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MINI-REVIEW

Relationship between gut microbiota, probiotics, and type 2 diabetes mellitus

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Abstract

The worldwide prevalence of type 2 diabetes mellitus (T2DM) is constantly increasing, and it has become a major concern, with several implications for public health, economy, and social well-being. It is well-known that several factors such as lifestyle, increased intake of fat and sugar-rich foods, and host genetics can lead to T2DM. Some recent studies have suggested that the composition of the intestinal microbiota can trigger T2DM. Since then, considerable effort has been made to understand the link between the composition of intestinal microbiota and T2DM, as well as the role of probiotics in modulation of intestinal microbiota. This mini-review summarizes the major findings and discusses the close relationship between intestinal microbiota, probiotics, and T2DM.

Keywords Type 2 diabetes · Gut microbiota · Probiotic · Chronic disease

Introduction

Diabetes is a chronic disease caused by inherited or acquired deficiency in the production of insulin by the pancreas or the inability of the body to make adequate use of the insulin produced (WHO 2016). Diabetes is a chronic condition, and affected individuals must routinely manage their lifestyle (ADA 2009; Ahola et al. 2017).

Diabetes affects more than 420 million people worldwide and this number may continue to increase in the future (WHO 2016). It is predicted that about 630 million people will be affected by the illness worldwide by the year 2045 (IDF 2017). In this context, diabetes is a global concern which strongly impacts public healthcare expenditures with an estimated cost of $827 billion worldwide (Seuring et al. 2015).

The three main types of diabetes are type 1, type 2, and gestational diabetes; however, there are some other types of diabetes such as autoimmune latent in adults (LADA), for example. Type 1 diabetes (also called insulin-dependent, juvenile, or childhood onset) is characterized by low insulin production and requires daily administration of this hormone. The cause of type 1 diabetes is still unknown and cannot be prevented with current knowledge (WHO 2016). Diabetes LADA is a special subtype of type 1 diabetes and it is characterized by slow β cell damage in the islets (Xiang et al. 2015). Therefore, patients with LADA usually show early signs that mimic type 2 diabetes, resulting in a non-negligible diagnostic rate. In fact, it has been estimated that the incidence of LADAs is about 6% among newly diagnosed patients with type 2 diabetes (Martinell et al. 2016).

Maturity-onset diabetes of the young (MODY) is a subtype of diabetes, characterized by early onset (usually under 25 years of age) and autosomal dominant transmission (determined in at least three generations). It corresponds to a primary defect in insulin secretion associated with pancreatic β cell dysfunction (Nyunt et al. 2009). Another type of diabetes, the gestational diabetes, is characterized by hyperglycemia (increased blood sugar) that appears during pregnancy and reaches values that, although higher than normal, are lower than those established for the diagnosis of diabetes. Women with gestational diabetes have a higher risk of complications during pregnancy and delivery. In addition, they and their children are at greater risk of developing type 2 diabetes in the future (WHO 2016).

The T2DM is a metabolic disorder characterized by high blood glucose that results from a combination of insufficient

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insulin secretion and insulin resistance (Asemi et al. 2013). Although T2DM is most commonly diagnosed in older adults, the incidence of this pathology has been increasingly observed in children, adolescents, and young adults due to increasing levels of obesity, physical inactivity, and poor diet (IDF 2017). The factors and mechanisms that trigger T2DM have been intensely discussed, and the major risk factors are genetic factors, high caloric intake, and physical inactivity (Lyssenko et al. 2008).

Obesity is one of the most important triggers for T2DM diabetes development. Obesity is a complex condition that is explained by risk factors, such as total energy expenditure, level of physical activity, food intake, genetics, socioeconomic status, or level of education, in addition to an unconventional but highly studied factor, which is the intestinal microbiota, which has been related to obesity (Dugas et al. 2018). There are differences between the composition of the intestinal microbiota of thin and obese individuals, so a correlation between obesity and the composition of the microbiota was observed and suggested (Peters et al. 2018). The majority of studies have found a higher proportion of *Firmicutes* phylum and a lower amount of *Bacteroidetes* in obese microbiota when compared to the lean (Schwiertz et al. 2010; Bervoets et al. 2013). However, according to recent revision about obesity and microbiota, the *Firmicutes/Bacteroidetes* ratio can change depending on the obese population under study, and therefore, a more detailed study of the intestinal microbiome, covering bacterial families, genera, and species, is required for a better understanding of the relationship between obesity and the gut microbiota (Bianchi et al. 2018).

Therefore, exercise is often prescribed for weight loss and maintenance. Some evidence suggests that chronic exercise usually causes partial, but incomplete, compensation for energy intake, and this is likely to be due to beneficial changes in appetite-regulating hormones (Stensel 2010). It is worth noting that the type of physical activity has a different impact on the intestinal microbiota, it has been reported that some moderate intensity exercises reduce intestinal transit (time) and increase the diversity of the microbiota (Evans et al. 2014; Campbell et al. 2016), while strenuous (prolonged) exercises may increase bowel permeability resulting in bacterial translocation of the colon, diarrhea, and gastrointestinal bleeding (Martin 2011). According to Matsumoto et al. (2008), he showed that voluntary physical exercise can stimulate species of butyrate-producing bacteria and, consequently, the production of AGCC (n-butyrate).

The intestinal microbiota profile may be associated with specific dietary patterns and responds to diet (David et al. 2014). Thus, beneficial microbes, such as probiotics and their metabolites, modify the microbiota profile and consequently influence metabolic parameters, such as the improvement of insulin sensitivity (Asemi et al. 2013). Probiotics are living microorganisms that, when administered in adequate amounts, confer benefits to an individual's health (Hill et al. 2014). Two of the main probiotic strains that are advantageous to health include *Lactobacillus* and *Bifidobacterium*. However, others microorganisms, such as yeast, can be used as probiotic. The good example is *S. cerevisiae* also known as *S. cerevisiae* var. *boulardii* (Edwards-Ingram et al. 2007; Bernaola et al. 2010).

In this context, the impact of probiotic microorganisms on T2DM acquires special interest, since strategies aimed at the use of probiotics can alter the microbial balance in favor of the host. Thus, the goal of this review is to discuss the use of probiotics and their impact on the microbiota and on major biomarkers as a strategy for the prevention of T2DM as well as to prescribe probiotic use for the amelioration of illness progression.

Relationship of intestinal microbiota with T2DM

The intestinal microbiota, often referred to as a hidden organ harboring trillions of microorganisms, are arguably as important to the metabolic health of the host as the organs that sustain them (Patterson et al. 2016). The adult intestine has approximately 500–1000 different bacterial species and may have 10^{12}–10^{14} microorganisms with a mass weight of about 1–2 kg (Blaut and Clavel 2007). Metagenomic studies have revealed that approximately 90% of the bacterial species present in the adult intestine belong to the phyla of *Bacteroidetes* and *Firmicutes*. In addition, other phyla such as *Actinobacteria*, *Proteobacteria*, and *Verrucomicrobia* are found in low abundance (HUMAN MICROBIOME PROJECT C 2012a, 2012b; Kalinkovich and Livshits 2019). Depending on the anatomy, abiotic environment, and diverse functions of different parts of the intestine, the microbial composition may vary (Blaut and Clavel 2007). The gut microbiota is characterized by a significant interpersonal variability and depends on differences attributed to genetics, diet, lifestyle, health status, and hygiene (Kalinkovich and Livshits 2019).

A healthy gut commensal microbiota is beneficial to the host, and it is linked with vital activities, such as digestion, harvesting energy from food components, xenobiotic degradation, production of water-soluble vitamins, and production of metabolites. These vital activities can promote intestinal barrier integrity, support the functional capacity of the gut epithelium, and provide protection from pathogens (van de Wiele et al. 2016).

On the other hand, dysbiosis is a disruption of the host-microbiota equilibrium due to gut inflammation, use of antibiotics, stress, menopause, toxin, and others triggers (Hegde et al. 2018). In addition, dysbiosis has been linked with a range of disorders such as cardiovascular (Battson et al. 2018) and autoimmune disorders (Opazo et al. 2018), autism

(Sgritta et al. 2019), obesity (Bianchi et al. 2018), and T2DM (Karlsson et al. 2013), among others.

T2DM may be linked to the composition of the intestinal microbiota and is directly responsible for the induction of low-grade inflammation. Further, the composition of the intestinal microbiota plays a significant role in the development of pre-diabetic conditions, such as insulin resistance (Roager et al. 2017). In this context, studies on the characterization of the intestinal microbiota of individuals with T2DM as well as the evaluation of possible correlations between the abundance of certain microorganisms and metabolic aspects are fundamental to clarify and strengthen the role of the microbiota in this clinical condition (Sabatino et al. 2017).

According to Sabatino et al. (2017), the main characteristics of the microbiota of T2DM patients are reduced butyrate-producing bacteria (especially *Roseburia intestinalis* and *Faecalibacterium prausnitzii*); moderate dysbiosis; pro-inflammatory environment with increased expression of microbial genes involved in oxidative stress, reduced expression of genes involved in vitamin synthesis, and increased serum LPS concentration; and increased intestinal permeability.

In addition, the major alterations in the intestinal microbiota that are associated with T2DM include a significantly lower prevalence of *Firmicutes* and an enrichment of *Bacteroidetes* and *Proteobacteria* (Roager et al. 2017). In terms of marker species in the microbiota of T2DM patients, some studies have observed a high number of opportunistic pathogens, such as *Clostridium clostridioforme*, *Bacteroides caccae*, *Clostridium hathewayi*, *Clostridium ramosum*, *Clostridium symbiosum*, *Eggerthella* sp., and *Escherichia coli* (Larsen et al. 2010; Karlsson et al. 2013). Larsen et al. (2010) showed that *Betaproteobacteria* family was highly enriched in T2DM patients compared to non-diabetic individuals.

Dysbiosis in T2DM patients, caused by the interaction of the intestinal microbiota with environmental and genetic factors, leads to increased intestinal permeability and altered mucosal immune response, which may result in the development or worsening of T2DM (Razmpoosh et al. 2018). It is important to highlight the interactions between the microbiota and the immune system since factors hampering these interactions can lead to metabolic disturbances. The lipopolysaccharide (LPS) of Gram-negative bacteria can stimulate the inactive immune system by activating toll-like receptors and inducing the release of inflammatory cytokines. Further, LPS promotes the activation of the nuclear factor kappa-B and c-Jun N-terminal kinase pathways, both of which are linked to the development of insulin resistance and the deficiency of insulin signaling in the muscle, adipose tissue, liver, and hypothalamus (White 2002; Caricilli and Saad 2013; Newsholme et al. 2016).

It is important to highlight that the gut microbiota is also responsible to produce and contribute to energy by short chain fat acids (SCFA) production, which involves the anaerobic breakdown of dietary fiber, protein, and peptides. The most produced by colonic bacteria are acetate, propionate, and butyrate (Baxter et al. 2019). Acetate and propionate are mostly produced by *Bacteroidetes phylum*, while butyrate is produced by the *Firmicutes phylum*. When the gut microbiota is in dysbiosis is directly related with alteration of SCFA production (Alexander et al. 2019). According to Gao et al. (2009), SCFA, particularly butyrate, improves insulin sensitivity and secretion by stimulating the secretion of peptide 1 like glucagon (GLP-1) and reducing the inflammation of adipocytes (Ríos-Covián et al. 2016; Tolhurst et al. 2012; Wang et al. 2015). Further, Qin et al. (2012) showed that Chinese patients with T2DM demonstrated a decrease in SCFA-producing bacteria, mainly butyrate-producing bacteria (*Clostridiales* sp. SS3/4, *Eubacterium rectale*, *F. prausnitzii*, and *R. intestinalis*, among others). These studies suggest that factors that are able to increase levels of SCFA, especially butyrate, are important for relieving T2DM symptoms. In additional, dietary butyrate supplementation has been associated with decrease of weight gain in animals fed high-fat diets (HFD). Although numerous bacterial strains have been analyzed for their butyrate-producing capacities, such as *Faecalibacterium prausnitzii* (a member of *Clostridium cluster* IV) and *Eubacterium rectale*/*Roseburia* (*Clostridium cluster* XIVa) (Lu et al. 2016).

Besides insulin resistance/sensitivity, the intestinal microbiota and its metabolites can affect other factors involved in T2DM, such as body weight, pro-inflammatory status, and the modulation of intestinal hormones. In this sense, the modulation of intestinal microbiota composition and metabolites using beneficial microorganisms, such as probiotics, can have advantageous effects on glucose metabolism and insulin resistance. The physiological functions of probiotics might lead to modulation of intestinal microbiota and can affect appetite, food intake, body weight, and metabolic functions of the body by means of gastrointestinal pathways (Rad et al. 2017; Kobyliak et al. 2016).

The use of probiotics for the management of T2DM

Probiotics were recognized for conferring health benefits; however, based on a large number of well-designed clinical trials, it was agreed that certain health beneficial effects of various strains of various well-studied microbial species can be attributed to probiotics as a general class (Hill et al. 2014; Fijan 2014). Several species of the genera *Bifidobacterium* and *Lactobacillus* claim to have a major benefit in healthy intestinal microbiota, creating a favorable intestinal environment. In addition, strain-specific probiotics support positive health outcomes, including the maintenance of a healthy immune system (Hill et al. 2014; McFarland et al. 2018). Probiotics are considered as complementary and alternative

medicine, along with vitamins, minerals, and other food supplements (April et al. 2012).

In this context, some studies have suggested that probiotics, as good intervention options in metabolic diseases, can positively alter intestinal microbiota safely and effectively and as a consequence a positive response in diseases (Reyes et al. 2016; Dahiya et al. 2017; Bianchi et al. 2018). In general, probiotics have shown beneficial effects, and various mechanisms have been proposed for T2DM therapy (Panwar et al. 2013). The possible relationship between probiotics, gut microbiota composition, and reduction of T2DM symptoms is shown in Fig. 1. After ingestion of probiotics, an improvement in T2DM symptoms is usually observed, such as improved intestinal integrity, decreased systemic LPS levels, decreased endoplasmic reticulum stress, and improved peripheral insulin sensitivity (Park et al. 2015; Balakumar et al. 2018; Lim et al. 2016).

The levels of LPS are closely related to intestinal integrity. Thus, it is known that the translocation of LPS from the intestinal lumen to the circulatory system is prevented by the intestinal barrier during homeostasis (Vera et al. 2018). This barrier possesses an intestinal permeability that is usually regulated by tight junction proteins and adhesion between the epithelial cells of the intestine, which create a barrier that prevents bacteria, toxins, and intestinal lumen products from reaching circulation (Vancamelbeke and Vermeire 2018). The translocation of LPS into circulation due to disruption of the intestinal barrier might trigger inflammation, leading to the development of various diseases, such as obesity (von Scholten et al. 2013), atherosclerosis (Wiesner et al. 2010), and diabetes (Creely et al. 2007). One hypothesis is that the T2DM can be improved by decreasing the concentration of LPS in the blood (Trøseid et al. 2013). Amar et al. (2011) showed, using an animal model for insulin resistance and T2DM, that treatment with the probiotic *Bifidobacterium animalis* subsp. *lactis* 420 for 6 weeks can reduce metabolic endotoxemia, inflammation, and translocation of LPS and improve the overall metabolism.

Different probiotic strains showed a beneficial impact on T2DM both for clinical models and for animal models (Table 1 and Table 2) such as reduction in plasma lipids and pro-inflammatory genes (TNF-α, IL-6, IL-β) and increase production of short chain fatty acids (SCFA). In addition, some studies have shown that a mixture of different probiotic strains has a better and broader impact on human health when

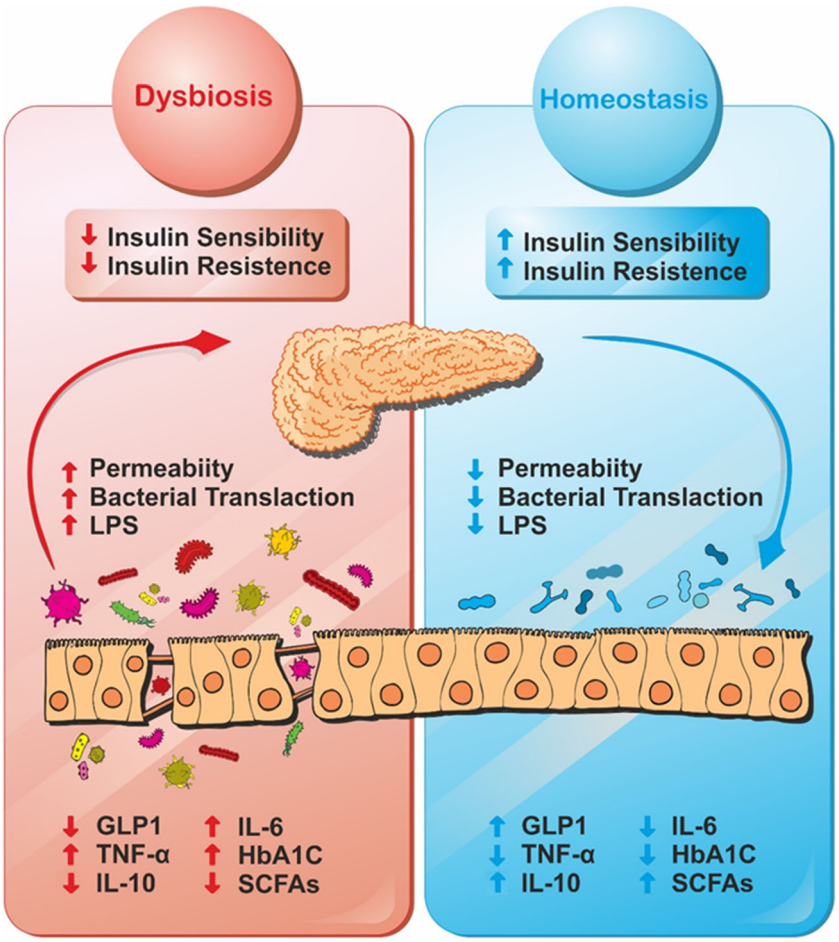

Fig. 1 Intestinal microbiota in homeostasis and dysbiosis promoted by type 2 diabetes and consequent impact on the development or prevention of T2DM. Intake of probiotics can positively modulate the intestinal microbiota, resulting in increased production of saccharolytic fermentation, short chain fatty acids (SCFA), and improved function of the intestinal barrier. Increased SCFAs are implicated in the release of glucagonal peptide-1 (GLP-1), which have an important impact on satiety, hunger, insulin sensitivity, and also improve intestinal barrier function. Consequently, increased bowel barrier function may reduce translocation of bacteria and liposaccharide (LPS), and thus reduce pro-inflammatory markers (interleukin-6 (IL-6), tumor necrosis factor (TNF)), and increase anti-inflammatory markers (interleukin-10 (IL-10)), as well as increase glycosylated hemoglobin A1c (HbA1c)

Table 1 Effects of different probiotic strains on diabetes mellitus type 2 parameters (clinical trial)

Probiotic/probiotic candidate	Subject	Dose/duration	Main findings after treatment with probiotic candidate, probiotic group compared with placebo group:	Authors
Lactobacillus casei	20 people with diabetes 2 type	1×10^8 CFU for 8 weeks.	↓FBG ↓IC ↓IR	Khalili et al. (2019)
Multiprobiotic "Symbiter" (concentrated biomass of 14 probiotic bacteria genera: *Bifidobacterium*, *Lactobacillus*, *Lactococcus*, *Propionibacterium*)	53 people with diabetes 2 type	*Lactobacillus* + *Lactococcus* (6×10^{10} CFU g^{-1}) *Bifidobacterium* (1×10^{10} CFU g^{-1}) *Propionibacterium* (3×10^{10} CFU g^{-1}) *Acetobacter* (1×10^6 CFU g^{-1}) For 8 weeks.	↓TNF-α ↓IL-1β ↓IL-6 ↓HOMA-IR ↓HbA1c	Kobyliak et al. (2018)
Lactobacillus reuteri DSM 17938	46 people with diabetes 2 type	*L. reuteri* DSM 17938 10^{10} CFU g^{-1} for 12 weeks.	↑ISI ↑DCA in subgroup with higher microbial diversity at baseline.	Mobini et al. (2017)
7 viable strains of *Lactobacillus, Bifidobacterium* and *Streptococcus.*	30 people with diabetes 2 type	*Lactobacillus acidophilus* (2×10^9 CFU) *Lactobacillus casei* (7×10^9 CFU) *Lactobacillus rhamnosus* (1.5×10^9 CFU) *Lactobacillus bulgaricus* (2×10^8 CFU) *Bifidobacterium breve* (3×10^{10} CFU) *Bifidobacterium longum* (7×10^9 CFU) *Streptococcus thermophilus* (1.5×10^9 CFU) For 6 weeks.	↑HDL-C ↓FPG	Razmpoosh et al. (2019)
Lactobacillus casei	68 people with diabetes 2 type	*Lactobacillus casei* (4×10^{10} CFU)-fermented milk for 16 weeks.	Partially improved bowel disbiosis in type 2 diabetes.	Sato et al. (2017)
Lactobacillus acidophilus La 5 *Bifidobacterium lactis* Bb-12	64 people with diabetes 2 type	*Lactobacillus acidophilus* La5 (7×10^6 CFU/day) *Bifidobacterium lactis* Bb-12 (6×10^6 CFU/day) For 6 weeks	↑Erythrocyte SOD ↑GPx ↑TAC ↓FBG ↓HbA1c	Ejtahed et al. (2012)

Note: ↓decrease, ↑increase, *FBG* fasting blood glucose, *IC* insulin concentration, *IR* insulin resistant, *TNF-α* tumor necrosis factor-α, *IL-1β* interleukin-1β, *IL-6* interleukin-6, *HOMA-IR* homeostasis model assessment-estimated insulin resistance, *HbA1c* glycosylated hemoglobin A1c, *ISI* sensitivity index, *DCA* serum levels deoxycholic acid, *HDL-C* high density of lipoprotein cholesterol, *FPG* fasting plasma glucose, *SOD* superoxide dismutase, *GPx* glutathione peroxidase, *TAC* total antioxidant capacity, *FBG* fasting blood glucose

used individually (Kobyliak et al. 2018; Razmpoosh et al. 2018; Ejtahed et al. 2012; Bagarolli et al. 2017).

According to Bagarolli et al. (2017), the treatment with the probiotics *L. rhamnosus*, *L. acidophilus*, and *B. bifidum* in animal model increase of *Bacteroidetes* and decrease of *Firmicutes* abundance. In addition, the authors showed that a high-calorie diet promotes changes in gut microbiota that are reflected in increased intestinal permeability, translocation of the SPL, and low-grade systemic inflammation, resulting in decreased glucose tolerance. In addition, according to Firouzi et al. (2016) and O'Connor et al. (2017), probiotics may modulate intestinal microbiota, which, through cascading metabolic processes, may result in improved lipid profiles (decreased LDL, CT normalization, increased HDL), reduced fasting glucose levels, hemoglobin A1c, fasting insulin levels, and levels of C-reactive protein (CRP).

In addition, the elegant study realized by Brandão et al. (2018) showed for first the time that administration of *Saccharomyces Boulardii* is strongly associated with glycemic control, cardiovascular protection, and improvement of inflammatory profile in animal model.

The strengths and distinctions of this review include the inclusion of the specific medium (animal or clinical) dose and duration of each probiotic intervention, providing insight into the probiotic that may be clinically relevant and beneficial for blood glucose. However, the specific relationship between microbiota-probiotic-T2DM has not been clarified. There are few experimental studies on microbiota modulation by probiotic and DM2 ingestion and we found many studies (clinical or animal) on probiotic ingestion and biochemical parameters. Finally, further studies are needed to identify which specific microorganisms and mechanisms of action are involved in preventing DM2 and probiotic ingestion.

Table 2 Effects of different probiotic strains on diabetes mellitus type 2 parameters (anima model)

Probiotic/probiotic candidate	Subject	Dose/duration	Main findings after treatment with probiotic candidate, probiotic group compared with placebo group:	Authors
Lactobacillus casei CCFM419	32 male mice (C57BL/6J) divided into four groups: -mice receiving normal diet; -Diabetic control group; -Pioglitazone group; -*L. casei* CCFM419 group.	8×10^{10} CFU mL^{-1}. For 12 weeks.	↓FBG ↓PBG ↓HbA1C ↓Leptin levels ↓HOMA-IR ↓Serum insulin level ↑Glucose tolerance ↑SCFAs Improvement of the compromised pancreas. Adjustment for normal HDL-C and LDL-C levels	Li et al. (2017)
Lactobacillus plantarum Ln4	Male C57BL/6J mice, divided into three groups (5–7 mice per group): fed normal chow diet, high-fat diet (HFD) and group Ln4.	5×10^{8} CFU. For 5 weeks daily.	↑insulin resistance ↓FPG ↓Total TG	Lee et al. (2018)
Lactobacillus rhamnosus *Lactobacillus acidophilus* *Bifidobacterium bifidum*	Animals [male Swiss mice ($n = 6$ per group)] composed of two groups: - one group on chow diet; - second group on an HFD (high-fat diet)	6×10^{8} CFU of each strain, final concentration of 1.8×10^{9} CFU of bacteria, for 5 weeks daily.	↓TNF-α ↓IL-6 ↓plasma LPS ↓TLR4 ↓JNK ↓IRS-1 ↓IL-1β	Bagarolli et al. (2017)
Lactobacillus casei CCFM419	48 three-week-old male C57BL/6J mice: - 8 mice were fed a normal diet and the others were given a high-fat diet.	10^{10} CFU mL^{-1}, 10^{9} CFU mL^{-1}, 10^{8} CFU mL^{-1}, once daily from weeks 1 to 12.	↑IL-6 ↑TNF-α ↑GLP-1 ↑*Bacteroidetes*	Wang et al. (2017)
Probiotic/probiotic candidate	Subject	Dose/duration	Main findings after treatment with probiotic candidate, probiotic group compared with placebo group:	Authors
Lactobacillus paracasei TD062	$n = 8$ per group: -diabetes mellitus group: rats with diabetes and treated with saline; -high dose group: rats with diabetes and treated with 10^{9} CFU mL^{-1} -myd dose group: rats with diabetes and treated with 10^{8} CFU mL^{-1} -low dose group: mice with diabetes and treated with 10^{7} CFU mL^{-1}	10^{9} CFU mL^{-1} (high dose) 10^{8} CFU mL^{-1} (medium dose) 10^{7} CFU mL^{-1} (low dose). All doses for 8 weeks.	↓ Insulin levels ↓HbA1C ↑glucose tolerance ↑HDL-C Normalized of TC, LDL-C and TG	Dang et al. (2018)
Saccharomyces boulardii	$n = 6$–12 per group: -control; - diabetes; -control + *S. boulardii*; -diabetes + *S. boulardii.*	0.5×10^{8} CFU/day, for 8 weeks.	↓ Control glycem ↓ TG No effect on cholesterol ↓ IL-6 ↑ IL-10	Brandão et al. (2018)
Lactobacillus plantarum MTCC5690 *Lactobacillus fermentum* MTCC5689 *Lactobacillus rhamnosus* (LGG)	Animals [male C57BL/6J mice ($n = 6$ per group)], composed of seven groups comprising feeding on: -Normal Pellet diet (NPD); -High-fat diet (HFD); -HFD with LGG; -HFD with MTCC5690; -HFD with MTCC5689; -HFD with metformin; -HFD with vildagliptin .	$1{,}5 \times 10^{9}$ colonies/mouse/day. For a period of 6 months.	*Lactobacillus plantarum* MTCC5690: ↑GLP-1, ↓gut permeability *Lactobacillus fermentum* MTCC5689: ↓IR, ↓ development of diabetes *Lactobacillus rhamnosus* (LGG): ↓HbA1c, ↑glucose tolerance	Balakumar et al. (2018)

Note: ↓decrease, ↑increase, *FBG* fasting blood glucose, *PBG* postprandial blood glucose, *HbA1c* glycosylated hemoglobin A1c, *HOMA-IR* homeostasis model assessment-estimated insulin resistance, *SCFAs* short-chain fatty acids, *HDL-C* high density of lipoprotein cholesterol, *LDL-C* density lipoprotein cholesterol, *FPG* fasting plasma glucose, *TG* triglyceride, *TNF-α* tumor necrosis factor-α, *IL-6* interleukin-6, *LPS* lipopolysaccharide, *TLR4* toll-like receptors 4, *JNK* jun N-terminal kinases, *IRS-1* insulin receptor substrate 1, *IL-1β* interleukin-1β, *IL-10* interleukin-10, *GLP-1* glucagon like peptide 1, *IR* insulin resistance, *TC* total cholesterol, *CFU* colony forming unit

Conclusions and future prospects

T2DM is an important and widespread chronic disease. This mini-review shows that gut microbiota composition is essential for understanding the mechanisms involved in the pathology of T2DM. Compared to various other means of controlling T2DM, the consumption of probiotics is a promising strategy with a beneficial impact on the intestinal microbiota. Several different probiotic strains, especially those belonging to *Lactobacillus* and *Bifidobacterium* spp., have demonstrated the ability to improve parameters related to T2DM, highlighting the importance of studying probiotics for diabetes prevention, progression, and symptom amelioration. With the emergence of molecular biology and the "omic" era, a better understanding of the mechanisms involving T2DM and gut microbiota is expected, making it possible to advance our knowledge of the relationship between microbiota composition and diabetes with more determination and detail. Finally, the intestinal microbiota can be key to the management of this chronic disease.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The article does not contain any studies with human participants or animals performed by any of the authors.

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