**Probiotics with anti-type 2 diabetes mellitus properties: targets of polysaccharides from traditional Chinese medicine**

WU Lun¹, GAO Yue², SU Yang²,³*, LI Jing², REN Wen-Chen², WANG Qiu-Hong⁴, KUANG Hai-Xue²*

¹Institute of Traditional Chinese Medicine, Heilongjiang University of Chinese Medicine, Harbin 150040, China;  
²School of Pharmacy, Heilongjiang University of Chinese Medicine, Key Laboratory of Medicinal Materials, Chinese Academy of Sciences, Harbin 150040, China;  
³Faculty of Microbiology and Immunogenetics, University of California, Los Angeles, CA 90095, USA;  
⁴School of Traditional Chinese Medicine, Guangdong Pharmaceutical University, Guangzhou 510000, China

Available online 20 Sep., 2022

**[ABSTRACT]** Traditional Chinese medicine polysaccharides is a biologically active ingredient that is not easy to be digested. It is fermented by intestinal microflora to promote qualitative and selective changes in the composition of the intestinal microbiome, which often result in beneficial effects on the health of the host. People call it “prebiotics”. In this review, we systematically summarized the anti-diabetic effect of traditional Chinese medicine polysaccharides. These polysaccharides regulate the metabolism of sugar and lipids by inter-influence with the intestinal microflora, and maintain human health, while improving type 2 diabetes-like symptoms such as high blood glucose, and abnormal glucose and lipid metabolism.

**[KEY WORDS]** Traditional Chinese medicine polysaccharide; Prebiotics; Intestinal microflora; Type 2 diabetes mellitus

**[CLC Number]** R965  
**[Document code]** A  
**[Article ID]** 2095-6975(2022)09-0641-15

---

**Introduction**

Polysaccharide is a carbohydrate polymer made up of more than ten monosaccharides connected by glycoside bonds, which are widely found in traditional Chinese medicines (TCM) [¹]. In previous studies, polysaccharide was considered as an inactive ingredient. In the 1950s, researches indicated the immunomodulatory effects of fungal polysaccharides, and then increasing attention was gradually drawn towards the structure and function of polysaccharides. After the 1980s, new studies started to unravel the other characteristics of plant polysaccharides. Since then, many bioactivities of polysaccharides have been confirmed, including antioxidation, immunomodulation and anti-tumor effects, while their corresponding mechanism and structure relationship become of interest to scientific researchers. Furthermore, microbiologists such as Kaoutari reported the presence of carbohydrate active enzymes in intestinal microorganisms, as human body is unable to digest some polysaccharides due to lack of appropriate enzymes. The intestinal microbiota is involved in the biological function of polysaccharides, which consequently promotes the studies concerning the interaction between polysaccharides and intestinal microorganisms [², ³]. As a new type of “dietary fiber”, TCM polysaccharides improve the environmental stability of the intestine and selectively induce probiotics in the intestine to exert health benefits, which is in line with the characteristics of prebiotics; and may be developed into new prebiotic agents [⁴].

Diabetes is a chronic, metabolic disease characterized by elevated levels of blood glucose, and mainly attributable to defects in insulin secretion and/or utilization [⁵]. In recent years, the number of patients with diabetes is increasing year by year due to population growth, aging, urbanization, decreased physical activity and unhealthy diet changes. The predominant form is type 2 diabetes mellitus (T2DM), which manifests as a metabolic disorder of sugar and lipids. Since 1980, the global prevalence of T2DM has risen from 4.7% to 9.3% in the adult population. So it is essential to investigate the pathological mechanisms and effective methods for the prevention and treatment of T2DM [⁶]. Studies have found
that the lack of good eating habits, abuse of antibiotics, stress and environmental changes can result in intestinal microflora imbalance, which seriously affects the body’s metabolism and immunity, causing obesity, insulin resistance, and T2DM. Therefore, intestinal microbial disorders become one of the important triggers of T2DM [7-9].

At present, many commercial hypoglycemic agents are effective in the treatment of T2DM. However, a single chemical composition is not advantageous in modulating gut microbiota. For example, sulfonylureas can significantly reduce blood glucose levels in obese patients, but often cause hypoglycemia, and even secondary failure after long-term medication. Troglitazone can effectively enhance the function of insulin in patients with T2DM, but result in liver injury at the same time. In contrast, compared with the above-mentioned drugs, Chinese herbal medicines with complex chemical composition are more effective in regulating the composition and structure of microorganisms. TCM has the advantages of long-term beneficial effect and mild adverse reaction, and is less likely to develop drug resistance. In the current review, we summarizes the research progress on polysaccharide with anti-diabetic effect, and expounds the “prebiotic” characteristics of TCM polysaccharides. From the perspective of the intestinal microflora, the possible mechanisms of TCM polysaccharides for the prevention and management of T2DM are discussed, which will provide reference to researchers in relevant fields.

**Intestinal Microflora and T2DM**

**Effect of the intestinal microflora in the development of T2DM**

The human intestinal tract is home to a vast, diverse microbial community, including bacteria, fungi, viruses and protozoa. These microorganisms account for 80% of the human microbiome and together with the parasitic intestinal environment form the intestinal micro-ecosystem. Maintaining the homeostasis of the system is very important for the host’s nutrient digestion and absorption, immune response, biological antagonism and other life activities [10]. The intestinal microflora can be regarded as “microbial organs” in host organisms, which have positive or negative effects on human health. Modern studies have shown that changes in intestinal microflora can affect the host’s insulin sensitivity and insulin secretion, and play an important role in the development of T2DM [11, 12]. For example, aseptic and antibiotic-treated mice were more insulin sensitive than conventionally reared or untreated mice [13, 14]. Vijay-Kumar et al. investigated the relationship between the intestinal microflora and insulin resistance in mice with Toll-like subject 5 defects (T5KO) [15]. Results showed that the composition of the intestinal microflora in T5KO mice was changed, with abnormal glucose tolerance and insulin resistance. However, insulin resistance was recreated when the intestinal microflora of T5KO mice was transplanted into the intestines of wild mice. In addition, prolonged high-fat diet (HFD) feeding can cause changes in the intestinal microflora in mice, such as reduction of Akkermansia muciniphila. Meanwhile, sterile mice developed sugar metabolic disorders and significant insulin resistance after transplantation of the intestinal microflora from long-term HFD-fed mice [16]. Ramos-Romero et al. found that HFD and high fructose diet caused insulin resistance in rats, which is consistent with an increase in Escherichia coli in the intestine [17]. Qin et al. found through metagenome-wide association study (MWAS) that the disorder of the intestinal microflora in T2DM patients led to an increase in intestinal permeability, which allowed the translocation of a large number of intestinal bacteria into the blood and tissue, causing insulin resistance [18, 19].

With the rapid development of genomics technology, the biological function of the intestinal microflora has been deeply investigated. Studies indicated that the absence of Akkermansia muciniphila compromised the integrity of the intestinal barrier, increased intestinal permeability, and reduced beneficial bacteria such as Faecalibacterium prausnitzii, Roseburia faecis, and Anaerostipes butyraticus, which eventually led to insulin resistance. In contrast, supplementation with Akkermansia muciniphila repaired the damaged intestinal barrier, reduced intestinal inflammation, and restored normal insulin sensitivity [19]. Similarly, Eubacterium hallii improved the insulin resistance of db/db mice (T2DM mice), increased butyric acid content in the feces, and regulated the metabolism of bile acids (BAs) to treat diabetes [20]. Other probiotics such as Lactobacillus acidophilus, Bifidobacterium bifidum, Lactobacillus plantarum MTCC5690, Lactobacillus fermentum MTCC5689 and Lactobacillus rhamnosus improved the imbalance of intestinal microbiota in obese mice induced by HFD, reduced intestinal permeability, inhibited the displacement of intestinal lipopolysaccharide (LPS), and reduced systemic low inflammation [21-23]. In addition, pathogenic bacteria such as Escherichia coli W3110 induced abnormal blood sugar and insulin tolerance, and promoted macrophage differentiation into proinflammatory phenotype (M1 polarization) [24]. The underlying mechanism of damaged glucose tolerance in mice by Staphylococcus aureus infection may be that the extracellular structure (eLtaS) of LtaS cells bound to insulin and induced insulin resistance [25].

**Modern drug research based on the prevention and treatment of T2DM in the intestinal microflora**

T2DM is one of the most common metabolic diseases characterized by chronic hyperglycemia, which can be attributed to genetic and/or environmental factors, and associated with metabolic diseases due to the intestinal microflora. In recent years, the role of intestinal microflora in T2DM has attracted more and more attention. Current treatment options for T2DM (especially hypoglycemic agents) are determined based on various pathophysiological processes. Therefore, understanding the relationship between commonly used hypoglycemic agents and the intestinal microflora is helpful to evaluate the effect of intestinal microenvironment on T2DM. Currently, metformin is a first-line glucose-lowering drug and
recommended by the American Diabetes Association and the European Association for Diabetes Research, with recognized efficacy, safety and low cost [29]. Metformin can affect the intestinal microenvironment by regulating the uptake and utilization of glucose, increasing the levels of glucose like peptide-1 (GLP-1) and BAs and changing the intestinal microbiota. Its hypoglycemic effect is partly mediated by the intestine, while the intestinal flora can function as a new factor in alleviating the adverse effects of metformin and thus improving patient compliance [27, 28]. In addition, the classic -glucosidase inhibitor acarbose lowered blood glucose levels after meals by delaying glucose absorption, promoted host health by altering the diversity and composition of the intestinal microflora of diabetics, reduced the levels of inflammatory cytokines and regulated BA metabolism [29, 30]. Other hypoglycemic agents like pioglitazone, improved the intestinal microflora structure of KKAy mice and reduced the insulin resistance of T2DM patients through binding to the peroxisome proliferators-activated receptors- (PPAR) [31, 32].

In addition, with the continuous development of TCM, increasing attention has been drawn towards the use of TCM in the treatment of T2DM. Specifically, compared with a single chemical component, TCM polysaccharides are advantageous in regulating the intestinal flora. TCM polysaccharides are difficult to digest and absorb, but can be used as a carbon source of the intestinal microflora to promote beneficial bacterial growth. Through their metabolites, TCM polysaccharides play a prebiotic role, regulating the intestinal microenvironment and changing the diversity of intestinal microbiota. Therefore, in light of the changes in the intestinal microflora as a key process of pathogenesis and progression of metabolic diseases, it is important to explore the interaction of TCM polysaccharides with the intestinal microbiota for better understanding the etiology, treatment, and prognosis of T2DM.

**TCM Polysaccharides Play a Prebiotic Role in the Treatment of T2DM**

**Physicochemical properties of TCM polysaccharides against T2DM**

TCM polysaccharides are widely found in plants, animals, microorganisms and algae. Polysaccharides are not only an important nutrient of organisms, but also play an important role in the life activities of organisms. Together with proteins, lipids, and nucleotides, they are called the four most important biological macromolecules in the organism. Polysaccharides exert a variety of activities such as immunomodulation, anti-tumor, anti-viral, anti-aging, hypoglycemic, and lipid-lowering effects. In particular, plant polysaccharides, characterized in a wide range of sources, mild adverse reactions, and long-lasting efficacy has attracted a lot of attention. As the human body is incapable of digesting polysaccharides obtained from plants, they rely on microbes in the intestinal tract to metabolize. On the other hand, selective digestion of polysaccharides by different types of intestinal microorganisms also affects the colonization and reproduction of microorganisms in the gastrointestinal tract. Therefore, polysaccharides are a viable intestinal micro-ecological regulator that plays a prebiotic role [33].

Current studies concerning polysaccharides from TCM usually focus on their extraction, purification, structure, modification and biological activity, and the methods used above are diverse and always affect the type and characteristics of the final polysaccharides [34]. Through different extraction and purification methods, polysaccharides may produce various biological activities, which is a prerequisite for the analysis of polysaccharide biological activities. For example, ultrasonic extraction significantly affected and improved the antioxidant activity of *Schisandra chinensis* polysaccharide, which may result from ultrasonic degradation. Ultrasonic extraction decomposed high molecular weight polysaccharides into appropriate fragments, reduced the influence on hydrogen bond, and improved the scavenging rate of hydroxyl radicals [35]. Furthermore, the polysaccharides obtained by different purification methods were different. For example, *Schisandra chinensis* polysaccharides were separated by gel chromatography with different particle sizes (such as Sephadex G-100 and Sephadex G-150), resulting in homogenized polysaccharides (SCPP11 and BPS1-1) with different physicochemical properties. Results showed that SCPP11 and BPS1-1 were remarkably different in molecular weight, monosaccharide composition, and structural properties [36, 37]. The physicochemical properties of polysaccharides often determine their biological activities. For example, the (1→3) glycosidic bond in the glucose chain and the (1→6) glycosidic bond in the branched chain are necessary for anti-tumor activity. The highly ordered structure (triple helix) of high molecular weight (1→3)-D-glucose is essential for immunomodulatory activity. Polysaccharides with a molecular weight of 100–200 kDa exhibit the strongest activity, while those from the same source with amolecular weight ranging from 5–10 kDa have no bioactivity [38].

In recent years, more and more investigations have been conducted, which discuss the biological activity of crude or refined polysaccharides from TCM [39, 40]. The absorption and degradation of TCM polysaccharides are related to their molecular weight, monosaccharide composition, connection, polymerization, spatial structure, solubility and the adaptability of the intestinal microflora to polysaccharides [41]. As human genome cannot encode gastrointestinal enzymes that metabolize polysaccharides, the degradation of polysaccharides requires a series of enzymes from the intestinal microflora. For example, the proposed polysaccharide utilization loci “PULs” by Nicolas Terrapon are a group of gene clusters related to polysaccharides catabolism and located in specific areas, including starch utilization system (SusC), SusD, and genes encoding outer membrane glycoprotein binding proteins and carbohydrate active enzymes [42]. The PULs widely exist on Bacteroides, where many PULs are used to encode different enzymes. These enzymes are specifically used to degrade specific polysaccharides. Therefore, the absorption and
transit time and the type and quantity of the intestinal micro-
SCFAs may vary through anaerobic digestion of the colon. Bac-
teroids have become the main target of polysaccharides dur-
ing regulating the intestinal microflora. Therefore, under-
standing the physicochemical properties of TCM polysac-
charides is helpful to explain the relationship between the in-
testinal tract and polysaccharides. The basic information
about TCM polysaccharides with anti-diabetic effects, includ-
ing plant sources, separation, purification and analysis meth-
ods, molecular weights, monosaccharide composition and
structural characteristics are showed in Table 1. TCM polysac-
charides play a prebiotic role in the prevention and treatment of T2DM

TCM polysaccharides and intestinal microflora are inter-
active. On the one hand, polysaccharides provide adequate nutrition for the fermentation and growth of intestinal microorganisms, and reshape the structure of the intestinal microflora by changing the types of polysaccharides. On the other hand, intestinal microflora degrade TCM polysaccharides that the body itself cannot digest into a variety of active metabolites. Therefore, it is important to investigate the interaction between polysaccharides and the intestinal microflora, so as to reveal the characteristics of polysaccharide prebiotics. We summarized the current research progress on TCM polysaccharide-regulated intestinal microflora for T2DM treatment and the corresponding pharmacological findings, as showed in Table S2. TCM polysaccharides can increase the number of beneficial bacteria in the intestinal tract, reduce harmful bacteria, and restore the disturbance of the intestinal microflora, so as to restore the imbalance of the intestinal ecosystem, and regulate the sugar and lipid metabolic disorders in T2DM. The key to these effects lies in the interaction between polysaccharides and the intestinal microflora, improvement in the pathogenesis of diseases and gastrointestinal endocrinology, so as to provide basic data for TCM polysaccharides to improve intestinal microflora disorders.

Study on the Possible Mechanism of T2DM Prevention and Treatment by TCM Polysaccharides Based on the Intestinal Microflora

Short-fatty acids (SCFAs)

Short chain fatty acids (SCFAs), also known as volatile fatty acids, belong to organic fatty acids composed of 1–6 carbon atoms, and are mainly produced by indigestible and unabsorbed carbohydrates (such as non-starch polysaccharides, resistant starch, sugar alcohols and oligosaccharides) through anaerobic digestion of the colon. SCFAs may vary depending on the type of fermentation substrates, intestinal transit time and the type and quantity of the intestinal microflora. For instance, the intestinal tract of germ-free mice produced almost no fatty acids. The main SCFAs produced through TCM polysaccharide fermentation by intestinal microflora were acetate, propionate and butyrate at a ratio of 4 : 1.7 : 1. Gram positive Firmicutes and gram-negative Bacteroides are the most abundant bacteria in the intestine, accounting for 98% of the total intestinal microflora, and the dominant bacteria involved in the production of SCFAs in the intestinal tract. Acetic acid is the main fermentation product of most bacteria, while propionic acid and butyric acid are the main metabolites of Bacteroides and Firmicutes, respectively. Polysaccharides from TCM can not only increase the number of the bacteria mentioned above, but also act as fermentation substrates to form more SCFAs. The conversion of polysaccharides into SCFAs is described in Fig. 1. The bacteria associated with SCFAs belong to Bacteroides, Clostridi-
um sensu stricto 1, Ruminococcus 1, Butyribrio, Bifidobacterium, Peptococcus, Streptococcus, Prevotella 9, Roseburia, Faecalibacterium, Allobaculum, Blautia and Phascolarctobacterium in the human intestine. SCFAs not only provided energy for intestinal epithelial cells, promoted their proliferation, and maintained intestinal barrier function, but also main-
tained intestinal stability and improved immune tolerance. In addition, SCFAs directly or indirectly regulated T cell differentiation by regulating metabolism, inhibited dendrites and activated fatty acid receptors, so as to promote the production of Th1 or Th17 cells, stimulate T cells to produce anti-in-
flammatory factor IL-10, enhance the body’s immune response and reduce the incidence of T2DM. On the other hand, there are many SCFA receptors on the intestinal cells, such as GPR41/43. GPR43 promotes the release of GLP-1 from L-cells, stimulates insulin secretion, and enhances insulin sensitivity. SCFAs also reduced PPARγ in fat and liver tissue, stimulated metabolism and reduced the incidence of obesity or T2DM. Therefore, targeting SCFA-producing bacteria, appropriate interventions can be used to control T2DM (Fig. 2).

Liu et al. reported that Pumpkin polysaccharides im-
proved the insulin tolerance of T2DM rats through regulating the intestinal microflora, promoting the absorption of SCFAs, reducing serum glucose levels, total cholesterol levels and LDL levels, and increasing HDL levels. Gu et al. investigated the therapeutic mechanism of Polygonatum kingianum polysaccharide on diabetes mellitus through regulating the intestinal microflora. Studies have shown that PS and PSF regulate the diversity of the intestinal microflora by increasing the relative abundance of the bacteria that produce SCFAs. They also affected the concentration of SCFAs, which relieved the levels of high blood glucose in DM rats by regulating the intestinal microflora and subsequent SCFA alter-
tnation. The same results were also found in AERP, POP and GFP studies. Furthermore, Shi et al. demonstrated that Ophiopogon polysaccharide MDG-1 improved T2DM-related metabolic syndrome, while the indigestible fiber was mediated by SCFA and acted as the main end product of intestinal-related bacterial fermentation to prevent...
<table>
<thead>
<tr>
<th>Polysaccharide</th>
<th>TCM source</th>
<th>Part of the plant</th>
<th>Analysis method</th>
<th>Mw (Da)</th>
<th>Monosaccharide composition</th>
<th>Structure and composition characteristics</th>
<th>Producing/ Purchasing areas</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>AERP1</td>
<td>Astragalus</td>
<td>Industrial Astragalus membranaceus-extracted waste residue</td>
<td>HPLC-SEC-RID, HPLC-C18-UV, FT-IR, and NMR</td>
<td>$2.01 \times 10^6$</td>
<td>Man : Rha : GaL : Glc : Gal : Ara = 1.00 : 2.59 : 12.15 : 2.60 : 3.07 : 4.54</td>
<td>Glycosidic bonds of $\rightarrow 3/5-\alpha$-araf-(1→, T-\alpha-araf-(4→, 6-β-manp-(1→, $\rightarrow 3/3, 6-\beta$-galp-(1→, $\rightarrow 4\alpha$-rhap(1→, $\rightarrow 3/4, 6\alpha$-glcp-(1→, $\rightarrow 4\alpha$-galpA-(1→ and $\rightarrow 4\alpha$-galpA-(1→ linkage.</td>
<td>Guangdong, China [44]</td>
<td></td>
</tr>
<tr>
<td>AERP2</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>$2.11 \times 10^5$</td>
<td>-</td>
<td>AERP2 was a glucan by $\rightarrow 4\alpha$-glcp-(1→ linkage.</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>PS</td>
<td>Polygonatum kingianum</td>
<td>Rhizome of P. kingianum</td>
<td>GPC and HPLC</td>
<td>$1.79 \times 10^5$</td>
<td>Man, GaLA, Gal and Fuc (with an unknown ratio)</td>
<td>Containing 30.80% carbohydrates, with the protein content of 10.91% and the uronic acid content of 25.06%.</td>
<td>Yunnan, China [45]</td>
<td></td>
</tr>
<tr>
<td>PSF</td>
<td>Polygonatum kingianum</td>
<td>Rhizome of P. kingianum</td>
<td>GPC and HPLC</td>
<td>$1.35 \times 10^5$</td>
<td>Man, GaLA, Gal and Fuc (with an unknown ratio)</td>
<td>Containing 39.17% carbohydrates, with the protein content of 7.65% and the uronic acid content of 27.81%.</td>
<td>Yunnan, China [45]</td>
<td></td>
</tr>
<tr>
<td>HLP</td>
<td>Holothuria leucospilota</td>
<td>Bodies of Holothuria leucospilota</td>
<td>SEM and FT-IR</td>
<td>$5.28 \times 10^5$</td>
<td>Rha : Fuc : Glu acids : Gal : Glu : Xyl = 39.08% : 35.72% : 10.72% : 8.43% : 4.23% : 1.83%</td>
<td>Total sugar was the main constituent (71.68%), and protein was the minor constituent (16.80%).</td>
<td>Haikou, China [46]</td>
<td></td>
</tr>
<tr>
<td>GFP</td>
<td>Grifola frondosa</td>
<td>G. frondosa fruiting body</td>
<td>HPSEC-MALLS, FT-IR and HPLC-DAD</td>
<td>$1.59 \times 10^5$ : $2.81 \times 10^5$ : $1.82 \times 10^5$ = 0.85% : 3.96% : 95.29%</td>
<td>Man : Rha : GlcUA : GalUA : Glc : Gal : Fuc = 25.49 : 9.49 : 7.30 : 27.59 : 15.02 : 9.92</td>
<td>GFP showed a broad crystalline area at 20 value of 21°, which is the characteristic crystallization region of polysaccharide, ascribing to the hydrogen bonds interactions among the $\rightarrow$OH groups of polysaccharide chains in the XRD spectra.</td>
<td>Zhejiang, China [47]</td>
<td></td>
</tr>
<tr>
<td>MFP</td>
<td>Mulberry fruit</td>
<td>Mature black mulberry fruit</td>
<td>HPGPC</td>
<td>$2.10 \times 10^5$ : $1.00 \times 10^5$ : $6.25 \times 10^4$ : $2.08 \times 10^4$ : $4.28 \times 10^3$ = 16.33% : 41.37% : 29.54% : 12.76% : 0.79%</td>
<td>Ara : Gal : Glu : Rha : Gal-acid = 28.37% ± 0.12% : 27.51% ± 0.17% : 17.36% ± 0.19% : 12.59% ± 0.13% : 14.07% ± 0.08%</td>
<td>The carbohydrate and protein contents in MFP were 84.67% and 0.79%, respectively</td>
<td>Xinjiang, China [49]</td>
<td></td>
</tr>
<tr>
<td>PAS</td>
<td>Adlay seed</td>
<td>Adlay seed powder</td>
<td>-</td>
<td>$2.55 \times 10^5$</td>
<td>-</td>
<td>Rich in oligosaccharides and arabinoxylans</td>
<td>Hangzhou, China [50]</td>
<td></td>
</tr>
<tr>
<td>Polysaccharide</td>
<td>TCM source</td>
<td>Part of the plant</td>
<td>Analysis method</td>
<td>Mw (Da)</td>
<td>Monosaccharide composition</td>
<td>Structure and composition characteristics</td>
<td>Producing/Purchasing areas</td>
<td>Ref.</td>
</tr>
<tr>
<td>---------------</td>
<td>------------</td>
<td>------------------</td>
<td>----------------</td>
<td>---------</td>
<td>----------------------------</td>
<td>------------------------------------------</td>
<td>---------------------------</td>
<td>------</td>
</tr>
<tr>
<td>MDG-1</td>
<td>Ophiopogon japonicus</td>
<td>Root of O. japonicus</td>
<td>NMR and UPLC-Q-TOF-MS</td>
<td>$3.40 \times 10^3$</td>
<td>Fru : Glc = 35 : 1</td>
<td>It was composed of Fru (2→1) and a branch of Fru (2→6) Fru (2→) per average 2.8 of main chain residues. It also contained a trace amount of α-D-GLc, which may be connected to its reducing terminal. Composed of two α-D-galactopyranosyl, one α-D-glucopyranosyl, and one β-D-fructofuranosyl linked as α-Gal (1→6) α-Gal (1→6) α-Glc (1→2) β-Fru</td>
<td>Zhejiang, China</td>
<td>[51]</td>
</tr>
<tr>
<td>STS</td>
<td>Stachyose</td>
<td>Rehmanniae Radix</td>
<td>UPLC</td>
<td>-</td>
<td>-</td>
<td>The molecular weight ranged from 1.00 to 1308.98 kDa, with the weight-average molecular weight and number-average molecular weight of 39.56 and 3.57 kDa, respectively</td>
<td>Henan, China</td>
<td>[52]</td>
</tr>
<tr>
<td>GP</td>
<td>Ginseng</td>
<td>Fresh ginseng</td>
<td>HPGPC</td>
<td>-</td>
<td>Man : Rha : GalA : Glc : Gal : Ara : Fuc = 1.11 : 1.00 : 7.11 : 15.95 : 4.40 : 6.12 : 2.42</td>
<td>The molecular weight ranged from 1.00 to 1308.98 kDa, with the weight-average molecular weight and number-average molecular weight of 39.56 and 3.57 kDa, respectively</td>
<td>Jilin, China</td>
<td>[53]</td>
</tr>
<tr>
<td>MSP</td>
<td>Maydis stigma</td>
<td>Maydis stigma</td>
<td>HPLC</td>
<td>$8.00 \times 10^4$</td>
<td>Rha, Ara, Man, Gal and Xyl (with an unknown ratio)</td>
<td>MSP was a homogeneous polysaccharide with a purity of 98% by area normalization method and contained 83.2% carbohydrate.</td>
<td>Liaoning, China</td>
<td>[54]</td>
</tr>
<tr>
<td>POP</td>
<td>Polygonatum odoratum</td>
<td>A variety of marine plants, especially seaweeds</td>
<td>HPLC</td>
<td>-</td>
<td>-</td>
<td>A crude polysaccharide</td>
<td>Shanghai, China</td>
<td>[55]</td>
</tr>
<tr>
<td>PSPK</td>
<td>Rhizome of P. kingianum</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>A crude polysaccharide</td>
<td>Yunnan, China</td>
<td>[56]</td>
<td></td>
</tr>
<tr>
<td>PPSB</td>
<td>Physalis alkekengi</td>
<td>Calyces of P. alkekengi L. var. francheti</td>
<td>HPLC</td>
<td>$2.7 \times 10^4$</td>
<td>Ara : Gal : Glc : GalA = 2.60 : 3.60 : 2.00 : 1.00</td>
<td>PPSB contained 92.5% carbohydrate, without nucleic acid and proteins.</td>
<td>Dalian, China</td>
<td>[57]</td>
</tr>
<tr>
<td>LGPP2-2</td>
<td>Pumpkin</td>
<td>Fresh pumpkin (C. pepo, lady godiva variety) fruits</td>
<td>GC-MS and SEC-MALLS</td>
<td>-</td>
<td>-</td>
<td>Composed of 1,6-linked-glucosyl, 1,2,6-linked-mannosyl, 1,2,6-linked-mannosyl, 1,2,6-linked-galactosyl, 1,2,6-linked-galactosyl, terminal fucosyl and terminal glucose.</td>
<td>Beijing, China</td>
<td>[58]</td>
</tr>
<tr>
<td>PLP</td>
<td>Plantago asiatica</td>
<td>P. asiatica L. seeds</td>
<td>HPGPC, FT-IR and HPLC</td>
<td>$1.89 \times 10^6$</td>
<td>-</td>
<td>PLP contained 29.2 g kg$^{-1}$ protein and 145.8 g kg$^{-1}$ uronic acid.</td>
<td>Jiangxi, China</td>
<td>[59]</td>
</tr>
</tbody>
</table>
Fig. 1  The conversion of polysaccharides from traditional Chinese medicine into SCFAs by the intestinal microflora

Fig. 2  TCM polysaccharides interact with the intestinal microflora for T2DM treatment
and manage obesity \[51\]. Acetic acid and propionate have been shown to stimulate fat production in fat cells and increase leptin release in adipose tissue in mice. Butyrates may affect the proliferation and differentiation of epithelial cells and regulate energy metabolism in the mammalian colon. As a prebiotic, MDG-1 was completely fermented by the intestine into SCFAs, so as to effectively treat T2DM \[81\].

**Bile acids (BAs)**

BAs are an important component of bile and a major endogenous metabolite for cholesterol degradation in the liver, and act as an important signaling molecule that regulates energy metabolism and inhibits excessive proliferation of the intestinal microflora \[54\]. The intestinal bacteria participated in the transformation of BAs in the body and hepatic circulation, and effectively hydrolyzed foreign bodies cleared by BAs \[59\]. BA regulation is a complex process that requires the joint action of the intestinal microflora, the intestinal tract, and the liver, primarily through two BA receptors: farnesoid X receptor and G protein-coupled BA receptor 1 (GPBAR-1 or TGR5), which are involved in the synthesis of lipid metabolism. The synthesis of BA in the liver and the reabsorption of BA in the intestine play an important role in the metabolism of lipids, glucose and energy \[96\]. BAs maintained the barrier function of the intestine and prevented the overgrowth and migration of the intestinal microflora \[57\]. As a result, intestinal microflora disorders led to a decrease in the secondary production of BAs, followed by a decrease in activation of BA receptors, which then accelerated the severity of glucose metabolic disorders and T2DM \[7\]. Studies have shown that the metabolism of BAs changed in T2DM patients, and blood sugar levels were improved through regulating the type and content of BAs in T2DM patients \[70\]. Jones and other researchers found that intestinal dysbacteriosis and the reduction of intestinal microbiota containing bile salt hydrolases led to BA metabolic disorders, inducing glycolipid metabolic diseases. Therefore, regulation of the intestinal microflora involved in BA metabolism may be a potential target for the treatment of diabetes \[70\].

BAs have long been thought to regulate cholesterol metabolism in humans and animals, and the increased synthesis of BAs improves the utilization of cholesterol as a substrate, which is considered the main metabolic pathway for cholesterol degradation (Fig. 2). Medicinal plant polysaccharides interacted with BAs, which inhibited enterohepatic circulation and increased the excretion of BAs in the feces \[80\]. Hu et al. investigated the effects of a new polysaccharide (PLP) from seed of Asiatic plantain on intestinal function in vitro. Results showed that PLP was able to bind to BAs and possibly lower cholesterol levels, which was essential for slowing glucose diffusion, inhibiting amylase activity, prolonging blood sugar reactions and thus controlling the concentration of postprandial blood glucose. This finding demonstrated that PLP may have potential benefits from human intestinal function and can be used as a potential ingredient in functional food applications \[81\]. Nakahara et al. evaluated the effects of *Pleurotus eryngii* polysaccharides on obesity and intestinal microflora in HFD-fed mice, where most of cholesterol was converted into BAs by liver cells in the mice \[82\]. The metabolic disorders caused by obesity play a significant role in T2DM. Experimental results showed that *Pleurotus eryngii* polysaccharides treated obesity and lowered LDL cholesterol in obese mice, and prevented diabetes by increasing the excretion of BAs and lipids and changing the body’s microbiome. Moreover, Shi et al. confirmed that MDG-1 absorbed BAs in the intestinal cavity and reduced their re-absorption, so as to promote cholesterol catabolism and inhibit the expression of farnesol X receptors and the activation of liver X receptors. These findings provide new thoughts for the mechanism of MDG-1 in lipid control \[83\].

**Endotoxin theory**

Endotoxin is a component of LPS which constitutes the outermost cell wall of gram-negative bacteria \[84\]. HFD and other factors lead to intestinal microflora disorders, reduce Bifidobacteria, lactic acid bacteria and other beneficial bacteria proportion, increase the proportion of gram-negative bacteria and increase intestinal wall permeability or displacement of the intestinal microflora. Metabolic endotoxinemia occurs by producing and absorbing more LPS and inhibiting the function of the intestinal barrier. LPS and glucose phosphate isomerases form a complex of protein CD14, which is identified by the tool-like subject TLR-4 on the surface of monocyte macrophages, working on skeletal muscle cells and fat cells, and identifying inflammation and insulin resistance through the TLRs and mitogen-activated protein kinase (MAPK) signaling pathways \[85, 86\]. Studies have shown that disorders in the intestinal microflora can lead to decreased function of the intestinal physical barrier, microbial barrier, and metabolic endotoxinemia. The destruction of the bacterium leads to decreased levels of the intestinal tight junctional protein ZO-1 and Occludin, disrupts the intestinal microbial barrier consisting of membrane flora (mainly Bifidobacterium and Lactobacillus) and cavity flora (mainly E. coli and Enterococcus) and the colonization of pathogenic bacteria in the intestinal mucosa. Impairment of the function of the intestinal barrier led to the displacement of intestinal microflora, endogen infection, and eventually metabolic endotoxinemia \[7\]. Cani et al. \[85\] introduced a concept of “metabolic infection” to define the role of the intestinal microflora in endotoxinemia related inflammation and insulin resistance in T2DM (Fig. 2).

In summary, intestinal microflora disorders can lead to T2DM by weakening intestinal barrier function and activating endotoxinemia, inflammation, and insulin resistance induced by the TLRs and MAPK signaling pathway \[87\]. Studies have shown that *Polygonatum kingianum* polysaccharides PS and PSF improve the integrity of the intestinal barrier in HFD-fed rats, and enhance the interactions with NF-κB to prevent their nuclear translocation and the production of activated IκB-α. Inhibiting the TLR4/NF-κB immune response reduced endotoxinemia and inflammatory ability to improve
glucose and lipid metabolic disorders [45]. Liu et al. investigated the regulation of intestinal microbiota in T2DM rats to improve inflammation, and found that STS reduced the mRNA expression of IL-6 and TNF-α and endotoxin LPS levels in pancreatic tissue through key strains in the intestinal microbiota, so as to treat T2DM. This mechanism of action is similar to metformin. This action is similar to metformin [92].

**Low-grade inflammation**

Insulin resistance and T2DM are closely related to low levels of “inflammation”, characterized by abnormal cytokine production, increase in reactants and other mediators in the acute phase and activation of inflammatory signaling pathways [89]. TCM polysaccharides can regulate the secretion of some inflammatory factors during the treatment of T2DM. Some cytokines such as IL-6, INF-α and IFN-γ are important indicators for evaluating the immune of the intestine, where TNF-α acts as a key inhibitor of insulin action. Deficiency in TNF-α function leads to improved insulin sensitivity and glucose stability, indicating that this inflammatory response plays a key role in the regulation of insulin action in obesity. There also have been numerous reports which indicated insulin resistance is a low-level inflammatory response [89, 90]. In addition, changes in the intestinal microflora may affect satiety and blood glucose controlled intestinal hormone levels, such as glucosin-like peptide-1 (GLP-1). GLP-1 is a hormone secreted by L cells at the end of the small intestine and colon. Its release is a potential mediator mechanism that explains the effect of SCFAs on glucose homeostasis, such as appetite control and stomach emptying, and stimulates insulin secretion in the pancreas to produce anti-diabetic effects [91]. There are also intestinal hormones like glucose-dependent insulintropic polypeptide (GIP), recombinant peptide YY (PYY), human cholecystokinin (CCK) and vasoactive peptide (VIP), all of which are associated with blood glucose regulation. Some polysaccharides played a direct or indirect role in regulating blood sugar by regulating the secretion of these hormones [92].

In general, TCM polysaccharides can treat T2DM by relieving low-grade inflammation and regulating endocrine levels in the gastrointestinal tract (Fig. 3). For example, Hino et al. found that GLP significantly reduced the levels of inflammatory factor interferon (IFN)-γ, interleukin (IL)-2 and IL-4, and reduced the serum level of amine oxidase (DAO), so as to improve the immune function of the intestine [90]. Xu et al. investigated the effect of *Ganoderma lucidum* polysaccharides on insulin resistance in HFD-fed mice [94]. Results showed that *Ganoderma lucidum* polysaccharides reduced the concentration of insulin in HFD-fed mice, reversed insulin resistance, alleviated low-grade inflammation, reduced decomposition in adipose tissue, restrained the mRNA expression of TNF-α and IL-6, and reduced the outflow of plasma triglycerides and non-esterified fatty acids. All of these mentioned above may be related to the composition of intestinal microflora associated of T2DM. Zhang et al. demonstrated that chrysanthemum powder reduced the levels of fasting blood glucose in diabetic rats induced by streptozocin (STZ) combined with HFD, relieved glucose intolerance, increased GLP-1 levels, reduced the levels of IL-6 in epididym adipose tissue, and the expression of phosphoenol pyruvate carboxykinase and glucose-6-phosphatase catalytic subunit in the liver, while regulating the intestinal microflora, so as to play a therapeutic role in T2DM [90].

**Synergistic conversion of TCM components**

TCM polysaccharides can restore the disturbance of in-

---

**Fig. 3** Mechanism of traditional Chinese medicine polysaccharide and compound combined with the intestinal microflora in the treatment of T2DM
intestinal microflora, while promoting the transformation of small molecular substances of Chinese medicine and playing a collaborative role in the treatment of diabetes (Fig. 3). It has been reported that some plant polysaccharides can enhance the absorption of drugs used simultaneously. Currently, traditional Chinese medicine is often administered by decoction preparation, where polysaccharides and small molecules exist together. There is no doubt that the chemical complexity of decoctions is the basis for the multi-target application module of TCM, and the small molecules and polysaccharides of TCM, the two important and dominant types of chemicals in TCM decoctions are usually separately investigated. But in a recent study, Li et al. investigated the synergistic anti-diabetic effects of ginseng polysaccharides and ginseng saponin Rb1 in T2DM rats induced by HFD and STZ. Ginseng saponin Rb1 has significant hypoglycemic activity, but disorders in the intestinal bacteria of diabetics may affect the metabolism and absorption of ginseng saponin Rb1, thereby affecting its hypoglycemic function. So Li Jing et al. observed the effects of ginseng saponin Rb1 and ginseng polysaccharides on fasting blood glucose in diabetic rats, and the conversion of ginseng saponin Rb1 in the intestinal flora of rats. Results showed that ginseng polysaccharides improved the hypoglycemic activity of ginseng saponin Rb1 by regulating the intestinal microflora, changed the bio-transformation pathway to ginseng saponin Rb1, improved the bio-conversion rate of ginseng saponin Rb1 into CK, promoted the activity of β-D-glucosidase in the feces, and improved the absorption of CK. At the same time, Chen and Qian et al. confirmed that the combination of pumpkin polysaccharide and puerarin was more effective for T2DM treatment than the two substances used alone, which improved blood glucose tolerance and insulin resistance in T2DM mice.

**Prevention and treatment of T2DM with Chinese herbal compounds based on the intestinal microflora**

Chinese herbal compounds exhibit beneficial effects of enhancing insulin sensitivity, protecting β cells, simulating insulin secretion, correcting glycolipid metabolic disorders, improving the immune system and regulating the structure of intestinal microflora in T2DM. Compared with simple TCM, Chinese herbal compounds conforms to the recently proposed principle of “multi-component and multi-target”, and the synergy of TCM includes efficiency and detoxification. In order to improve the efficacy, the mixed biological active ingredients present in TCM can play a multi-objective role, such as improving β cell function, hormone secretion, free radical scavenging and microcirculation. In the current research, there are two main ways for Chinese herbal compounds to treat T2DM based on the intestinal microflora. First, Chinese herbal compounds treat T2DM by adding and enriching beneficial bacteria, and reducing harmful bacteria (Table 2). For example, Gao et al. applied a new Chinese herbal compound Qijian mixture in the treatment of T2DM, and evaluated its safety and effectiveness. The mechanism of Qijian mixture was investigated by 1H NMR-based metabolomic methods. Results showed that Qijian mixture played a role in regulating metabolic disorders and regulating the concentration of different metabolites in amino acid and carbohydrate metabolism, while inducing structural changes in the intestinal bacteria, enriching beneficial bacteria, and playing a positive role in reducing sugar. Second, Chinese herbal compounds regulate the intestinal microflora, improve the intestinal barrier function and inflammatory response and then treat T2DM. For example, Wei et al. investigated the mechanism by which Xieixin decoction reduced blood glucose levels in T2DM rats. Results indicated that Xieixin decoction improved insulin resistance and T2DM by enhancing the function of the intestinal barrier and improving intestinal permeability and inflammation. In short, TCM may play a variety of health-promoting roles, and treat T2DM in the form of Chinese herbal compounds. We have summarized the therapeutic effect of current traditional Chinese prescription on T2DM based on the intestinal microbiota, so as to further explore the anti-diabetic mechanism of Chinese medicine from the perspective of the intestinal microbiota.

**Conclusion**

To sum up, TCM polysaccharides can interact with the intestinal microflora, which play therapeutic effect on the treatment of T2DM, while polysaccharide components can improve host health by optimizing the structure of intestinal bacteria. Intestinal microflora can be considered as “microbial organs” in host organisms, where probiotics play a positive role in human health. At the same time, TCM polysaccharides exhibit significant effect on the enrichment of probiotics, and participate in a series of stability recovery process in the intestinal micro-environment. These findings prove its role as prebiotics and open up a new perspective on the possible ways for TCM polysaccharides to participate in the treatment of human diseases. These advances have the potential to create new therapeutic thoughts about T2DM and its complications; that is, reducing the inherent rate of deterioration and mortality risk of metabolic diseases through two-way regulation of polysaccharides and intestinal microflora, and bringing innovative drug treatments and more effective treatment options to T2DM and obese patients.

People have long believed that the small molecular components of TCM are the material basis for the pharmacologic effect of a drug, while polysaccharide components have a large molecular weight, which are not easy to be absorbed, and less effective for the treatment of diseases. In addition, polysaccharides are characterized by low separation and purification efficiency, diverse structure, complex identification process, lack of chromophores or fluorophores, difficult component detection, and unclear market standards. In recent years, with the development of industrial production and extraction of TCM polysaccharides, a large number of new discoveries have been done in the field of purification and iden-
Table 2  Prescription of traditional Chinese medicine for the treatment of T2DM based on the intestinal microbiota

<table>
<thead>
<tr>
<th>Compound</th>
<th>Important drug composition</th>
<th>Model</th>
<th>Does</th>
<th>Prevention and treatment of type 2 diabetes</th>
<th>The influence of the gut microorganism</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wenyangqiuxue Fang</td>
<td>Prepared monkshood, Prepored licorice, ginseng and other 12 herbs (Increase and decrease with certificates) Pueraria lobata,</td>
<td>Patients</td>
<td>400 mL·d⁻¹</td>
<td>FBG↓, postprandial 2 h plasma glucose↓</td>
<td>Bifidobacterium↑, Bacteroides↑, Enterobacteriaceae↓, Enterococcus↓, Saccharomyces↓</td>
<td>[109]</td>
</tr>
<tr>
<td>Gegenqinlian Decoction</td>
<td>Scutellaria baicalensis, rhizome of Chinese goldthread, prepared Pueraria lobata,</td>
<td>T2DM patients</td>
<td>300 mL·d⁻¹</td>
<td>FBG↓ and Hba1c↓, maintain blood glucose homeostasis</td>
<td>Faecalibacterium prausnitzii↑, beneficial bacteria↑, such as Faecalibacterium spp.</td>
<td>[100]</td>
</tr>
<tr>
<td>Zibupiyin Fang</td>
<td>Salvia miltiorrhiza Bge, Polygala tenuifolia Wild., Panax ginseng C. A. Mey. et al. 12 herbs</td>
<td>Fat ZDF rats</td>
<td>0.1 mL/10 g</td>
<td>Total AUC in glucose↓, insulin sensitivity↑ and BG↓</td>
<td>Firmicutes↑, Bacteroidetes↓, Firmicutes/Bacteroidetes ratio↓</td>
<td>[110]</td>
</tr>
<tr>
<td>Qijian Mixture</td>
<td>Astragalus membranaceus, Ramulus euonymi, Coptis chinensis and Pueraria lobata</td>
<td>Male KKAY diabetic mice</td>
<td>1.795–5.385 g·kg⁻¹</td>
<td>BG↓</td>
<td>Bacteroidetes, Eroides and other probiotics↑</td>
<td>[107]</td>
</tr>
<tr>
<td>Xiexin Tang</td>
<td>Chinese rhubarb, Scutellaria, Rhizoma coptidis</td>
<td>SD rat + HFD + STZ</td>
<td>10 g·kg⁻¹</td>
<td>The hyperglycemia, abnormal fat metabolism and inflammation of rats were significantly improved</td>
<td>Bacteroidetes↑, Proteobacteria↑, Actinomyces↑</td>
<td>[108]</td>
</tr>
<tr>
<td>AMC</td>
<td>Salvia miltiorrhiza, Anemarrhena, Schisandra and other 8 herbs</td>
<td>T2DM patients</td>
<td>1 unit of AMC formula</td>
<td>Significantly improved blood glucose and lipid levels, TC↓</td>
<td>Faecalibacterium spp↑, Blautia spp↑</td>
<td>[111]</td>
</tr>
<tr>
<td>Oil Tea</td>
<td>Green tea : ginger : peanut : oil : cooking oil : salt = 9 : 10 : 5 : 2 : 1</td>
<td>Db/db male mice</td>
<td>4 g·kg⁻¹</td>
<td>Inhibit postprandial elevation of blood sugar, FBG↓, TC↓, TG↓ and LDL-cholesterol↓</td>
<td>Lachnospiraceae↑</td>
<td>[112]</td>
</tr>
<tr>
<td>Jinqijiang Tang</td>
<td>Rhizoma coptidis, Astragalus and Honeysuckle</td>
<td>HFD + STZ male C57BL/6J mice</td>
<td>Clinical equivalent dose (2 times)</td>
<td>FBG↑ and Hba1c↓, Improve T2DM IR</td>
<td>Akkermansia spp↑, intestinal barrier function↑, Desulfovibrio↓ and host inflammatory response↑</td>
<td>[113]</td>
</tr>
<tr>
<td>Shengjiang Power</td>
<td>Stiff silkworm, cicada slough, turmeric, Chinese rhubarb</td>
<td>HFD + STZ rat</td>
<td>0.753, 1.506, 3.012 g·kg⁻¹</td>
<td>FBG↑, TNF-α↑, INS↑, the inflammatory state↑, BG↑</td>
<td>Gut Streptococcus and other Probiotics↑, Lactobacillaceae↑</td>
<td>[114]</td>
</tr>
</tbody>
</table>

CJNM – 651 –

Identification, while more biological activity has been explained by researchers. At present, studies about polysaccharides from TCM mainly focuses on pharmacological effects, while its exact chemical structure and physical and chemical properties have not been well explained. Although POP, PSPK, MFP, GLP and other polysaccharides have anti-diabetic activities, they simply work as crude polysaccharides. At the same time, the underlying mechanisms of many polysaccharides are not completely understood. For example, *Schisandrae chinensis* polysaccharide SSPW1 increased the weight of T2DM rats, improved glucose tolerance, reduced FBG, and improved the level of rat fins and ISI values, playing a significant role in T2DM treatment. Similar polysaccharides include okra polysaccharides, fenugreek polysaccharides, and wolfberry polysaccharides. Therefore, more preclinical and clinical trials are required to further explore the potential therapeutic mechanism of polysaccharides from TCM, in which the intestinal microflora can be considered as a priority mechanism because of the prebiotic properties of TCM polysaccharides. The human body suffering from T2DM will lead to intestinal endocrine disorders and beneficial bacteria imbal-
ance. Due to the destruction of probiotics, polysaccharides cannot be rapidly or more difficult to be decomposed and utilized, which brings limitations on the treatment of T2DM with polysaccharides. The disorder of internal microflora caused by diseases has also become a disadvantage of polysaccharide therapy. At the same time, the relationship between the types of polysaccharides, molecular weight, monosaccharide composition, glycosidic linkage and the regulation of intestinal microflora is still unclear. The mechanism by which natural polysaccharides play a variety of biological activities through regulating intestinal microflora needs to be further investigated. In recent years, a large number of prebiotics have entered everyone's field of vision, which maintain human health through the overall concept of the human body. In the future, more indigestible carbohydrates will be developed into new prebiotic products against diseases that are difficult to treat. It is essential to develop of Chinese prebiotics have entered everyone's field of vision, which maintain human health through the overall concept of the human body. In the future, more indigestible carbohydrates will be developed into new prebiotic products against diseases that are difficult to treat. It is essential to develop of Chinese medicine polysaccharide drugs that can be easily absorbed or used in combination with probiotics, so as to exert the biological activity of Chinese medicine polysaccharides to treat diseases in an fast and effective manner.

Supporting information

Supporting information of this paper can be requested by sending E-mails to the corresponding authors.

References

[27] McCleig LH, Bailey CJ, Pearson ER. Metformin and the
Food hydrocolloids, 2019, 89: 735-741.


[64] Shen H, Gao XJ, Li T, et al. Ginseng polysaccharides en-
hanced ginsenoside Rb1 and microbial metabolites exposure through enhancing intestinal absorption and affecting gut microbial metabolism [J]. *J Ethnopharmacol*, 2018, **216**: 47-56.


