Recent advances in biotransformation, extraction and green production of D-mannose

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ABSTRACT

D-mannose is a natural and biologically active monosaccharide. It is the C-2 epimer of glucose and a component of a variety of polysaccharides in plants. In addition, D-mannose also naturally exists in some cells of the human body and participates in the immune regulation of cells as a prebiotic. Its good physiological benefits to human health and wide application in the food and pharmaceutical industries have attracted widespread attention. Therefore, in-depth research on preparation methods of D-mannose has been widely developed. This article summarizes the main production methods of D-mannose in recent years, especially the in-depth excavation from biomass raw materials such as coffee grounds, konjac flour, acai berry, etc., to provide new ideas for the green manufacture of D-mannose.

1. Introduction

Nowadays, the incidence of chronic diseases such as diabetes, hyperlipidemia, and hypertension is rapidly increasing worldwide and is showing a trend of getting younger (Zhang et al., 2017b). The occurrence of these diseases is closely related to excessive intake of high-sugar and high-fat foods. People excessively pursuit of taste, but ignore certain healthy diet habits. At present, the public's awareness of the impact of diet on human health has been greatly increased. Functional sugar has attracted people's attention. D-mannose has excellent physiological properties and biological activities, such as low calorie and low sweetness (Sharma et al., 2018). It has a wide range of applications in the food, medicine and beverage industries (Huang et al., 2018) (Fig. 1). For example, mannose can effectively reduce the growth rate of tumor cells (Gonzalez et al., 2018) and play an important role in the chemical modification of anti-cancer drugs and nano-vaccines (Dong et al., 2019; Yang et al., 2018). Meanwhile, it also has a good antibacterial effect and can effectively adjuvant treat urinary tract infections (Kyriakides et al., 2020); it also has a positive effect on the treatment of type I diabetes (Zhang et al., 2017a), deficiency of mannose phosphate isomerase (MPI) (de Lonlay and Seta, 2009) and other diseases. On the other hand, mannose can also be used as an important raw material for the production of bioenergy, such as ethanol fermentation with mannan as a substrate under the combined action of β-mannanase and β-mannosidase (Ishii et al., 2016).

As a high-value product, D-mannose production is a research hotspot in food and pharmaceutical industry. So far, a variety of methods such as chemical synthesis, microbial fermentation, biotransformation, etc. had been developed (Hu et al., 2016a). Each of these methods has its unique advantages. However, the reagents used and by-products formed in the process of chemically synthesized mannose are likely to cause pollution to the environment. As far as the current social development is concerned, the demand for environmental requirements, sustainable development, and "zero waste economy" is getting higher, which also means prevention, assurance and sustainability are key indexes for green chemistry. Green chemistry principles (GCP) were created by Paul Anastas and John Warner, who had attempted to define a greener (or more environment-friendly) chemical process or products (Horváth and Anastas, 2007). It towards sustainable development has been promoted (Lozano et al., 2018). As a strategic approach, the implementation of "circular economy", a nascent concept to improve the resource and energy efficiency has been proposed by Leontief (Murray et al., 2017). Considering the aspect of green production and compared with methods such as microbial fermentation and biotransformation, production based on biomass such as agricultural by-products or production waste is more in line with the above social and industrial production needs. Therefore, this review aims to summarize the commonly used methods of producing D-mannose in recent years and more focused on the green processing of bulk cash crops such as spent coffee grounds (SCGs), konjac flour, acai berry, and other biomass as substrates, as well as
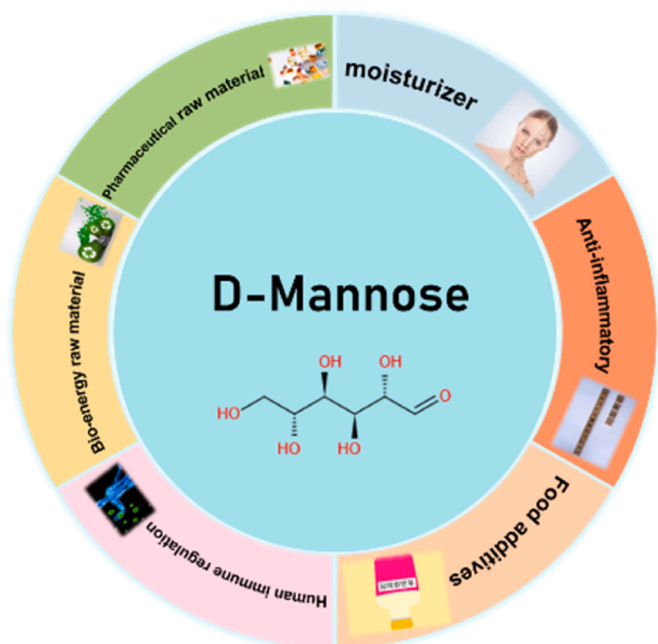
Fig. 1. Application of D-mannose.

discuss the important role of related enzymes and the optimal reaction conditions.

2. Methods of D-mannose production

2.1. Chemical catalysis

The traditional chemical preparation method uses molybdic acid or molybdate as a catalyst to prepare D-mannose by isomerizing D-glucose (Hu et al., 2016a). The researchers screened different types of molybdate catalysts and reaction conditions to increase the yield of D-mannose. For example, using ammonium molybdate as a catalyst to convert glucose (55%) at 98 °C and pH 2.0 for 150 min, the yield of D-mannose can reach 32.6% (Zhao, 2005). Using a mixed catalyst of ammonium molybdate and calcium oxide at 150 °C and pH 3.0 for 80 min, a D-mannose yield of 44.8% was obtained (Xu, 2014). However, the use of soluble molybdate will cause difficulties in the subsequent purification, which requires additional steps such as solvent replacement. Yin et al. used ethanol as an organic solvent for substitution and crystallization to obtain crude sugar crystals and then soaked in 60% ethanol again for a washing time of 20–30 min to obtain mannose with a purity of more than 99% and a yield of more than 60% (Yin et al., 2013). In addition, the chemical preparation method is only suitable for small-scale preparation in the laboratory due to the high production cost and cumbersome process, which is not conducive to industrialized large-scale production.

2.2. Enzymatic isomerization

D-mannose used as a dietary supplement or as a raw material for pharmaceuticals should avoid contamination by chemical extractants or other chemical by-products (Bicas et al., 2010). According to the Izumori strategy (Izumori, 2006), many high-value monosaccharides can be obtained by using sugar isomerase to convert common monosaccharides (such as glucose). Different substrate specificities of sugar isomerases can convert natural abundant sugars from raw materials. At present, many studies have shown that the bioconversion of D-mannose from D-glucose and D-fructose through isomerase has great potential for large scale production.

The isomerases currently used in the production of D-mannose

mainly include D-lyxose isomerase (LIase) (Guo et al., 2019; Huang et al., ; Park et al., 2010), D-mannose isomerase (Mlase) (Hu et al., 2016a,b), cellobiose 2-epimerase (CEase) (Park et al., 2011) and mannose 2-epimerase (Saburi et al., 2019), etc (Fig. 2). D-mannose isomerase, D-lyxose isomerase, and cellobiose 2-epimerase can be produced in large scale. Mlase can reversibly catalyze the isomerization of D-fructose and D-mannose. Currently, Mlases have been found in a variety of microorganisms, such as *Xanthomonas rubrilineans* S-48 (Takasaki et al., 1964), *Agrobacterium radiobacter* M-1 (Hirose et al., 2001), *Thermobifida fusca* MBL10003 (Kasumi et al., 2013) and *Marinomonas mediterranea* (Saburi et al., 2018), etc. In addition, some studies have shown that CEase can convert other β-1,4-linked disaccharides, such as lactose, through epimerization at the C-2 position, and catalyze the conversion of D-mannose and D-glucose as well (Park et al., 2011). The CEase extracted from the thermophilic microorganism *Caldicellulosiruptor bescii* and *Roseburia faecis* also showed good catalytic properties (Jameson et al., 2021).

Compared with the above isomerases, D-LIase is an aldose-ketose enzyme with a greater application value. It has broad substrate specificity which catalyzes the reverse isomerization of many functional sugars (Guo et al., 2019), such as D-xylulose and D-lyxose, D-fructose, D-mannose, L-ribulose, and L-ribose (Huang et al., 2018). The genes of D-LIase are widely distributed in many microorganisms such as *Aerogenes* PRL-R3 (Hirose et al., 2001), *Bacillus licheniformis* DSM13 (Patel et al., 2011), *Lactobacillus* RI-39 (Zhang et al., 2019), *Dictyostelium dilatum* DSM 6724 (Choi et al., 2012), *Escherichia coli* O157:H7 (van Staalduinen et al., 2010), *P. stuartii* KCTC 2568 (Kwon et al., 2010) and *S. proteamaculans* KCTC 2936 (Park et al., 2010), etc. In recent years, more and more studies have shown that D-LIases have better catalytic properties. For example, Guo et al. identified a D-LIase from *B. velezensis* CICC 24777, in the presence of 0.1 mM Co^{2+}, the genetic engineered D-LIase obtained exhibit maximum activity at 55 °C and pH 6.5. When using 25 U/mL enzyme and 500 g/L D-fructose as a substrate for 6 h, the reaction basically reached equilibrium and production rate of D-Mannose is 18.46 g/L/h (Guo et al., 2019). Hao et al. identified and characterized a novel putative D-LIase from the thermophilic strain *Caldanaerobius polysaccharolyticus* (Wu et al., 2020). It shows that D-LIase from *C. polysaccharolyticus* has a high mannose conversion rate of 25.6% and high thermostability (65 °C). Wenli et al. characterized a D-LIase from *Thermoflavimicrobium dichotomicum,* the results showed that the enzyme can form a homodimer structure, and showed strict metal coordination and conservation of substrate binding sites and metal independence (Zhang et al., 2019). The enzyme is very stable below 55 °C and has a high specific activity to D-mannose. The equilibrium ratio between D-mannose and D-fructose was 25:75. In a long-term reaction, 110.5 g/L of D-mannose was obtained from 500 g/L of D-fructose for 6 h, and the yield reached 22.1%. Lina et al. discovered a D-LIase with strong thermal stability in *Thermosediminibacter oceani*. It exhibits maximum activity at pH 6.5 and 65 °C, and is still active at 80 °C. Thermal stability experiments showed that the half-life of the enzyme at 70, 75, 80 and 85 °C was calculated to be 5.64, 2.82, 0.77 and 0.2 h, respectively (Yu et al., 2016). The enzyme shows the best activity with D-lyxose as a substrate, and can effectively catalyze the isomerization reaction between D-fructose and D-Mannose. Under the best conditions, 101.6 g/L D-mannose can be produced from 400 g/L D-fructose after 9 h of reaction, and the conversion rate can reach 25.4%. The isomerase method has become a new possible way for the industrial production of D-mannose through continuous transformation to adapt to industrial production conditions and reduce costs.

2.3. Enzymatic hydrolysis of mannose-rich polysaccharides

Mannan, glucomannan, and galactomannan derived from plant biomass are important renewable energy resources. These polysaccharides can be degraded by hydrolytic enzymes to generate manno-oligosaccharides or D-mannose (Fig. 3). β-mannanase and
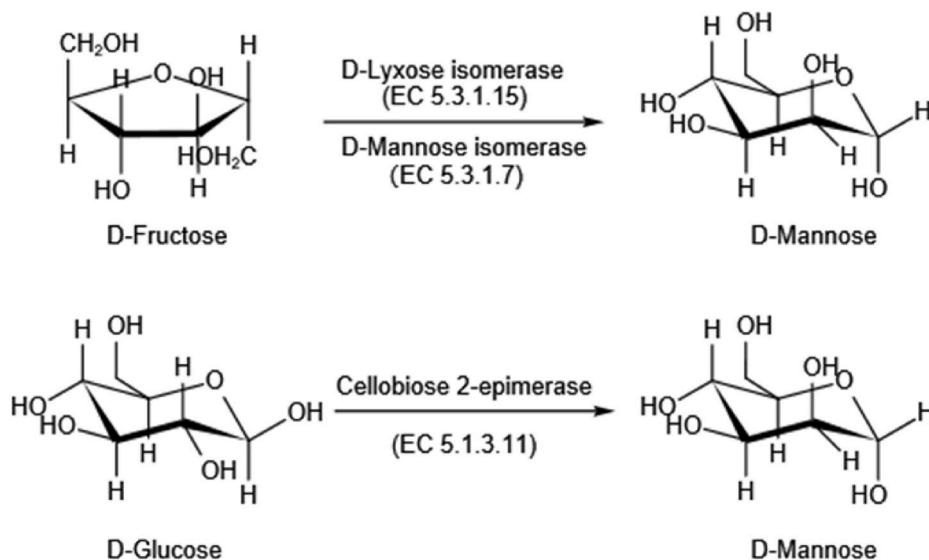
Fig. 2. D-mannose production by D-lyxose isomerase, D-mannose isomerase and cellobiose 2-epimerase.

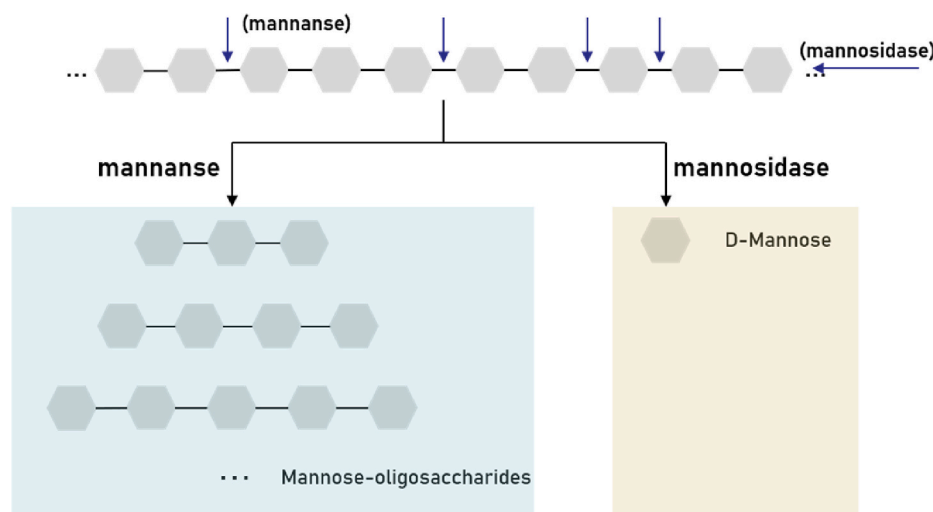**Fig. 3.** Schematic diagram of mannan degradation by mannase and mannosidase.

β-mannosidase are the main enzymes that are divided into different glycosyl hydrolase families (GH1, GH2, GH3, GH5, GH 26, GH113, etc.). In plants, these enzymes enhance plant metabolism mainly by degrading the mannan present in the cell wall (Moreira, 2008). Currently, mannanase has been isolated from plants, animals, and microorganisms (Jana et al., 2018; Kim et al., 2013; Wang et al., 2015b). At present, most commercial β-mannanase are produced by microorganisms. Among bacteria, most mannan-degrading enzymes come from Gram-positive bacteria, such as *Bacillus* (David et al., 2018). However, some Gram-negative bacteria, such as *Klebsiella oxytoca*, can also effectively degrade mannans (Tuntrakool and Keawsompong, 2018). Fungal mannanases mainly come from *Aspergillus*, *Trichoderma* and *Penicillium* (Agrawal et al., 2011; Blibech et al., 2011; Liu et al., 2020). The actinomycetes *Streptomyces* and *Nocardia* show significant mannan degradation ability (Gohel and Singh, 2015; Pradeep et al., 2016).

Genetic engineering can be used to improve the activity of mannanase. Wenting et al. found a GH 113 family β-mannanase *Ba*Man113A which exhibited a substrate preference for oligosaccharides compared with mannans, and produced mannose and mannosides as main hydrolysates. The study found that the amino acids W94, K174, and N236 at the reducing end of the +2 subsite of the recombinant protein of

*Ba*Man113A mutant form a spatial barrier that closes the substrate-binding tunnel (Liu et al., 2021). Compared with the wild-type enzyme, the catalytic activity on locust bean gum (LBG) and konjac glucomannan (KG) increased more than 100%, and the catalytic activity of the double mutant F101E/N236Y was significantly increased by 2.9 times and 4 times, respectively. It proves that high-efficiency conversion of mannose can be achieved through enzyme engineering. This green biotransformation method using renewable resources is of great significance for sustainable development. Therefore, it is critical to develop pretreatment and conversion technologies for mannose-rich biomass.

2.4. Mannose production from biomass

2.4.1. Spent coffee grounds

In recent years, the emergence of some new pretreatment technologies provides ideas for obtaining mannose from biomass. Coffee is the second most valuable commodity after oil (Murthy and Naidu, 2012), and the current global coffee consumption is about 9.98 billion kilograms ("World coffee consumption," 2021). However, the processing, roasting, and grinding of coffee beans produce a large amount of biological waste every year. The production of instant coffee and coffee

brewing generates approximately 8 million tons of spent coffee grounds (SCGs) per year worldwide (Burrows, 2015), which causes environmental pollution. In recent years, many studies have focused on the composition of SCGs and their secondary applications. SCGs contain a lot of organic matter such as oil fraction (7.9–26.4%), crude fiber (19.7–22.1%) and alkaloids (such as caffeine, trigonelline), protein, fatty acids (such as caffeine, trigonelline), phenol species, lignin, melanoidin and volatile compounds (Acevedo et al., 2013; Campos-Vega et al., 2015; Corrêa et al., 2014; Mussatto et al., 2011; Pujol et al., 2013). Among them, SCG is rich in cellulose and hemicellulose. It was shown that SCG contains 46.8% mannose, 30.4% galactose, 19% glucose, and 3.8% arabinose (Mussatto et al., 2011). The high content of the D-mannose component makes it a suitable source for the industrial production of mannose.

Quynh et al. developed a new integrated process that pretreated SCG through delignification and degreasing to remove almost all non-polysaccharide components (Nguyen et al., 2019). This process uses sodium chlorite and acetic acid to delignify SCG; use hexane for degreasing treatment, filtration and dehydration to obtain SCG-derived polysaccharides. Compared with raw SCG, the mannose component is enriched from 19.3% to 58.2%, which is significantly higher than that of palm kernel meal. The SCG-derived polysaccharides were subsequently subjected to continuous short-term and long-term saccharification. Studies have shown that under the conditions of cellulase-assisted hydrolysis, the highest conversion rates are about 77.8% and 73.9%, respectively.

The above research shows that valuable sugars, especially MOSs (manno-oligosaccharides) and mannose, can be obtained by improving pretreatment and regulating enzymatic hydrolysis. The reaction conditions are mild, and the maximum temperature in the delignification process is below 80 °C. The whole process shows high loading efficiency and the feasibility of large-scale production. In addition, acid pretreatment also has a good effect and helps the extraction of mannose. Dilute acid hydrolysis is one of the most effective methods to release hemicellulose sugars; however, the main problem of acid hydrolysis is that the decomposition of monosaccharides produced during the reaction and the hydrolysis of polysaccharides occur simultaneously. To prevent sugar decomposition, it is very important to perform the process under appropriate reaction conditions.

Simone et al. tested SCG hydrolysis in sulfuric acid, acetic acid, lactic acid and use cellulase to further convert carbohydrates into free sugars (Verhagen, 2018). The HPLC analysis proved that dilute acid hydrolysis can promote the efficient saccharification of SCG. In addition, Alchris et al. used sulfuric acid (3–5% v/v) to carry out hydrolysis at 95 °C with a substrate concentration of 10%. It showed that under the optimal condition with an acid concentration of 4% and a hydrolysis time of 120 min, the highest recoverable reducing sugar recovery rate is 86% (Go et al., 2016). These studies have shown that acid pretreatment has a great effect on the production of many types of reducing sugars including mannose by SCG.

Solange et al. tried to obtain the maximum hydrolysis efficiency of galactan, mannan, arabinan, and hemicellulose in SCG by optimizing conditions. Studies have shown that: at 163 °C, with 100 mg of sulfuric acid/gram of dry matter, 10 g of liquid-to-solid ratio extraction for 45 min. Under these conditions, the hydrolysis efficiencies of SCG galactan, mannan, arabinan, and hemicellulose were 100%, 77.4%, 89.5%, and 87.4% (Mussatto et al., 2011), respectively. Adane et al. used a combination of ultrasonic pretreatment and subcritical water hydrolysis to recover SCG polysaccharides (SCGPGs) from waste coffee grounds (Getachew et al., 2018; Getachew and Chun, 2017). Analyze the composition and saccharification efficiency of monosaccharides by HPLC, and determine the optimal treatment method of ultrasound from the pretreatment methods of ultrasonic, microwave, and supercritical carbon dioxide. The final study concluded that the maximum yield of SCGPSs can reach 18.25 ± 0.21% under the optimal extraction conditions of 178.85 °C, 20 bar, and 5min extraction time. The

monosaccharide composition shows that galactose (64.13 ± 0.56% mol) and mannose (29.82 ± 0.52% mol) are the main monosaccharides, followed by arabinose (3.33 ± 0.03% mol) and glucose (2.33 ± 0.03% mol). Current research shows that ultrasonic pretreatment can be used as an effective way to recover bioactive polysaccharides and monosaccharides from SCG.

Autohydrolysis technology has been widely used to extract polysaccharides and selectively produce oligosaccharides and monosaccharides (Rivas et al., 2013; Romaní et al., 2011). Lina et al. evaluated the effects of different process variables (including temperature, solid-liquid ratio, and extraction time) on the extraction rate of SCG polysaccharides to maximize the extraction rate of polysaccharides (Ballesteros et al., 2017). It was found that the extraction efficiency depends on different factors, including the type of coffee beans and their roasting degree, solid-liquid ratio, solvent, temperature, and extraction time. Compared with the percentage of total sugar extracted from SCG using alkali pretreatment, the percentage of total polysaccharides extracted from SCG using autohydrolysis technology is slightly lower (Ballesteros et al., 2015; Simões et al., 2009). However, when the optimal conditions are used, the amount of extracted mannose (31.88 mol%) is much higher than that obtained using alkaline pretreatment (4.43 mol%) (Ballesteros et al., 2015). These data indicate that autohydrolysis is an effective technique for extracting mannose from SCG (Table 1).

2.4.2. Konjac powder

Konjac is a kind of herb that grows in China, Southeast Asia, Japan and other places. It has been used as human food for more than 2000 years (Chua et al., 2010). It can be used as a food and dietary supplement, with functions of detoxification, tumor suppression, and asthma inhibition (Chen et al., 2006). The main polysaccharide found in konjac is glucomannan, in which glucose and mannose are connected by β-1, 4-glycosidic bonds in a ratio of 1:1.6 (Chen et al., 2013; Fang and Wu, 2004; Jian et al., 2013; Katsuraya et al., 2003). Methods to extract mannose include acid and enzymatic hydrolysis, oxidative degradation, physicochemical methods, and a combination of some newly emerged pretreatment technologies (Al-Sheraji et al., 2013; Al-Ghazzewi et al., 2007; Chen et al., 2005; Kranjčec et al., 2014; Oroskar et al., 2015; Roberfroid, 2007; Rolim, 2015; Wang et al., 2015a). Cuong et al. used the microwave radiation (MCR) technology (Kappe, 2004; Kappe and Dallinger, 2009; Kato and Matsuda, 1972) combined with hydrochloric acid as a catalyst to explore the reaction conditions for konjac flour hydrolysis and extraction of glucomannan oligosaccharides and mannose (Bui et al., 2016). Under the reaction conditions of 110 °C, 15 min, 1.2 M hydrochloric acid, 10% konjac powder, the yields of mannose and glucose were the highest, which were 35.8% and 30.2%,

Table 1
Summary of different preparation methods to obtain D-mannose from SCGs.

Methods	Advantages	reference
Delignification, Degreasing, Saccharification	High loading efficiency, the feasibility of large-scale production, can prevent sugar decomposition.	Nguyen et al. (2019)
Dilute acid hydrolysis	Acid pretreatment has a great effect on the production of many types of reducing sugars including mannose by SCG.	(Go et al., 2016; Verhagen, 2018)
Ultrasonic pretreatment and subcritical water hydrolysis	Effectively improve energy efficiency, high conversion rate, fast reaction, no solvent pollution, save time and manpower.	(Getachew et al., 2018; Getachew and Chun, 2017)
Autohydrolysis technology	Compared with alkali pretreatment, the yield can be greatly increased, environmental friendly.	Ballesteros et al. (2017)

respectively. Under this condition, only a small portion of 5-HMF was formed (0.3%). The combination of microwave radiation and acid hydrolysis can effectively hydrolyze konjac flour into glucomannan, mannose, and glucose in a short reaction time. In addition, this method can also be used to extract most of the carbohydrates in konjac flour under relatively mild reaction conditions.

2.4.3. Acai palm seed

Palm kernel meal is a by-product of the palm oil production process and is a biomass rich in mannose. The mannose component can reach about 48% of the total weight (Zhang et al., 2009). Acai palm is one of the representative plants, which is widely distributed in northern South America. The quality of ripe acai berry pulp only accounts for about 15% of the weight of the ripe fruit, while the seeds account for 85% (Pessoa et al., 2010; Pompeu et al., 2009). The annual storage of acai palm seeds in the Amazon region exceeds 1 million tons (de Lima Yamaguchi et al., 2015). However, there is currently no suitable and efficient utilization method for this valuable resource. Alvaro et al. used a combined strategy of acid hydrolysis and enzyme catalysis to analyze the chemical composition of the hydrolysate, optimized conditions and developed a conversion method. It was found that mannan is the main component of the mature seeds, and its content accounts for 50% of the total dry weight and 80% of the total carbohydrates. Using 3% sulfuric acid to hydrolyze at 121 °C for 60 min, 41 g/L of mannose can be obtained, and the yield is about 30%. Enzymatic hydrolysis of the remaining 70% of the mannan in the seeds can increase the mannose concentration to 146.3 g/L, and the yield can reach 96.8%, which is the highest concentration of mannose extracted from plant residues reported so far. This work confirmed that high-concentration and high-yield mannose can be obtained from acai berries (Monteiro et al., 2019).

2.4.4. Other biomass

Fungi have a variety of biologically active compounds (lectins, alkaloids, polysaccharides, lactones, etc.) (Ferreira et al., 2015; He et al., 2017; Yan et al., 2014). The active polysaccharides are mainly heterogalactan, glucan and mannan. The most common polysaccharides in basidiomycetes are mannan and fucoidan (Komura et al., 2010; Smiderle et al., 2008; Zhang et al., 2007). The main heteropolysaccharides of ascomycetes are glucomannan and galactomannan (Barreto-Bergter and Gorin, 1983). Gülsen Tel-Çayan et al. reported two new galactomannans separated from R. luteolus and G. adspersum, and their structures were characterized by infrared spectroscopy and nuclear magnetic resonance. The results showed that the molar ration of mannose/galactose of galactomannan i and ii were 0.81:1.0 and 1:1.4, respectively (Tel-Çayan et al., 2020). This research provides a new idea for the production of mannose from fungi. Meanwhile, the first extracted galactomannan ii has been proved to have medical value and can be used as a new natural anticholinesterase drug for the treatment of Alzheimer's Natural medicine for silent disease. Compared with galantamine used as a standard, it has high acetylcholinesterase and BChE inhibitory activity.

In addition to the above biomass, there are also studies on extracting mannose from fruits. D-Mannose is usually the main component of polysaccharides in fruits and can be separated by a variety of extraction methods. For example, Ya et al. extracted a new heteropolysaccharide from *Passiflora foetida,* through hot water extraction, ethanol precipitation and column chromatography. Furthermore, the composition of monosaccharides of this heteropolysaccharide was determined by gel permeation chromatography. Among them, the mannose content is 48.83% (Song et al., 2019). In addition, Yang et al. used *Malus micromalus Makino* fruit wine as raw material to extracted water-soluble polysaccharide MWP-2 by fractionated extraction, alcohol precipitation, and macroporous resin purification. The structure of MWP-2 was preliminarily analyzed by high performance gel-permeation chromatography (HPGPC), ion chromatograph (IC) and FT-IR. It showed that MWP-2 is composed of galactose, glucose, mannose and fructose in the mole ratio of 1:33.2:8.4:7.2 (Hui et al., 2019). It also proved that MWP-2

has anti-aging function. Moreover, there are examples of extracting different parts of fruits such as Chinese quince fruits (Qin et al., 2020), Chinese jujube (B. Wang, 2011), *Aotinidia arguta* (Zhu et al., 2019), longan pulp (Huang et al., 2019), *Opuntia flcus indica* fruit (Salehi et al., 2019), black mulberry fruit (Wang et al., 2018), citrus peel (Park et al., 2017), etc. The mannose yields are 22.86 ± 1.11%,12.90%, 9.60%, 9.27 ± 0.25%, 2.40%, 1.46%, 1.24% (Table 2). It can be derived from the above data that mannose can be extracted from fruits to some extent. Although some methods are not very environmentally friendly, they can be expected in the future. Through further research, improving production methods, increasing extraction efficiency and reducing costs, fruits and their processing by-products can become another major source of mannose.

3. Conclusion

As a functional sugar, mannose is widely used in food, medicine, cosmetics and other fields. The use of chemical methods in the production of D-mannose has the advantages of rapid and convenient application, but due to environmental problems, some consumers do not support the production of edible raw materials through chemical methods. As far as sustainable development is concerned, energy-saving cycles, pollution reduction and waste reduction have become the goals pursued by people. Therefore, attention should be paid to the development of the way to produce mannose from biomass, and to increase its productivity as much as possible. It is suitable for the conditions of industrial production, increases waste utilization, and realizes the recycling of economic resources. And, in terms of safety, the preparation methods that use more toxic chemical reagents should be avoided as much as possible. At present, the biological method of using biomass to produce D-mannose has gradually attracted more and more interest and has become a more promising method. However, the yield and process

Table 2
Other Sources for preparing D-mannose.

Source	Percentage	Main methods	Reference
Konjac power	35.80%	Microwave radiation	Bui et al. (2016)
Acai	NR	Hydrolysis, Enzyme catalysis	Monteiro et al. (2019)
Fungi	NR	Chemical extraction	Tel-Çayan et al. (2020)
China passiflora foetida	48.83%	Hot water extraction, column chromatography	Song et al. (2019)
China quince fruits	22.86 ± 1.11%	Chemical extraction, HPAEC	Qin et al. (2020)
Chinese jujube	12.90%	Boiled water extraction and ethanol precipitation	(Wang, 2011)
Aotinidia arguta	9.60%	Distilled water extraction, enzymatic hydrolysis	Zhu et al. (2019)
Longan pulp	9.27 ± 0.25%	Superfine grinding-assisted enzymatic extraction	(Huang et al., 2019)
Malus micromalus makin fruit wine	8.40%	Fractionated extraction, HPGPC	Hui et al. (2019)
Litchi peel	4.01%	NR	Somboonkaew & Terry (2010)
Opuntia flcus indica fruit	2.40%	Microwave digestion, gas chromatograph	Salehi et al. (2019)
Black mulberry fruit	1.46%	Hot water extraction, HPLC	(Wang et al., 2018)
Citrus peel	1.24%	Chemical and enzymatic degradation, dialysis, HPLC	(Park et al., 2017)
Ponkan peel	0.40%	High temperature extraction, GLC	Colodel et al. (2018)

NR: Not reported.

of using biomass production need to be optimized. It is suitable for high yield and simple processes. The optimal preparation plan for industrial production is still to be studied.

The use of economically acceptable and effective methods to produce value-added products is not only attractive to society, but also to industry. The trend in recent years is aimed at achieving a "zero waste economy." One can expect that focusing on the research and use of biomass as a substrate for energy production will help the circular economy and avoid or minimize waste generation. At present, when people are concerned about the consequences of depletion of natural resources, renewable energy should be accepted and used wisely as a "value-added product".

The wide application of D-Mannose has created a broad market prospect. In particular, D-mannose can be used as a substitute for high-calorie sugar to reduce obesity caused by excessive sugar intake and as a new food adjuvant, it has great market application value. D-mannose can not only reduce costs in the application of fine chemicals, but its naturalness and good skincare effect will also bring good economic benefits to enterprises. In the field of medical applications, D-mannose-modified drugs have been proven to have positive effects on anti-inflammatory, anti-cancer, and anti-tumor effects, and have the potential for better application prospects in the development of new drugs for certain diseases in the future.

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CRediT authorship contribution statement

Peiyao Wang: Writing – original draft, wrote the article. All authors read and approved the final article. **Yuting Zheng:** Writing – original draft, wrote the article. All authors read and approved the final article. **Yanping Li:** Writing – original draft, wrote the article. All authors read and approved the final article. **Ji Shen:** collected literature. All authors read and approved the final article. **Meiling Dan:** collected literature. All authors read and approved the final article. **Damao Wang:** Conceptualization, conceived and designed the project. All authors read and approved the final article.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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