Research progresses on the effect of drying technology on α-glucosidase inhibitors in plants

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Abstract. Diabetes is a metabolic disease characterized by hyperglycemia. It is one of the chronic non-communicable diseases after tumor and cardiovascular diseases, which seriously threatens the life and health safety of human beings. Alpha-glucosidase inhibitors can reduce fasting blood glucose and postprandial blood glucose. Compared with traditional inhibitors, the hypoglycemic components extracted from plants have less side effects, have an integrated mechanism of action, and the advantage of mild and lasting effects. Drying technology plays the role of controlling insects, mildew and not easy to deteriorate, which is conducive to the storage, transportation and dispensing of plants, so drying has become the essential operation unit of plants processing. Recently, various drying methods have been applied to the processing of hypoglycemic plants. The choice of drying technology affects the content and activity of active substances in plants, as well as the energy consumption, equipment investment, and drying cost. Therefore, this article reviews the effects of commonly used drying methods on substances with glucosidase inhibitory activity in hypoglycemic plants.

Keywords: Drying technique, diabetes mellitus, α-glucosidase inhibitors, medicinal and edible homologous plants, hypoglycemic active compounds.

1. Introduction

Diabetes mellitus, a metabolic disease characterized by hyperglycemia, is associated with factors such as insufficient insulin secretion and insulin resistance. In recent years, diabetes has become one of the chronic non-communicable diseases that seriously threaten the life and health safety of human beings after tumor and cardiovascular diseases [1]. Clinically, diabetes is mainly divided into type 1 diabetes and type 2 diabetes, among which type 2 diabetes accounts for about 90%–95% [2]. As an effective target for treating diabetes, α-glucosidase is key enzyme in the regulation of postprandial blood glucose, since it is able to convert complex carbohydrates into glucose [3]. Alpha-glucosidase inhibitors enable reversible competition with α-glucosidase, reduce carbohydrate degradation, decrease postprandial blood glucose, and effectively improve complications caused by hyperglycemia. Therefore, α-glucosidase inhibitors are the first-choice hypoglycemic drugs for type diabetes and auxiliary drugs for type I diabetes. Acarbose, voglibose, and miglitol are currently the three most clinically used α-glucosidase inhibitors. Unfortunately, they are often accompanied by various side effects such as diarrhea, abdominal discomfort, bloating and flatulence [4]. Therefore, it is particularly important to find novel α-glucosidase inhibitors with slight or no adverse effects.

Currently, the methods of obtaining α-glucosidase inhibitors include extraction from natural substances, microbial fermentation, and chemical synthesis [5]. Among them, the hypoglycemic components extracted from plants have the advantage of integration mechanism, mild side effects, and lasting effect. With the development of modern instrumental analysis technology, a large number of substances with α-glucosidase inhibitor activity have been isolated from different plants, mainly including polysaccharides, flavonoids, alkaloids, polyphenols and saponins, etc. [6, 7]. This provides a rich source for safe, efficient α-glucosidase inhibitor screening with small side effects. The drying of plants is an important and essential unit operation in the food processing industry. It extends the shelf life of the material by reducing microbial spoilage and enzymatic activity. On the other hand, dried products are greatly reduced in size, saving money on packaging, transportation, and storage costs, as well as maintaining higher nutrient concentrations. However, how to maintain the original
physical and chemical properties and biological functions of plants when drying is crucial. The effects of drying techniques and drying parameters on α-glucosidase inhibitors caused much attentions. In this paper, the current status of the chemical components of α-glucosidase inhibitors and the effects of drying technology in hypoglycemic plants were reviewed.

2. Alpha–glucosidase inhibitors from active ingredient of plants

2.1. Polysaccharides

Polysaccharides are widely found in almost plants and are one of the main functional and active components of plants. It has been proved that the polysaccharides of many medicinal and edible homologous plants have various biological activities such as lowering blood lipid, lowering blood sugar, antioxidant and enhancing immunity. Many studies have shown that polysaccharides are important active substances with α-glucosidase inhibitory activities. Hu et al. [8] studied the structural characteristics of mulberry leaf polysaccharide and its inhibitory effect on α-glucosidase activity, and found that mulberry leaf polysaccharide had good dose-effect relationship on α-glucosidase in the range of 0-5 mg/mL. Xu et al. [9] reported several native polysaccharides, which were isolated from Ribes nigrum L. and exhibited apparent α-glucosidase, α-amylase and glycation inhibitory activities in vitro. Moreover, the inhibitory effects on α-amylase and α-glucosidase of the isolated polysaccharides would be further enhanced when modified by nitric acid-sodium selenite method. Tian et al. [10] found that the inhibition of Lycium barbarum polysaccharides (LBP) on α-glucosidase was non-competitive inhibition. About 52% and 88% of α-glucosidase activities could be inhibited by 0.4 mg and 2 mg of LBP, respectively. Kou et al. reported that the preparation method would obviously affect the physical and chemical properties and biological activities of polysaccharides. The polysaccharide that extracted from L. barbarum with 6% ionic liquid had the highest inhibitory activities on α-glucosidase, α-amylase, and aldose reductase.

2.2. Flavonoids

Flavonoids are another active compounds exist in plants. According to their chemical structure, flavonoids can be further divided into many subclasses, such as flavonoids, isoflavones, flavonols, flavanols and anthocyanins [11]. Numerous studies have shown that flavonoids can inhibit α-glucosidase, improve cellular insulin resistance, and are considered as an effective supplement to prevent diabetes and effectively reduce complications [12]. For example, the total flavonoids (TF) of Ampelopsis Grossedentata and their derivatives have good effects on α-glucosidase inhibition and hypoglycemic activity. Chang et al. [13] found that the TF content contained in mulberry leaves in different origins was positively correlated with its α-glycosidase inhibitory activity. Tartary buckwheat is an efficient antihyperglycemic plant. Han et al. identified 12 potential α-glucosidase inhibitors from Tartary buckwheat, among which myricetin and quercetin had the highest activity. Moreover, they also found that different polyphenols had synergistic effect on the inhibitory activity of α-glucosidase. For example, the combination of competitive inhibitor myricetin with non-competitive inhibitor kaempferol-3-O-racoside had higher α-glucosidase inhibitory rate than that of the combination of competitive inhibitor myricetin combined competitive inhibitor isoquercetin. Hamed et al. [14] studied the inhibitory effect of flavonoids extracted from Moringa oleifera leaf (FMOL) on α-glucosidase, which indicated that 800 μg/mL FMOL could non-competitively inhibit up to 99.1% of α-glucosidase activity. Meanwhile, the combination of FMOL with acarbose significantly reduced the IC50 value and required concentration of acarbose.

2.3. Polyphenolic compounds

Polyphenols are common natural bioactive substances in plants and have aroused plenty of attentions in reducing the risk of obesity and diabetes. Studies have showed that polyphenols could inhibit α-glucosidase by interacting with enzymes or substrates, and the inhibitory activity was related to the structure of polyphenol substances [15]. Zheng et al. [16] confirmed the inhibitory effect...
of ferulic acid on α -glucosidase. Miao et al. found that tea polyphenols were potential drugs for the prevention and control of type 2 diabetes, and both have obvious inhibitory effects on glucosidase activity. Zhu et al. [17] found that phenolic compounds of Perilla seeds and roseminic acid extract of Perilla leaf could effectively inhibit α -glucosidase activity, showing great potential for prevention and treatment of diabetes. Rapeseed oil is rich in active phenolic compounds. Fluorescence quenching spectra and fourier-transform infrared spectroscopy analysis showed that the phenolic substances in rapeseed oil, including sinapic acid, canolol, canolol dimer, could induce conformational alterations in α-glucosidase and consequently cause the non-competitive inhibition on α–glucosidase . Han et al. detected 9 kinds of phenolic compounds presented in the free or bound states from 7 colored quinoa varieties, among which gallic acid and ferulic acid were the main components. However, free phenol extracts of colored quinoa showed higher α -glucosidase inhibitory activity than bound phenolic extracts. This result was attributed to free phenolic extracts contain more as phenolics with higher α -glucosidase inhibitory activity, including gallic acid, p-hydroxybenzoic acid, ferulic acid and rutin, etc.

2.4. Alkaloids

The alkaloids are structured similarly to sugars and thus are highly likely to replace the position of the sugar in humans and combined with α -glucosidase. With the deepening of modern pharmacology research, the alkaloid components with α -glycosidase inhibitory activity have been continuously excavated, and the mechanism of hypoglycemic action has also been deeply investigated [18]. In China, different part of mulberry plants have been widely applied in the treatment of diabetes since ancient times, including mulberry leaves, branches, root skins and fruits . Polyhydroxy alkaloids have been proved as one of the main active components of anti-diabetes, especially represented by 1-deoxynojirimycin (DNJ), which can effectively inhibit the absorption of sugar in small intestine and reduce the dietary blood sugar. Jia et al. [19] reported that the alkaloid extract of mulberry branch had some α-glucosidase inhibitory activity and antioxidant activity. And the active compounds were mainly distributed in ethyl acetate, followed by n-butanol part, and few in aqueous phase. The alkaloids contained in bamboo pepper also have a good inhibitory effect on α-glucosidase, which can reduce the enzyme activity by binding with the enzyme and the substrate complex to achieve the inhibition of α-glucosidase .

2.5. Saponins

Saponins are glycosides composed with sugars, uronic acids or other organic acids. Because the hydroxyl structure of saponin itself may be the action site of some enzyme, it has good physiological activity. Previous studies have confirmed that saponin was the main material basis for the inhibition of α-glucosidase activity, and can effectively inhibit the activity of α-glucosidase and aldose reductase. Han et al. reported that saponins extracted from quinoa had strong inhibitory effect on α -glucosidase comparable to acarbose. Dong et al. [20] found that the inhibitory effect of quinoa saponins was significantly stronger than that of the positive drug acarbose. Moreover, the inhibitory types of quinoa saponins extract and acarbose on α -glucosidase were mixed inhibition and competitive inhibition, respectively. A new oleanane-type triterpenoid saponin with α-glucosidase inhibitory activity was extracted from Camellia nitidissima, which showed potent inhibitory activity against α-glucosidase with an IC50 value of 185.9± 44.5 µmol/L. Two new stigmastane-type steroid saponins, asparagine K and asparagine L, were isolated from the leaves of Vernonia amygdalina, which showed significant inhibition on α-glucosidase, comparable to the positive control acarbose [21].

3. Effect of drying on α -glucosidase inhibitors in plants

At present, hot air drying, heat pump drying, vacuum drying, microwave drying, freeze drying are the common drying techniques of plants. In addition, combined drying technologies also have widely applied in order to further improve the drying efficiency, reduce energy consumption, and maximize
the content and activity of active compounds in plants. Moreover, a large amount of researches on the effects of drying on the active components with α-glucosidase inhibitory properties in plants have also been conducted.

3.1. Hot air drying

Hot air drying method, also namely oven-drying method, is the most common method applied for plants drying at present. It has the advantages of strong applicability, high economy, high automation degree, simple operation, and large processing capacity. Currently, hot air drying has been widely used in the drying of hypoglycemic plants. Gu et al. [22] proposed that polyphenols in the bitter gourd that dried at 50℃ had the highest content and the strongest removal ability of DPPH free radicals, while, the highest flavonoids content was obtained when dried at 60℃. The dried bitter gourd powder could significantly inhibit the activity of α-glucosidase and α-amylase. After comparing the effects of four different drying methods, namely freeze drying, vacuum drying, microwave drying and hot air drying, on the active ingredients of mulberry leaves Qin et al. found that hot air drying is more suitable for the drying of large quantities of mulberry leaves in industrial production. Wu found that the total flavonoids content in mulberry leaves decreased continuously with the prolonged hot air drying temperature and drying time. However, the drying factors had less influence on the inhibition rate of α-glucosidase. Shang et al. [23] dried the Medicago sativa L. (MS) with hot air drying (HD), freeze drying (FD) and vacuum drying (VD), and the results indicated that the alfalfa polysaccharide extracted from the hot air dried MS (HD-MSPs) had higher inhibitory activity on α-amylase and α-glucosidase than VD-MSPs and FD-MSPs. Miao et al. comprehensively evaluated the effects of different methods, including hot air drying at different temperatures, vacuum drying and air drying, on the chemical composition, antioxidant activity and anti-α-glucosidase activity of Coreopsis tinctoria Nutt. It was concluded that 30℃ hot air drying was considered more energy-saving and more time-saving. However, generally speaking, hot air drying has the problem of low thermal efficiency and energy utilization. Meanwhile, hot air drying has several disadvantages including poor quality of dried products, easy loss of heat-sensitive nutrients, and direct discharge of air after drying.

3.2. Vacuum freeze drying

The vacuum freeze drying process is carried out at low temperature and vacuum conditions, so it is the preferred drying method for some plants containing heat-sensitive compounds and easy oxidation components [24]. Li et al. treated fresh mulberry by vacuum freeze drying (VFD), hot air drying (HAD) and heat pump drying (HPD), and the results indicated that the flavonoids content in the mulberries dried by VFD was very close to that in fresh mulberry. Zhao et al. found that VFD could better retain the total phenol, chlorogenic acid and derivatives, flavonoids, vitamin D3, α-lactocopherol, ascorbic acid and other functional components in the sweet potato leaves, so that the dried leaves still have strong antioxidant capacity. Meanwhile, the total amount of free phenolic acid in sweet potato leaves under VFD was 25.6 times that of hot air drying at 60℃. Wu et al. [25] comprehensively evaluated the Lycii Fructus samples dried by 9 different methods, and found that the VFD method could retain the multi-type functional components in Lycii Fructus to the maximum extent.

However, compared to other drying methods, vacuum freeze drying method typically have the problems of higher costs, longer time consumption, and higher energy consumption. Therefore, vacuum freezing drying method always combined with other drying method, such as microwave drying, heat pump drying, hot air drying, etc.

3.3. Microwave-assisted drying

Microwave-assisted drying (MAD) method mainly uses the strong microwave penetration. When penetrating into the medium, the dielectric molecules in a high microwave frequency internal violent vibration generated heat energy to achieve the purpose of drying. Microwave-assisted drying method has the advantages of high thermal efficiency and low pollution. However, the local overheating
during MAD would lead to the carbonization phenomenon and damage the quality of raw materials [26]. Therefore, suitable drying parameters of MAD are important for maintaining the content and efficiency of α-glucosidase inhibitors in hypoglycemic plants. He et al. compared the effects of different drying methods on the total flavonoids content (TFC) of *Scutellaria baicalensis Georgi* Leaves and found that TFC in the microwave dried leaves was the highest. Qin et al. [27] investigated the effect of four drying methods, including freeze drying, vacuum drying, microwave drying and hot air drying, on the hypoglycemic active ingredients of mulberry leaves. The results showed that MAD had slight influence on the hypoglycemic composition and color of mulberry leaves. The highest contents of DNJ and polysaccharide in mulberry leaves were obtained when treated by MAD at 140 W for 10 min. Wang et al. reported that compared to artichoke powder that dried by hot air drying method, vacuum drying method, vacuum freeze drying method, the artichoke powder dried by MAD method had the highest polyphenols content and best antioxidant capacity of free phenol and combined phenol.

### 3.4. Ultrasonic drying method

As a single drying method to process food, ultrasonic drying is characterized by the removal of water from solids without heating up. It can accelerate the water removal speed and minimize the residual water content in the solid. Therefore, it is benefit for improving the drying efficiency and reducing the energy consumption and drying cost [28]. In addition, ultrasound is often used in the pretreatment of other drying, such as low-temperature drying, freeze drying, infrared radiation drying, osmotic dehydration, etc. [29, 30]. In summary, this is a promising technology to minimize cost with a high degree of quality improvement in the dried product. Recently, the ultrasonic drying technology has also been widely used in the drying of hypoglycemic plants. Zhang et al. found that the total phenolic content of wolfberry (*Lycium barbarum* L.) when dried with ultrasonic far-infrared synergistic drying method at 40 kHz was increased by 44.9% compared with that of dried with natural drying method. Gong et al. [31] found that ultrasound-assisted vacuum drying method could shorten the drying time of *Flos Sophorae Immaturus* (FSI) by 40%. Meanwhile, the content and inhibitory effect on α-glucosidase and α-amylase of total flavonoids, rutin, quercetin and kaempferol were also significantly enhanced. However, it was found that extending the ultrasound time at the same ultrasonic power had no obvious effect on the content of flavonoids and other substances.

### 4. Conclusion

This article summarizes the research progresses in the drying techniques of hypoglycemic plants rich in natural α-glucosidase inhibitors. The characteristics of different drying techniques and their effects on the content and α-glucosidase inhibitory activity of active substances in different hypoglycemic plants were reviewed. In the future, combined drying techniques will be the research and development trend of hypoglycemic plant, which integrate the advantages of various single drying techniques. Combined drying techniques can further enhance the drying efficiency and energy utilization ratio, improve the content and activity of α-glucosidase inhibitors of the dried stocks, and reduce energy consumption and drying costs. However, currently, most combined drying techniques are only in the laboratory stage. Therefore, in the future, it is necessary to strengthen the design and industrial application of integrated equipment for combined drying techniques.

### References


