**Review Article** 

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**Functional and Therapeutics Potential of Inulin** 

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# Abstract

In recent years, there has been a growing interest in inulin, a type of fructan carbohydrate, due to its potential for both functional and therapeutic applications. Inulin is extracted from various plant sources such as chicory roots, Jerusalem artichoke, and agave. It possesses unique physiochemical properties that make it versatile for a wide range of uses in the food, pharmaceutical, and nutraceutical industries. Our understanding of the human intestinal commensal microbiota and their metabolic products has deepened, shedding light on their role in maintaining host health. As this knowledge has expanded, new health-associated bacteria have emerged. In the pharmaceutical and nutraceutical sectors, inulin has shown promise as a delivery system for various bioactive compounds, including probiotics, antioxidants, and drugs.

Keywords: Inulin, Fructan, Prebiotic, Functional Food, Gut Health, Therapeutics Potential, Delivery System, Bioactive Compound and Beneficial Microbes

# **1. Introduction**

Health and nutrition represent one of the most formidable challenges in our contemporary world, and this challenge is expected to persist in the coming years. A crucial area of research focuses on enhancing and preserving the nutritional value of our food. While energy-dense and refined foods may offer immediate comfort, they often lack essential nutrients, which can contribute to the development of various health issues such as hyperglycemia, hypercholesterolemia, colorectal cancer, and bowel diseases. In recent decades, the escalating demand for functional foods has spurred various food processing industries to develop methods aimed at preserving the nutritional quality of food [01].

Inulin is a type of polysaccharide composed of fructosyl units linked together in a linear chain through  $\beta$  (2 $\rightarrow$ 1) linkages. Typically, each inulin molecule features one terminal glucose moiety attached via an  $\alpha$  (1 $\rightarrow$ 2) linkage [02]. The discovery of inulin traces its origins back to the early 19th century when the German scientist Valentine Rose identified it as a storage carbohydrate in the roots of the Inula helenium plant. The carbohydrate was subsequently named "inulin" by Thomson. In 1864, plant physiologist Julius Sachs observed ethanol-precipitated spherocrystals of inulin under a microscope. Since then, inulin has been isolated from various sources, including tubers of plants like Inula helenium, Dahlia pinnata, and Helianthus tuberosus. Inulin can be found in approximately 45,000 plant species, constituting around 15% of all flowering plants. Some common examples of plants containing significant amounts of inulin include Helianthus tuberosus (Jerusalem artichoke), Dahlia pinnata (Dahlia), Polymnia sonchifolia (Yacon), and Cichorium intybus (Chicory) [03].

Inulin's structure consists of oligo- and polysaccharides made up of fructose monomers linked together by glycosidic bonds with a  $\beta$ -configuration at the anomeric C2 position. This particular β-configuration renders inulin resistant to hydrolysis by human gastrointestinal enzymes, classifying it as a non-digestible carbohydrate [04]. The degree of polymerization (DP) of fructan inulin can vary, ranging from 2 to 60 units, with an average value typically falling within the range of 10-12 units. The DP value holds significance as it can impact the functionality of inulin and is influenced by factors such as the plant source, the timing of harvesting, climatic conditions, the duration of the growing season, and storage time after harvest. Fructooligosaccharides, also known as oligofructose, have low DP values, typically around 10 units or less. It's worth noting that inulin derived from chicory tends to have lower DP values compared to inulin obtained from artichoke and globe thistle [05].

## **Major Sources of Inulin**

*Jerusalem Artichoke:* The Jerusalem artichoke (JA), also known as sunchoke or sun root, is a versatile crop that can thrive in various climatic conditions. It belongs to the Compositae family and is native to temperate regions of North America [06]. The tubers of Jerusalem artichoke are notably rich in inulin, with levels ranging from 17% to 20.5%. Fresh Jerusalem artichoke

tubers are primarily composed of approximately 80% water and contain around 1-2% protein. Furthermore, these tubers boast a significant mineral content, including iron, calcium, potassium, and sodium. In terms of calorie content, JA tubers are low in calories due to their relatively low starch and fat content or even the absence of these components. Inulin serves as the primary carbohydrate reserve in Jerusalem artichoke tubers. Pure inulin consists of approximately 3% glucose and about 97% fructose units. Most of the inulin found in JA tubers has a degree of polymerization (DP) of less than 9, making it suitable for fermentation. Additionally, the tubers contain inulin with medium DP values (ranging from 10 to 40) and high DP values (greater than 40), which can be utilized for fat replacement [02].

Jerusalem artichoke has been discovered to put forward a range of health benefits. Research indicates that it can help reduce cholesterol levels, maintain a healthy balance of intestinal microflora, combat intestinal infections, address obesity concerns, regulate blood sugar levels among diabetic individuals, and improve the composition of blood lipids. Moreover, supplements containing inulin and fructo-oligosaccharides derived from Jerusalem artichoke have the potential to bolster the immune system and contribute to the prevention of various diseases, including ulcerative colitis, inflammatory bowel diseases, and colorectal cancer [07].

# Chicory

Chicory (Cichorium intybus L.) stands out as a major reservoir of inulin, a type of dietary fiber predominantly present in its roots. Chicory root boasts a substantial inulin concentration, typically comprising around 68% of its composition when fresh, and up to an impressive 98% when dried. This rich inulin content positions chicory as a pivotal commercial source for inulin extraction. The process involves harvesting and processing the roots of the chicory plant to obtain this valuable inulin. The extracted inulin finds applications across various industries, including the food and beverage sector, where it serves as a prebiotic, sugar substitute, or fat replacer. Furthermore, it plays a role in dietary supplements and pharmaceutical formulations.

Cultivation of chicory as a crop is widespread in numerous countries, especially across Europe and Asia. The plant's robust adaptability to diverse climatic conditions underscores its reliability as a primary source for inulin production. While chicory remains a prominent inulin source, it's essential to recognize that other plants and sources also contain inulin, such as Jerusalem artichoke, dandelion root, and burdock root.

## **Extraction and Precipitation of Inulin**

Due to the increasing industrial applications of inulin, substantial research has been dedicated to its extraction, quantification, and utilization [08]. Numerous studies have delved into optimizing extraction conditions, encompassing factors like temperature, extraction duration, and solvent-to-solid ratios, all geared toward enhancing inulin yield [09]. One widely adopted method for inulin extraction involves hot water diffusion. Elevating the extraction temperature enhances inulin's solubility; while it remains insoluble at 25°C, it can dissolve up to 35% when the temperature reaches 90°C. Consequently, many industrial extraction processes rely on hot water diffusion systems [10]. Continuous stirring is often employed to improve extraction efficiency. A typical extraction process entails using distilled water at temperatures of 80-85°C for an hour while maintaining a pH of 6.8 to prevent inulin hydrolysis, which is prone to occur at pH levels below 6 [11]. Ultrasound-assisted extraction has also been explored to enhance extraction efficiency. Variables such as temperature, sonication amplitude, and time are adjusted to optimize the process. For instance, in the extraction of inulin from burdock roots, increasing sonication amplitude and extraction time improved efficiency, while the temperature remained relatively constant. Care should be taken to avoid the fragmentation of inulin caused by direct ultrasound action. Direct waves are preferred for depolymerizing inulin to obtain low molecular weight byproducts, while the indirect method is better suited for preserving intact inulin molecules [12]. Following extraction, inulin recovery typically involves precipitation through temperature reduction or different solvents, followed by centrifugation [12]. Phase separation can be a common issue when concentrated inulin solutions are cooled or frozen. To mitigate this, inulin precipitation through freezing or cooling can be followed by centrifugation and spray drying to obtain powdered inulin. Alternatively, freezing/thawing of inulin followed by centrifugation can serve as another precipitation method. High concentrations of organic solvents like ethanol, acetonitrile, methanol, acetone, and propanol can also be used for the precipitation of long-chain inulin molecules. Among these solvents, acetone stands out for effectively preserving the natural degree of polymerization (DP) of inulin, followed by methanol and ethanol. Acetone's advantage lies in its low boiling point, facilitating its recovery through distillation. Inulin recovery from Jerusalem artichoke tubers has shown promising results with a combination of acetone and ethanol. Ethanol is often preferred for food applications due to its Generally Recognized as Safe (GRAS) status. Ethanol has been used to recover inulin with DP values of 25 and 40 from chicory and dahlia, respectively. It's important to note that the yield of inulin powder can vary depending on the plant species and extraction methods employed [13].

## Inulin and lipid metabolism

Insulin resistance and elevated cholesterol levels are key factors contributing to metabolic disorders. High levels of cholesterol can lead to the accumulation of fat in the inner walls of arteries, contributing to vascular dysfunction, atherosclerosis, strokes, and cardiac issues. It's estimated that increased cholesterol levels underlie approximately 18% of strokes and 56% of cardiovascular complications.

In the current perspective, dietary guidelines are being emphasized as a means to lower elevated triglycerides and cholesterol in the bloodstream. This approach is gaining traction due to the costs and potential side effects associated with medications. Inulin and fructo-oligosaccharides have demonstrated their effectiveness in reducing triglyceride concentrations, particularly by decreasing very low-density lipoproteins (VLDL) during the post-absorptive state.

The cholesterol-lowering effects of inulin and oligofructose are attributed to their ability to inhibit triglyceride synthesis by reducing lipogenesis and promoting the production of short-chain fatty acids (SCFAs) through colonic fermentation. During fermentation, acetates and propionates are generated, which are then absorbed by the colon's mucosal lining and transported to the liver. Acetate serves as a substrate for cholesterol synthesis, while propionates interfere with enzymes involved in cholesterol and triglyceride synthesis, thus inhibiting lipogenesis. The ratio of acetates to propionates is crucial in evaluating their combined potential to reduce triglycerides. Studies involving diets containing 1-5% chicory extract and 5% inulin have shown significant effects in reducing lipid content, cholesterol levels, and bile secretions when compared to fiber-free diets. Target groups exhibited a high HDL/LDL ratio compared to the control group.

An 8-week study involving twenty-two young and healthy volunteers who consumed pasta enriched with 11% inulin was conducted to assess its impact on gastrointestinal motility, lipid metabolism, and glucose metabolism [14]. At the study's conclusion, significant differences were observed between the control and treated groups in terms of glucose and lipid levels (including HDL/LDL ratio, cholesterol, and triglycerides). The treated group displayed a noteworthy reduction in these parameters compared to the control group. Additionally, the study found a delay in gastric emptying and improved insulin sensitivity among individuals consuming an inulin-enriched diet.

# **Newly Identified Health Associated Microbes**

Metagenomics and multiomics technologies have brought about a transformative era in the study of the human gut microbiome, enabling the identification and characterization of several beneficial gut bacteria species. Among these, three species have garnered considerable attention: Faecalibacterium prausnitzii, Ruminococcus bromii, and Akkermansia muciniphila. These bacteria are commonly found in the gut of healthy individuals and are believed to play pivotal roles in maintaining gut health.

•*Faecalibacterium prausnitzii:* This bacterium is renowned for its anti-inflammatory properties and ranks among the most abundant species in the human gut [15]. It belongs to the Firmicutes phylum and has been linked to several health benefits, primarily due to its production of butyrate, a short-chain fatty acid known to support gut health.

•*Ruminococcus bromii:* Also, a member of the Firmicutes phylum, this bacterium specializes in breaking down complex dietary fibers, particularly starch. Its presence is crucial for the efficient utilization of dietary carbohydrates in the gut, thereby benefiting the host's digestive system.

•*Akkermansia muciniphila:* Belonging to the Verrucomicrobia phylum, this species is distinguished by its ability to degrade gut mucus lining the intestinal walls. A. muciniphila has been associated with improved gut barrier function and has shown promise in preventing metabolic disorders such as obesity and type 2 diabetes.

Additionally, Roseburia hominis and Roseburia intestinalis have been identified as species capable of utilizing mucin as an energy source, indicating that mucin degradation is more widespread than previously thought [16]. Christensenella minuta and Oscillospira spp. have been linked to a lean phenotype, suggesting their potential as targets in combating obesity [17]. It is important to note that the proportions of these beneficial species can vary among individuals and may be influenced by factors such as diet, age, and overall health. For instance, Faecalibacterium prausnitzii can constitute more than 5% of the total gut microbiota in some individuals, while at the species level, A. muciniphila has been observed to make up to 8% of the gut microbiota [18]. Short-chain fatty acids (SCFAs) are the result of the fermentation of dietary fibers and complex carbohydrates by gut bacteria.

#### These SCFAs offer a range of benefits, including:

• Lowering luminal pH: They help maintain a healthy acidity level in the gut.

• **Increasing calcium and magnesium absorption:** SCFAs support the body's ability to absorb these essential minerals.

• **Reducing pathogenic bacteria:** They contribute to the control of harmful bacteria in the gut.

• **Providing energy for colonocytes:** SCFAs serve as an energy source for the cells lining the colon.

• Modulating the immune system: They play a role in regulating the immune system's activity.

Butyrate, a specific SCFA produced by certain Firmicutes bacteria, such as those found in Clostridium clusters XIVa and IV, plays a crucial role in protecting against diseases like colon cancer and colitis. Furthermore, many gut bacteria engage in cross-feeding interactions. This means they utilize various substrates produced by other microbes to generate useful metabolites, enhancing the overall ecosystem of the gut microbiome.

#### **Inulin containing plants**

Inulin is naturally present in a variety of plants, primarily in their root or underground parts. Here are some common plants known to contain inulin

- Chicory Root: Chicory root stands out as one of the most abundant natural sources of inulin and is frequently used in commercial inulin production.
- Jerusalem Artichoke: Also referred to as sunchokes, Jerusalem artichokes boast a high concentration of inulin, primarily stored in their tuberous roots.

• **Dandelion Root:** Dandelion root, commonly used in herbal preparations, contains inulin and is recognized for its diverse health benefits. It's sometimes utilized as a coffee substitute.

• **Burdock Root:** Burdock root is another plant that contains inulin. It finds applications in traditional medicine and culinary dishes.

• Asparagus: Asparagus spears contain modest amounts of inulin, contributing to their dietary fiber content.

• Garlic: Garlic, celebrated for its unique flavor and health advantages, contains a small quantity of inulin, in addition to other valuable compounds.

• **Onion:** Onions, particularly their bulbous part, contain inulin alongside other types of dietary fiber.

## 2. Conclusion

Inulin offers promising technological and functional attributes that can be effectively harnessed in specific food applications, particularly in the realms of bakery and dairy products. Furthermore, dietary sources rich in inulin can be explored as beneficial ingredients to promote health, given their abundance in dietary fiber and their adaptability for crafting various therapeutic and functional food recipes. Additionally, inulin can serve as a valuable fat replacement component in the formulation of low-calorie foods, all while maintaining the health aspects important to consumers. This can contribute significantly to reducing the risks associated with conditions like hypercholesterolemia and hyperglycemia. In summary, the incorporation of inulin into food products holds immense potential for addressing various lifestyle-related disorders, making it an ideal ingredient for the development of customized, health-promoting foods.

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