Exploring the role of inulin as a nutraceutical for enhancing nutritional and health benefits - a review

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Abstract

This review explores the role of inulin, a natural prebiotic, delving into its transformative impact on the food industry, especially in creating functional products and assessing its impact on public health. Inulin, a versatile carbohydrate compound, not only acts as a fat replacer but also serves as a dietary fiber source, enhancing the overall nutritional value of the foods. Furthermore, inulin's fermentation by beneficial gut bacteria results in the production of short-chain fatty acids, contributing to colorectal cancer prevention and glycemic control, catering to the evolving preferences of health-conscious consumers.

Keywords: inulin, functional food, nutraceuticals, prebiotics

Introduction

Throughout history, developed civilizations have exhibited a significant level of fascination and concern regarding the quality and reliability of food sources. Historically, societies have long pondered the connection between nutrition and health. Even before the rise of nutritionism, philosophers like Hippocrates emphasized the importance of understanding the role of food in maintaining health and preventing diseases. He highlighted the significance of balancing nutrients to promote well-being (Adams, 1886). The human organism is composed of various substances that contribute to its unique chemical composition. Biologically active substances of natural origin play a pivotal role in maintaining normal physiological functions in plants, animals, and humans. These substances can also be utilized as external resources to achieve specific results in the organization of biological processes. As recognized more than 2000 years ago by Hippocrates, a fundamental connection exists between food and health. He emphasized that „... differences in diseases depend on the nutrients taken in..." (Andlauer and Fürst, 2002). Despite this understanding, the boundary between what constitutes food and what constitutes a potential cure remains a topic of ongoing research and discussion.

The term "nutraceuticals," introduced in 1989 by the Foundation for Innovation in Medicine, an organization dedicated to advancing medical discovery, outlines an ever-growing realm within biomedical research (Alissa and Ferns, 2012). Broadly defined, nutraceuticals encompass bioactive compounds inherent to food, granting significant health benefits, including disease prevention, treatment, and the maintenance of essential physiological processes vital for human well-being (DeFelice, 1992). Beyond their nutritional content, nutraceuticals manifest indisputable pharmacological effects. When the safety and suitable bioavailability upon ingestion are demonstrated, they can show significant effectiveness in preventing and treating specific pathological conditions. Nutraceuticals operate in the realm denoted as 'beyond diet, before therapy' (Santini, 2014). Integrating these agents into daily dietary practices not only forestalls disease progression but could potentially lead to postponing the necessity for pharmaceutical interventions. Nutraceuticals appeal to individuals seeking non-pharmacological alternatives for managing health conditions, aligning with the concept of proactive medicine (Santini et al., 2017).

Functional foods and nutraceuticals

In the latter half of the 20th century, accompanied by increased food accessibility, lifestyle shifts, and the emergence of new dietary practices, notably characterized by the overconsumption of specific nutrients detrimental to human health (such as foods rich in saturated and unsaturated-trans fatty acids, as well as added and refined sugars), a necessity arose to conceptualize "optimal nutrition." Optimal nutrition, the term highly popularized in the 1970s., focuses on a set of dietary guidelines advocating the modification, either reduction or augmentation, of specific foods or food components. Such modifications aim to enhance an individual's overall health and well-being (Ridgway et al., 2019; Jiménez-Colmenero et al., 2010). This concept signifies the ability to optimize particular physiological functions through nutrition, thereby improving health and mitigating the risk of disease development. It was within this framework that the concept of „functional food" emerged for the first time, gaining traction since the 1980s and serving as a pivotal catalyst for the development of innovative food products (Daliri and Lee, 2015). Functional food refers to food prepared using a scientific approach, wherein one or more nutraceuticals are incorporated, demonstrating established health benefits for a specific population (Kalra, 2003). Functional food, to gain acceptance, must adhere to the format of conventional food while incorporating added, substituted, or subtracted nutrients or other ingredients, facilitating consumption as part of the regular diet (Jiménez-Colmenero et al., 2001.; Siró et al., 2008). This evolution signifies a shift in the traditional conception of food, as functional food takes on the character of a "therapeutic ally," addressing diverse individual needs (Kalra, 2003.). While recommended intake guidelines exist for numerous substances today, adherence to these guidelines is limited among the general population. A significant challenge to adherence lies in the extended duration of consumption required to yield positive effects, as foods rich in nutraceuticals must be consumed daily over an extended period to achieve the desired outcomes (Jiménez-Colmenero et al., 2010). Consequently, it is more plausible for consumers to meet their nutritional requirements by consuming foods that naturally incorporate these biologically active substances, thereby expanding the variety of available options.

Effect of dietary fibers as nutraceuticals

Dietary fibers are non-digestible carbohydrates that provide structural support to plants. There are two primary categories: insoluble and soluble fiber, both of which are crucial for a balanced diet (Dhingra et al., 2012). Insoluble fibers, including lignin, hemicellulose, and cellulose, absorb water, enhancing fecal bulk, and facilitating efficient movement through the digestive tract. Rich sources encompass wheat, whole grains, seeds, berries, nuts, and various fruits and vegetables, which are excellent sources of insoluble fiber. Soluble fiber, on the other hand, undergoes breakdown during its journey through the digestive tract, forming a viscous gel that impedes cholesterol absorption and regulates blood sugar levels. Water-soluble fibers consist of compounds such as fructans (e.g., inulin), pectins, gums (e.g., agar), and mucilage (as could be found in psyllium). Some fruits and vegetables, legumes (such as lentils, beans, chickpeas, green beans, and peas), and grains like oats and barley provide substantial sources of soluble fiber. Notably, human digestive enzymes cannot metabolize dietary fiber, allowing it to reach the large intestine. Insoluble dietary fiber contributes no caloric value, while soluble dietary fiber contains some calories. Furthermore, high-fiber sources could play a pivotal role in contemporary meat processing technology for several reasons: certain fibers offer prebiotic and probiotic functions, have favorable nutritional attributes, and some of them have the potential to comply with regulatory guidelines regarding enrichment claims (Tiefenbacher, 2017).

Inulin: Functional Properties and Applications

Inulin belongs to the group of oligosaccharides within the so-called fructan compounds that contain 2-60 fructose molecules interconnected by a $\beta(2\rightarrow1)$ bond and a terminal glucose molecule that is connected to fructan units by an $\alpha(1\rightarrow2)$ glycosidic bond (Esmaeilnejad Moghadam et al., 2019). The functionality of inulin is related to its degree of polymerization, which is highly variable among inulins and depends on many factors, such as the plant species from which it is isolated (Chi et al., 2011). As a carbohydrate, inulin is present in many plant species, such as Jerusalem artichoke, dahlia, and chicory root, which represent the three main commercial sources of inulin production (Rubel et al., 2014), while in nature they can be found in a large number of other plants such as unripe wheat, rye and unripe barley, onions, garlic, leeks, bananas, asparagus (González-Herrera et al., 2015). Chicory is a plant that has been exploited on an industrial scale for extracting inulin-type fructans. Inulin is one of the surface-active oligosaccharides and has long been considered a functional food ingredient used in the food industry as a substitute for sugar or fat. Its adoption serves to enhance the nutritional profile of food products by reducing their caloric content (inulin typically possesses an energy content of 1.5 kcal/g), providing a source of dietary fiber, and offering prebiotic benefits. From a technological standpoint, inulin has proven to be an excellent gelling agent, viscosity modifier, and texturing agent in various foods (Tiefenbacher, 2017; Melilli et al., 2021). The effectiveness of inulin in fat replacement is closely linked to its capacity to form highly stable gels. However, the gel properties are highly dependent on temperature, concentration, and the degree of polymerization of the inulin compound (Yousefi et al., 2018). These molecules have the ability to create a robust interfacial film surrounding dispersed oil droplets, resembling networks of fat crystals in oil (McClements and Gumus, 2016). For instance, due to this similarity, inulin gels have been identified as an interesting ingredient in the preparation of new, functional meat products and contribute to flavor and creaminess similar to those containing animal fats (Yousefi et al., 2018). The advantage of using inulin is that, although proteins as emulsifiers have better emulsifying properties when used at low concentrations and create smaller oil droplets, these fructan-type molecules can generate emulsions that are stable to higher variations in environmental conditions such as pH, temperature (up to 80°C), and freezing (McClements and Gumus, 2016). The degree of polymerization is related to both the technological properties of inulin and the potential to cause positive health effects. Consumption of long-chain inulin, such as that isolated from the root of chicory (*Cichorium intibus*), offers a range of potential health benefits that will be discussed in detail later in this article.

Inulin and health clames

In the global market, particularly over the last two decades, it is estimated that nutraceuticals of natural origin, acting as bioactive compounds, and especially in the form of functional foods, have become integral components of the multi-billion dollar food industry (Awuchi and Okpala, 2022). The substantial economic expansion in this field has necessitated proper and legally defined nutritional labeling, along with assessments of health effects and recommendations regarding the consumption of functional foods containing nutraceuticals. Both the scientific community and regulatory authorities, including the European Food Safety Agency (EFSA), the American Food and Drug Administration (FDA), the World Health Organization (WHO), and individual national regulatory bodies, are actively engaged in addressing these issues. Inulin is a compound tested at high doses in animals with no reported toxic effects (Coussement, 1999). The US Food and Drug Administration (FDA) has categorized it as a substance "Generally Recognized as Safe" (GRAS).

Moreover, to date, only one prebiotic - inulin from chicory - has received an approved health claim from EFSA. The following wording reflects the scientific evidence: "Chicory inulin contributes to the maintenance of normal defecation by increasing stool frequency." To achieve the intended effect, a daily intake of 12 grams of "native chicory inulin" is recommended (EFSA, 2015). However, concerning its laxative properties, inulin is generally well-tolerated at single doses of 5 grams, with a total daily intake reaching up to 15-20 grams. It's worth noting that increasing flatulence may occur at higher doses (Yousefi et al., 2018).

Prebiotic Inulin: Impact on Gut Health

Increased awareness of the complex interactions between diet, the gut microflora of the gastrointestinal tract, and overall health have prompted the development of novel dietary approaches promoting the growth of specific beneficial bacterial groups (Boeckner et al., 2001). The definition of prebiotics varies across scientific and political spheres worldwide. However, it is generally accepted that almost all prebiotics can be classified as dietary fibers, but not all fibers are considered prebiotics. According to the latest description, a prebiotic is "a substrate selectively utilized by host microorganisms to foster a health benefit" (Carlson et al., 2017). To be categorized as a prebiotic, a food ingredient should display certain attributes, such as resistance to low stomach pH, resistance to hydrolysis by enzymes of the gastrointestinal tract (GIT), and resistance to absorption in the upper GIT. Additionally, it should possess the ability to be fermented by the intestinal microbiota, selectively stimulating the growth and metabolic activity of colonic bacteria, such as bifidobacteria and lactobacilli, while at the same time inhibiting the growth of pathogens. This selective stimulation should directly correlate with positive outcomes for the host's health (Carlson et al., 2017; Kolida, 2002)

Given that the colonic bacterial microflora constitutes approximately 95% of the total cells in the human body and plays a pivotal role in the host's nutrition, health, and disease, prebiotic fermentation should target desirable bacteria in the human population, such as indigenous *Bifidobacterium* and *Lactobacillus,* known for their positive impact on the immune system of the GIT, lower-intestinal motility, plasma glucose and lipid level control, mineral absorption, and various intestinal diseases (Kolida, 2002; Scheid et al., 2013). The ultimate goal of nutritional supplementation/fortification with inulin is to modulate the intestinal microbiota, thereby enhancing digestive tract health and the overall state of the human organism (Kolida, 2002) while also leading to reducing the number of harmful species such as *Escherichia coli* and *Clostridium spp* (González-Herrera et al., 2015). Due to the susceptibility of bifidobacteria to changes when exposed to oxygen and heat, their application as food probiotics is limited compared to lactobacilli (which could be found as part of commercially available probiotics). Consequently, there has been substantial interest in bifidogenic factors in food that can withstand regular processing methods and exhibit efficacy within the human body following ingestion. Caused by the lack of prebiotic-hydrolyzing enzymes in the upper GIT, just like other insoluble dietary fibers, inulin passes through the upper GIT practically intact, and enters the large intestine, where it undergoes fermentation catalyzed by probiotic bacteria. This fermentation process yields short-chain fatty acids (SCFA) and gases, including methane, CO_2, and H_2. The fatty acids produced by this process are mainly butyrate, acetate, and propionates, which lead to a decrease in the pH level of the colon and serve as metabolic energy sources for colonocytes (Scheid et al., 2013).

The impact of SCFA on gastrointestinal health is evident in the energy generated within the intestinal mucosa by colonocytes upon absorption Additionally, SCFA contributes to mitigating inflammatory processes by reducing or inhibiting the activity of pro-inflammatory nuclear factor (NF-kB), which inhibits the synthesis of pro-inflammatory cytokines such as interferon-γ (macrophage activator) and IL-2 (which promotes further production of Th1 and Th2 leukocytes and leads to exacerbation of immune response). The increased presence of propionate and acetate leads to increased secretion of anti-inflammatory cytokine IL-10, which downregulates the expression of Th1 cytokines and can block the expression of NF-kB (Roberfroid et al., 2010; Scheid et al., 2013; Pothuraju et al., 2021). Consequently, this secretion reduces the synthesis of IgE and promotes the induction of non-inflammatory immunoglobulins, specifically IgA (Esmaeilnejad Moghadam et al., 2019). Furthermore, the stimulation of mucin production by propionate and butyrate plays a role in preserving the mucosal layer, providing protection to the epithelium (Scheid et al., 2013). SCFA can induce an osmotic effect within the large intestine, playing a pivotal role in absorbing water from the intestinal lumen and enhancing intestinal peristaltic movement (Boeckner et al., 2001). This effect is highly beneficial for individuals struggling with constipation or obstipation issues, as well as patients with diabetes mellitus experiencing gastroparesis. However, it can pose challenges for consumers dealing with irritable bowel syndrome (IBS) (Tiefenbacher, 2017).

Role of inulin in colorectal carcinoma

Intestinal microbiota-derived metabolites, notably bile acids, hold a crucial role in human metabolism. Synthesized from cholesterol, bile acids are conjugated with glycine or taurine to form bile salts, stored in the gallbladder, which are then released into the duodenum during digestion, aiding in fat solubilization (Sayin et al., 2013). Bile salts exhibit potent antimicrobial efficacy by disrupting the cellular membrane structure and inducing DNA damage. Conjugated bile acids undergo reabsorption in the intestines through apical bile salt transporters, with a fraction (5-10%) remaining unabsorbed and subject to metabolism within the intestinal microbiota, particularly by "harmful" bacteria such as *E. Coli, Enterococcus faecalis,* and *Clostridia* strains. This metabolism results in the generation of secondary bile acids, which exhibit pronounced toxicity towards the proliferation and development of "beneficial" bifidobacteria and lactobacilli. The presence of secondary bile acids is associated with an elevated risk of cancer, specifically in the context of a high-fat diet (Pothuraju et al., 2021). In contrast, inulin exhibits a prophylactic effect against colorectal cancer by stimulating bifidobacteria activity (Esmaeilnejad Moghadam et al., 2019). Furthermore, inulin fermentation and subsequent short-chain fatty acid production constitute a significant anticancer mechanism. This process modifies colonic microbiota and reduces pH, preventing abnormal cell proliferation (Boeckner et al., 2001).

Effects of inulin on serum glucose in patients with type 2 diabetes

Inulin's resistance to human intestinal enzymes arises from its $\beta(2\rightarrow1)$ glycosidic bonds between fructose molecules. Its passage through the upper digestive tract provides a sense of fullness without adding calories, resulting in a low caloric value (1.5 kcal/g or 6.3 kJ/g). This value is associated with energy obtained from the absorption of short-chain fatty acids in the colon (Yousefi et al., 2018; Shoaib et al., 2016).Top of Form Also, since the hormone insulin is not required for the inulin metabolism, it does not affect the postprandial blood glucose level, so people with diabetes tolerate it well (Rao et al., 2019). Based on scientific evidence, even the EFSA recognized inulin as a potent ally in which consuming foods containing non-digestible carbohydrates induces a lower postprandial glycemic rise after meals (EFSA, 2014). Inulin can reduce lymphocytic infiltration in pancreatic islets of Langerhans and increase the proliferation rate of β-cells, thereby improving insulin sensitivity and pancreatic β-cell function. A review of clinical trials also suggests that inulin supplementation has beneficial effects on metabolic syndrome in individuals with type II diabetes mellitus (Rao et al., 2019).

Inulin and its effect on mineral metabolism

Inulin fermentation in the large intestine enhances mineral absorption, primarily through a pH drop due to short-chain fatty acid production. In the upper gastrointestinal tract, inulin interacts with calcium (Ca^{+2}). Upon reaching the large intestine, this complex releases Ca^{+2}, increasing its availability for absorption (Miremadi et al., 2016). Studies suggest that SCFA, particularly butyrate, positively impacts the large intestine's surface, increasing epithelial cell count per crypt. This effect boosts calcium, magnesium, and iron absorption, a known mechanism inhibiting osteoporosis with prebiotic intake (Scheid et al., 2013).

Conclusion

Recognizing the potential of nutraceutical composition variations offers the industry a route for creating specialized functional foods aligning with evolving consumer preferences. This article delves into the positive aspects of inulin as a nutraceutical. It shows the dynamic relationship between diet, functional foods, and human health, highlighting the evolving significance of nutraceuticals and functional ingredients. Dietary fibers, notably inulin, emerge as versatile contributors to digestive health, gut microbiota modulation, and various physiological functions. Inulin's diverse properties, encompassing prebiotic effects, and favorable technological and functional attributes suitable for incorporation into specific food applications position it as a valuable component in functional foods prospectives. Utilizing inulin as a fat replacer proves effective in formulating low-calorie foods, mitigating the risk of hypercholesterolemia and hyperglycemia without adverse effects on consumer health. The evidence suggests that incorporating inulin in novel foods holds promise in preventing colorectal cancer, managing blood glucose levels in type 2 diabetes, and positively impacting mineral absorption, emphasizing its potential as an exciting player in proactive and personalized nutrition.

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