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Role of functional foods versus proton pump inhibitors in the management of irritable bowel syndrome: A review

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Abstract

Functional foods represent a transformative advancement in nutrition science, bridging the gap between diet and health. Irritable bowel syndrome (IBS) is a prevalent functional gastrointestinal disorder characterized by chronic abdominal pain, bloating, and altered bowel habits, significantly impacting quality of life. Functional foods, defined as foods that provide health benefits beyond basic nutrition, have emerged as promising adjuncts in the management of IBS. The functional foods examined in this study include commonly used spices such as ajwain (*Trachyspermum ammi*), cumin (*Cuminum cyminum*), and fennel seeds (*Foeniculum vulgare*), which are widely utilized in Indian culinary practices. This review explores the role of functional foods including dietary fiber, and bioactive plant-based components such as ajwain (*Trachyspermum ammi*), cumin (*Cuminum cyminum*), and fennel (*Foeniculum vulgare*) in modulating gastrointestinal function vs PPIs and alleviating IBS symptoms. Evidence suggests that soluble fibre can improve stool consistency and bowel regularity, while, enhancing intestinal barrier function and reducing inflammation. Additionally, traditional spices exhibit carminative, antispasmodic, and anti-inflammatory properties that may help reduce bloating and abdominal discomfort. Proton Pump Inhibitors (PPIs) are antisecretory agents that are used widely to diminish acid secretion. The most common side effects of PPIs may include headache, constipation, diarrhea, nausea and vomiting. In addition, long-term use of PPIs found to be associated with some serious and rare adverse effects including kidney diseases (acute kidney injury, acute interstitial nephritis, chronic kidney disease, end stage renal disease), cardiovascular disease (myocardial infarction, stroke), liver disease (hepatocellular carcinoma), fractures, infections.

Keywords: Functional foods, PPIs, Irritable bowel syndrome

Introduction

Functional foods represent a transformative advancement in nutrition science, bridging the gap between diet and health often termed nutraceuticals or designer foods stems from their potential to promote well-being and prevent non-communicable diseases. The escalating prevalence of lifestyle-associated disorders, particularly gastrointestinal disturbances such as hyperacidity, gastroesophageal reflux, and dyspepsia, highlights the limitations of symptom-oriented therapeutic models and underscores the need for preventive, nutrition-cantered strategies. Functional foods, defined by their capacity to deliver physiological benefits beyond basic nutrition, represent a critical innovation in this transition.

Proton Pump Inhibitors are used widely to manage many gastric acid-related conditions such as gastroesophageal disease, gastritis, esophagitis, Barrett's esophagus, Zollinger-Ellison syndrome, peptic ulcer disease, nonsteroidal anti-inflammatory drug-associated ulcers, and *Helicobacter pylori* eradication, around the globe. (Maideen NMP 2023) ^[9].

Human Digestive system - From food ingestion to nutrient absorption

The human digestive system is a highly sophisticated anatomical and physiological complex that has evolved over millions of years to efficiently process food, powder form of spices, absorb nutrients, and defend against gastric cells. It comprises multiple organs including the oral cavity

with salivary glands, the esophagus, stomach (also referred to as gaster or ventriculus), pancreas, small intestine, large intestine, rectum, liver, and the gallbladder (Thies, 1992). The digestive process initiates in the oral cavity where mastication mechanically breaks down food into smaller particles. Masticatory performance decreases with age, the loss of teeth, and denture-wearing; however, it shows great individual variations. The perceived masticatory ability appears to be related to dental status, denture quality, general health and a variety of personal determinants such as physiologic, social, economic, and psychological factors. (Altenhoevel A *et al* 2011)^[1]. Concurrently, salivary glands secrete saliva which contains the enzyme amylase, beginning the enzymatic digestion of carbohydrates by cleaving polysaccharides into simpler sugars (Gossrau, 1981). The bolus, a cohesive mass formed by food mixed with saliva, is propelled posteriorly by the tongue into the pharynx and subsequently the esophagus. The esophagus features a flexible lumen and multiple histological layers including mucosa, submucosa, and muscularis externa, the latter comprising two outer muscle layers responsible for peristaltic propulsion irrespective of body orientation (Gossrau, 1981; Thies, 1992). Structurally, the stomach resembles the esophagus but is specialized with three distinct muscle layers: longitudinal (outer), circular (middle), and oblique (inner), supporting mechanical churning and mixing of ingested food (Thies, 1992). The gastric mucosa contains rugae—folds enabling expansion during distension. Gastric glands within the mucosa secrete mucus that protects the stomach lining from corrosive gastric acid (hydrochloric acid, HCl). Gastric acid secretion is stimulated by sensory cues such as sight and smell of food, chemical stimuli like spices, and mechanical stretching of the stomach wall, producing approximately 1-2 liters of gastric juice daily (Thies, 1992).

The esophagus and stomach are separated by the lower esophageal sphincter, a muscular valve that relaxes to permit passage of the bolus into the stomach and contracts to prevent acid reflux. Gastric juice contains hydrochloric acid, pepsin (activated from pepsinogen by acid), intrinsic factor, and gastric lipase (Thies, 1992). Hydrochloric acid performs multiple functions including microbial defense by destroying ingested pathogens and converting the zymogen pepsinogen into active pepsin, facilitating initial proteolysis. Intrinsic factor is essential for vitamin B12 absorption in the ileum and thus critical for erythropoiesis and nervous system maintenance. Gastric lipase catalyzes the hydrolysis of triglycerides into diglycerides and free fatty acids, though this lipolysis is relatively minor compared to pancreatic lipase action in the small intestine (Thies, 1992).

Gastric motility involves periodic contractions every 20 seconds, mixing the gastric contents into chyme, a semi-fluid mass that slowly empties into the duodenum controlled by the pyloric sphincter. This sphincter permits only small aliquots, preventing passage of large particles and ensuring optimal digestion (Thies, 1992). In the duodenum, chyme mixes with bile and pancreatic secretions through the ampulla of Vater. Bile, synthesized by hepatocytes and stored in the gallbladder, emulsifies lipids into micelles, enhancing lipase accessibility and fat digestion. Pancreatic juice is rich in enzymes including proteolytic enzymes (trypsinogen, chymotrypsinogen), amylase, and pancreatic lipase as well as bicarbonate ions which neutralize gastric acid, raising the pH to approximately 7-8, optimal for pancreatic enzyme activity (Gossrau, 1981; Thies, 1992). Enterokinase from the duodenal mucosa activates trypsinogen to trypsin, which catalyzes protein degradation and activates other

pancreatic zymogens. Alpha-amylase continues carbohydrate hydrolysis initiated in the mouth, producing maltose and isomaltose (Thies, 1992).

The small intestine is divided into three segments—duodenum, jejunum, and ileum each with distinct absorption profiles. The duodenum and jejunum possess circular folds (plicae circulares), villi, and microvilli, dramatically expanding the mucosal surface area to maximize nutrient absorption. Villi are approximately 1 mm in length and contain capillaries for nutrient uptake into the bloodstream, as well as lacteals for lipid transport via chylomicrons. The ileum lacks prominent circular folds but efficiently absorbs electrolytes (e.g., calcium), trace elements (e.g., zinc), vitamin B12 bound to intrinsic factor, and bile salts, which are recycled back to the liver via enterohepatic circulation (Karmakar *et al.*, 2020)^[7]. Nutrients like glucose may be absorbed passively or via carrier-mediated processes involving proteins such as transferrin for iron transport (Wang *et al.*, 2019). Motility in the small intestine features coordinated peristaltic waves propelling chyme distally and segmentation contractions that mix chyme, facilitating enzymatic digestion and contact with absorptive surfaces (Thies, 1992).

The large intestine, about one meter in length and wider than the small intestine, surrounds the latter and connects via Bauhin's valve (ileocecal valve), regulating passage of contents. It lacks villi but hosts a rich microbiota on the order of 10^{11} bacteria—that produce vitamins, ferment fibers into short-chain fatty acids for energy, and support immune defenses by inhibiting harmful microbes (Cotozzolo *et al.*, 2020)^[2]. Through peristalsis, chyme advances through the ascending, transverse, and descending colon, during which water and electrolytes are absorbed and mucus secreted to facilitate fecal passage. Residual indigestible material is stored in the rectum and expelled via the anus (Thies, 1992). Thus, the human digestive system exemplifies an integrated network, combining mechanical, chemical, enzymatic, immunological, and microbial elements to effectively process nutrients and protect the organism (Cotozzolo *et al.*, 2020; Karmakar *et al.*, 2020; Thies, 1992)^[2, 7, 1].

Diet is increasingly recognized as a central determinant of gastrointestinal and metabolic health. Within this framework, functional foods have emerged as a scientifically validated approach to restoring physiological balance. Originating from pioneering research in India, the concept integrates nutrition with therapeutic potential, positioning food as a primary tool for disease prevention (Martirosyan & Singh, 2015)^[8].

Materials and Methods

This review focuses on selected functional foods, particularly spices such as cumin, ajwain, and fennel, traditionally used in ethno medicine for their digestive benefits. Contemporary research has validated their pharmacological potential, demonstrating their ability to regulate gastric function, enhance enzymatic activity, and maintain gastrointestinal homeostasis. These spices, rich in bioactive compounds, represent a convergence of traditional knowledge and modern scientific evidence, offering a promising strategy for maintaining digestive health and supporting internal pH equilibrium (Rather *et al.*, 2016; Bairwa *et al.*, 2012)^[10, 18].

The present study evaluates the therapeutic efficacy of cumin (*Cuminum cyminum*), ajwain (*Trachyspermum ammi*), and fennel (*Foeniculum vulgare*) in modulating gastric acidity and maintaining gastrointestinal pH balance. A systematic review of scientific literature reveals that bioactive compounds such as thymol, anethole, flavonoids, and terpenoids play a pivotal role

in enhancing digestive enzyme activity, regulating gastric secretions, and reducing inflammation. These functional spices contribute indirectly to acid–base homeostasis by optimizing digestion and preventing acid accumulation. The findings support the integration of these spices into daily dietary practices as a sustainable, low-risk, and effective approach to preventive healthcare and holistic well-being (Hasler, 2002; Capanoglu, 2024; Srinivasan, 2018) ^[3, 13, 11].

Enzymes involved in Gastric Acid Secretion

Gastric acid secretion is chiefly stimulated and regulated by parietal cells in the stomach lining, which secrete hydrochloric acid (HCl). While HCl itself is not an enzyme, it creates the acidic environment necessary for the activation of digestive enzymes. One critically important enzyme related to gastric acid secretion is pepsinogen, which is secreted by chief cells in the gastric glands. Pepsinogen is an inactive zymogen that is converted into its active form, pepsin, upon exposure to the acidic pH generated by hydrochloric acid. Pepsin then functions to hydrolyze dietary proteins into peptides, thereby initiating protein digestion within the stomach. Additionally, gastric glands produce gastric lipase, a lipolytic enzyme active in the acidic environment for the partial digestion of lipids by hydrolyzing triglycerides into free fatty acids and diglycerides. Moreover, the intrinsic factor, a glycoprotein produced by the same parietal cells, is essential for the subsequent absorption of vitamin B12 in the ileum but does not directly participate in hydrolytic digestion (Thies, 1992).

Modern healthcare systems predominantly emphasize disease management rather than prevention, leading to an increasing reliance on pharmacological interventions for gastrointestinal disorders. Although such treatments provide rapid symptomatic relief, they often fail to address the underlying etiological factors, particularly those associated with dietary habits and metabolic dysfunction (Henry, 2010; Granato *et al.*, 2020) ^[4, 6]. This has contributed significantly to the global rise in non-communicable diseases, including digestive disorders. Proton pump inhibitors (PPIs) play a significant role in modern healthcare due to their effectiveness in managing acid-related gastrointestinal disorders.

Proton Pump Inhibitors

Proton pump inhibitors (PPIs) are a class of pharmacological agents that suppress gastric acid secretion by inhibiting the H⁺/K⁺-ATPase enzyme system in gastric parietal cells. Gastric acid plays a crucial physiological role in digestion by facilitating the breakdown of food and contributing to the elimination of ingested pathogens. However, excessive gastric acid production or its abnormal reflux into the esophagus can lead to pathological conditions. Proton Pump Inhibitors are used widely to manage many gastric acid-related conditions such as gastroesophageal disease, gastritis, esophagitis, Barrett's esophagus, Zollinger-Ellison syndrome, peptic ulcer disease, nonsteroidal anti-inflammatory drug-associated ulcers, and *Helicobacter pylori* eradication, around the globe. Proton Pump Inhibitors (PPIs) are antisecretory agents that are used widely to diminish acid secretion. PPIs are prescribed commonly to manage gastric acid-related conditions such as gastroesophageal reflux disease (GERD), gastritis, esophagitis, Barrett esophagus, Zollinger-Ellison syndrome, peptic ulcer disease, nonsteroidal anti-inflammatory drug-associated ulcers, and *Helicobacter pylori* (*H. pylori*) eradication, around the globe ^[1]. Current PPIs may include omeprazole, esomeprazole, lansoprazole, dexlansoprazole, pantoprazole and rabeprazole

^[2]. PPIs diminish acid secretion by binding covalently to sulfhydryl groups of cysteines of proton pump in parietal cells of stomach, thereby inactivating H⁺/K⁺-ATPase (Proton pump). The adverse effects associated with the long-term use of proton pump inhibitors including renal disorders (acute interstitial nephritis, acute kidney injury, chronic kidney disease, and end-stage renal disease), cardiovascular risks (major adverse cardiovascular events, myocardial infarction, stent thrombosis, and stroke), fractures, infections (*Clostridium difficile* infection, community-acquired pneumonia, and Coronavirus disease 2019),

Results and Discussion

Pancreatic Enzymes and Active Compounds in Digestion:

Following gastric digestion, chyme enters the duodenum where pancreas-secreted enzymes continue nutrient breakdown. A key pancreatic enzyme is pancreatic alpha-amylase, which hydrolyzes complex carbohydrates such as starch into smaller disaccharides such as maltose and isomaltose, effectively continuing carbohydrate digestion initiated by salivary amylase. This digestion is further complemented by brush border enzymes expressed in the small intestinal epithelium, such as maltase and glucoamylase, which cleave maltose and other oligosaccharides into absorbable glucose units.

Furthermore, pancreatic secretions contain a spectrum of proteolytic enzymes that require activation in the alkaline environment created by sodium bicarbonate-rich pancreatic juice. For example, trypsinogen is converted to active trypsin by enterokinase located in the duodenal mucosa. Trypsin then activates other proenzymes to facilitate complete protein digestion. Pancreatic lipase, assisted by bile salts produced by the liver and stored in the gallbladder, catalyzes the efficient hydrolysis of triglycerides into free fatty acids and monoglycerides, products readily absorbed by the intestinal mucosa (Thies, 1992). Gastric acid secretion is essential for activation of pepsinogen to pepsin and optimal function of gastric lipase, while pancreatic alpha-amylase, maltase, glucoamylase, proteases like trypsin, and pancreatic lipase collectively enable comprehensive digestion of carbohydrates, proteins, and lipids along the gastrointestinal tract (Thies, 1992; Wang *et al.*, 2019). The development of processing technologies for functional foods like cumin, ajwain, and fennel seed powders aims to enhance their nutritional and therapeutic potential, particularly their effects on the digestive system. These seeds contain a plethora of bioactive compounds and phytochemicals that, when properly processed and delivered, can modulate digestion through enzyme interactions, antioxidant activity, antimicrobial properties, and stimulation of digestive secretions.

Impact of Processing Technologies on Bioactive Delivery

Processing approaches such as milling, drying (freeze-drying, air-drying), and encapsulation (nano- and micro-encapsulation) significantly enhance the stability, bioavailability, and controlled release of these bioactives in the gastrointestinal tract. For example, advanced encapsulation technologies protect sensitive compounds from degradation during digestion, enable targeted delivery, and improve absorption of phytochemicals that promote digestive enzyme activity and gut health. Cumin and ajwain compounds stimulate gastric secretions, promoting hydrochloric acid and pepsin release, facilitating protein digestion in the stomach. Certain phytochemicals, such as thymol from ajwain and cuminaldehyde from cumin, may enhance pancreatic enzyme secretion, including pancreatic amylase, lipase, and proteases, improving carbohydrate, fat, and

protein digestion in the small intestine (Liebow & Franklin, 1982).

Fennel seed extracts have shown inhibitory effects on pancreatic lipase and carbohydrate hydrolases, suggesting a modulatory role on nutrient absorption and metabolism, which is beneficial in managing digestive efficiency and metabolic disorders (Nartea *et al.*, 2023). These enzymatic activities complement endogenous digestive enzymes such as pancreatic alpha-amylase, which continues polysaccharide breakdown producing maltose and isomaltose, and intestinal brush-border enzymes like maltase and glucoamylase, which convert disaccharides into absorbable monosaccharides, completing carbohydrate digestion.

Active Compounds in Cumin, Ajwain, and Fennel Seeds

Cumin (*Cuminum cyminum*) seeds are rich in essential oils (3–4%), particularly cuminaldehyde (~45–50%), along with proteins, phenolics, and flavonoids. These bioactive compounds possess antioxidant, antiallergic, anti-platelet aggregation, and hypoglycemic properties. The seeds also contain fibers and other phytochemicals like steroids, saponins, tannins, and alkaloids, which contribute to their nutritional and medicinal benefits.

Ajwain (*Trachyspermum ammi*), closely related to cumin, contains thymol-rich essential oils that exert antimicrobial and carminative effects, aiding in digestion by increasing the secretion of gastric enzymes and bile. Likewise, fennel seeds are known for their volatile oils, notably trans-anethole, and contain phenolics and flavonoids with antioxidant activity, which have been shown to support digestive health through antispasmodic and carminative actions.

Enzymatic and Physiological Effects on Digestion

The active constituents in these spice powders stimulate digestive enzymes and secretions enhancing macronutrient breakdown.

Examples of Functional Benefits

Incorporation of powdered cumin and fennel seeds into food products or probiotic yogurts has been found to increase antioxidant capacity and modulate gut microbiota beneficially, which indirectly supports digestive health and nutrient absorption.

Bioactive Composition and Functional Properties

The analysis confirms that cumin, ajwain, and fennel seeds are rich in pharmacologically active constituents, including essential oils, phenolic compounds, and flavonoids. Ajwain contains thymol, a potent antimicrobial and carminative agent, while cumin is characterized by cuminaldehyde and terpenoids that stimulate digestive enzyme secretion. Fennel contains anethole, known for its anti-spasmodic and gastroprotective properties (Srinivasan, 2018; Rather *et al.*, 2016) ^[17, 16].

These compounds collectively enhance digestive efficiency, reduce gastric discomfort, and stabilize gastrointestinal processes, thereby contributing to improved metabolic health (Bairwa *et al.*, 2012) ^[18].

Implications for Gastrointestinal and Chronic Health

Regular dietary incorporation of cumin, ajwain, and fennel is associated with improved gastrointestinal function, reduced incidence of acidity, and enhanced metabolic stability. Unlike conventional antacids, which provide transient relief, these functional foods address underlying digestive dysfunctions, making them more effective for long-term health management

(Swanson *et al.*, 2020) ^[12]. Furthermore, their antioxidant and anti-inflammatory properties contribute to broader health benefits, including reduced risk of chronic diseases.

Preventive Healthcare Paradigm

The findings reinforce the importance of shifting from a curative to a preventive healthcare model. Functional foods, particularly those rooted in traditional dietary systems, offer a sustainable and accessible approach to health maintenance. However, challenges such as limited awareness, regulatory inconsistencies, and the need for clinical standardization must be addressed to ensure their widespread adoption (Hasler, 2002) ^[3].

Proton Pump Inhibitor

The most common side effects of PPIs may include headache, constipation, diarrhea, nausea and vomiting. ⁴ In addition, long-term use of PPIs found to be associated with some serious and rare adverse effects including kidney diseases (acute kidney injury, acute interstitial nephritis, chronic kidney disease, end stage renal disease), cardiovascular disease (myocardial infarction, stroke), liver disease (hepatocellular carcinoma), fractures, infections (*Clostridioides difficile* infection, Community-acquired pneumonia, COVID-19), micronutrient deficiencies (hypomagnesemia, anemia, vitamin B12 deficiency, hypocalcemia), dementia, and gastric cancer (Maideen NMP 2023) ^[9].

The adverse effects associated with the long-term use of proton pump inhibitors including renal disorders (acute interstitial nephritis, acute kidney injury, chronic kidney disease, and end-stage renal disease), cardiovascular risks (major adverse cardiovascular events, myocardial infarction, stent thrombosis, and stroke), fractures, infections (*Clostridium difficile* infection, community-acquired pneumonia, and Coronavirus disease 2019), micronutrient deficiencies (hypomagnesemia, anemia, vitamin B12 deficiency, hypocalcemia, hypokalemia), hypergastrinemia, cancers (gastric cancer, pancreatic cancer, colorectal cancer, hepatic cancer), hepatic encephalopathy, and dementia. Clinicians including prescribers and pharmacists should be aware of the adverse effects of taking proton pump inhibitors for an extended period of time.

Vitamin B12 malabsorption can occur from hypochlorhydria induced by the use of gastric acid inhibitors, specifically proton pump inhibitors (PPIs) and histamine-2 receptor antagonists (H2RAs). Basically, these drugs alter the release of vitamin B12 from its food-protein carriers, which prevents its liaison to the intrinsic factor (IF). Accordingly, observational studies have reported an increased risk for vitamin B12 deficiency among long-term users of gastric acid inhibitors (N Presse *et al* 2015) ^[19].

Conclusion

The synergy of bioactive compounds in cumin, ajwain, and fennel seeds actively supports digestion through stimulation of gastric and pancreatic enzymes, antioxidant protection, and modulation of gut microbiota. Sophisticated processing and encapsulation technologies optimize the extraction stability and delivery of these compounds, facilitating their functional roles in the digestive system and enhancing the development of effective functional foods.

Cumin, ajwain, and fennel seeds represent potent functional foods with significant potential in regulating gastric acidity and supporting gastrointestinal balance. Through their diverse bioactive compounds and multifaceted mechanisms of action, these spices enhance digestion, reduce acid-related disorders,

and contribute to overall physiological stability. Their integration into daily dietary practices offers a sustainable, cost-effective, and holistic approach to preventive healthcare. As global health systems increasingly recognize the importance of nutrition-based interventions, these traditional functional foods stand at the forefront of a transformative shift toward true healing and well-being.

While proton pump inhibitors (PPIs) are highly effective pharmacological agents for suppressing gastric acid secretion in conditions such as gastroesophageal reflux disease and peptic ulcer disease, long-term use has been associated with potential adverse effects, including impaired absorption of micronutrients such as vitamin B12 due to reduced gastric acidity required for its release from dietary proteins. Therefore, clinical guidelines recommend periodic evaluation and monitoring during prolonged PPI therapy to prevent nutritional deficiencies.

In contrast, traditional dietary adjuncts such as ajwain (*Trachyspermum ammi*), cumin (*Cuminum cyminum*), and fennel (*Foeniculum vulgare*) seeds, commonly used in powdered form, have been reported in ethnopharmacological and experimental studies to possess carminative, antispasmodic, and gastroprotective properties. These bioactive compounds (e.g., thymol, cuminaldehyde, and anethole) may help regulate gastrointestinal motility, reduce bloating, and provide symptomatic relief in functional dyspepsia and mild acidity-related disorders.

In modern healthcare practice, an integrated and evidence-based approach is considered optimal. This includes the rational use of PPIs for acid-related disorders, regular monitoring of long-term nutritional status, and the complementary use of dietary interventions such as ajwain, cumin, and fennel seeds to support gastrointestinal health and alleviate mild dyspeptic symptoms. While these spices are beneficial as supportive therapies for regulating gastric discomfort and acidity, their role should be considered adjunctive rather than a substitute for pharmacological treatment or as agents influencing micronutrient absorption.

Vitamin B12 deficiency

A positive association between Vitamin B12 deficiency and PPI use has been found in numerous cross sectional and cohort studies. For vitamin B12 insufficiency linked to PPIs, various mechanisms have been put forth. PPIs lessen the production of stomach acid, which is necessary for pepsinogen to turn into pepsin, which releases vitamin B12 from dietary proteins. Pepsinogen is converted into pepsin by the action of pepsinogen. Vitamin B12 absorption is ultimately decreased as pepsin production declines. (Maideen NMP 2023) ^[9].

Long-term use of PPIs may enhance the incidence of cancers including gastric cancer, pancreatic cancer, colorectal cancer and hepatic cancer (Maideen NMP 2023) ^[9].

The present study highlights the nutritional and phytochemical richness of ajwain, cumin and fennel seed powder, affirming their potential role as functional foods. Nutritional profiling revealed that all three spice seeds are valuable sources of macronutrients such as carbohydrates, proteins, fats, and dietary fiber, as well as micronutrients including calcium, iron, and vitamin C, which are essential for various physiological functions.

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