Food-Derived Protease Inhibitors

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Plant protease inhibitors (PI) are usually small water-soluble proteins having many roles in the host biology, and they appear widely in the plant kingdom. Among many other functions in plant physiology, PIs are components of plants' defensive systems. PIs protect plants against pathogens and also against herbivores; thus, several classes of PIs inhibiting mammal and insect digestive enzymes are often expressed in many plant tissues. PIs are present in many common food and feed plants. Many plant-derived PIs, such as Bowman-Birk inhibitors and Kunitz-type inhibitors, have been suggested to negatively affect dietary protein digestion by blocking the activity of trypsin and chymotrypsin in the human gastrointestinal system. In addition, some PIs may possess proinflammatory activities. However, there is also scientific evidence on some beneficial effects of PIs, for example, gut-related anti-inflammatory and chemopreventive activities in vitro and in vivo.

protease inhibitors | Bowman-Birk inhibitors | Kunitz-type inhibitors | α-amylase/trypsin inhibitors | trypsin | chymotrypsin | irritable bowel syndrome | inflammation | colorectal cancer

1. Introduction

Plant protease inhibitors (PI) protect plants against pathogens and also against herbivores; thus, several classes of PIs inhibiting mammal and insect digestive enzymes are often expressed in many plant tissues.[1][2] PIs are classified into families, clans, and subgroups based on their evolutionary backgrounds, protein structures, and catalytic sites. PIs in separate families may share their target proteases, while PIs within one family may inhibit many different proteases. The main PI families present in cereals and/or legumes (two most important plant protein sources in human diets) are the serpin superfamily, Bowman-Birk inhibitor (BBI) family, Kunitz-type inhibitor (KTI) family, potato type 1 inhibitor (PI1) family, and ∝-Amylase/trypsin (ATI) family. PIs naturally present in legume and cereal grains may affect the nutritional value of foods by inhibiting the action of digestive enzymes on proteins.[3][4] Serpins, BBIs, KTIs, SCIs, and ATIs inhibit trypsin and/or chymotrypsin, two serine proteases that are formed in the small intestine from their pancreatic proenzymes.[5] PIs are known to inhibit digestive enzymes mainly by competitive binding.[3][6][7] This means that they block the active site of proteases by binding to their critical portions, thus preventing the true substrates from binding.[6]

In addition to inhibiting human proteases, PIs have been found to upregulate the secretion of cholecystokinin and, consequently, to upregulate the secretion of trypsin and chymotrypsin.[6] It has been suggested that oversecretion of digestive enzymes potentially leads to inflammation.[10] Legume-derived PIs have been found to cause extensive

secretion of digestive enzymes, as well as hypertrophy and hyperplasia of the pancreas in rodents.[8][9] ATIs of wheat, for example, may cause inflammatory responses in sensitive individuals.[11]

2. Protease Inhibitors Used as Therapy in GI Diseases

Interestingly, protease inhibitors have also been successfully used as therapy in several GI diseases when administered orally, for example, in ulcerative colitis[10][12]; in addition, they may possess some anticarcinogenic properties[13]. Efficient digestive processes, as well as mucosal protection, are regulated by balancing the proteolytic activities in the lumen and the PI activities on the mucosal surfaces.[10] Even the proteases pepsin, trypsin, and chymotrypsin (enzymes participating in gastric and intestinal food digestion) can damage the lining of the GI tract, in case of the failure of natural protective mechanisms, and contribute to GI inflammation.[14] Controlling the activity of digestive enzymes by PIs may thus help to mitigate the inflammatory state. Colorectal cancer is one of the most common cancers in the Western countries, and many research efforts are now investigating the chemopreventive effects of food-derived PIs against this condition.[15][16] Especially BBIs from legumes have gained positive attention due to their good stability during food processing and digestion and due to their promising activities as lunasin-protecting agents.[17][18][15] Inhibition of the digestive enzymes leads to accumulation of undigested protein in the small intestine and to slower gastric emptying.[6] This way, PIs may help to regulate hunger and food intake and, thus, to tackle obesity.[6]

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