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Table of Contents

- 03** Proteases – Powerful Multifunctional Enzymes
 - 04** Plant-Based Enzymes for Comprehensive Digestive Support
 - 05** The Link Between FGIDs and Enzyme Deficiency
 - 06** Are Phyto-Proteases Nature’s Alternative to NSAIDs?
 - 07** Beyond Protein Catabolism
 - 08** Enzyme Potency Determines Dose
 - 09** Inflammacidin™ - A Comprehensive Phyto-Protease Formula
 - 10** Inflammacidin™ Premier Ingredient Profiles
- 



Proteases – Powerful Multifunctional Enzymes

Proteases are a group of enzymes that **hydrolyze and break apart complex proteins** into smaller peptides and amino acids. These enzymes are also referred to as proteases or proteolytic enzymes. Proteolytic enzymes are involved in numerous biological processes in all living organisms. In humans, proteases are important for digestion as they can breakdown the protein in foods to **liberate amino acids** needed by the body **for energy** and to **build muscle**. Without enzymes, proteins are too complex for the body to break apart. It is no surprise that the malabsorption of proteins can cause gas, stomach pain or cramping as well as bloating and nausea.

Recent statistics indicate that nearly 20% of the global population are affected by functional gastrointestinal disorders (FGIDs), particularly women and elderly individuals. FGIDs include upper GI disorders such as gastric reflux, stomachache/dyspepsia, delayed gastric emptying, nausea, and vomiting, as well as lower GI disorders such as irritable bowel syndrome (IBS), and inflammatory bowel disease (IBD), which often includes constipation, indigestion, bloating, and diarrhea.

Plant-Based Enzymes

for Comprehensive Digestive Support

Increased intestinal permeability, also known as "leaky gut," has been associated with various health conditions, including **inflammatory bowel disease** (IBD), irritable bowel syndrome (IBS), and autoimmune disorders. Plant-based proteolytic enzymes, or **phyto-proteases**, help to alleviate mild gastrointestinal discomfort and **support optimal absorption of dietary proteins**. Phyto-proteases are classified based on the type of amino acid they act upon to break apart these complex proteins.

Cysteine proteases, such as **bromelain, papain, and actinidin** not only improve protein digestion and assimilation, but they also deliver **inflammation-modulating effects** to the gastrointestinal tract initially, then systemically, post-digestion. Some clinical evidence indicates that using a combination of **plant-based enzymes**, including papain and bromelain, was found to improve symptoms and modulate **inflammatory response** in patients suffering from FGIDs of the lower gastrointestinal tract.

Additionally, these **phyto-proteases** may also **improve gut dysbiosis**, an imbalance of gut microflora often due to enteropathogens or antibiotic use. Gut dysbiosis, coupled with inflammation, is a common cause of leaky gut syndrome and is also linked to SIBO (small intestine bacterial overgrowth), and SIFO (small intestine fungal overgrowth). Evidence supports that phyto-proteases may be **helpful for preventing diarrhea** caused by common enteropathogens associated with food-borne and water-borne illnesses.





The Link Between FGIDs and Enzyme Deficiency

Functional gastrointestinal disorders (FGIDs), as irritable bowel syndrome (IBS) and functional dyspepsia (FD). Clinical studies on individuals with FD or IBS reveal that these conditions correlate to low levels of pancreatic enzymes when compared to healthy individuals. While the exact relationship between pancreatic enzyme deficiency and FGIDs is not yet fully understood, it's possible that impaired digestion and absorption of nutrients may play a role in the development of symptoms in some patients with these conditions.

Pancreatic enzymes require supplementation when the pancreas is unable to produce adequate enzymes for proper digestion of nutrients, especially proteins and fats. When deficient, physicians typically prescribe antacids along with pancreatic lipase enzymes, to stabilize their susceptibility to become inactivated when pH becomes too acidic. However, this creates other digestive issues such as reducing HCl production in the stomach. The concomitant use of pancreatic enzymes and plant-based proteolytic enzymes, like bromelain and papain, is considered safe and can be used in lieu of antacids to stabilize their resilience to breaking down too quickly. Additionally, clinical evidence suggests that bromelain/proteolytic enzymes may be able to support protein absorption in elderly individuals who inherently have lower HCl production and weaker digestive systems.

Given both the incidence of protein malabsorption and the importance of amino acids to maintain and repair muscle, produce hormones, enzymes and maintain energy, there is an immediate need for safe, effective, food-based interventions for not only enzyme deficient conditions like FGIDs, but also those that suffer from conditions that illicit a prolonged or excessive immune response to inflammatory illnesses.



Are Phyto-Proteases Nature's Alternative to NSAIDs?

A prolonged or excessive immune response resulting in an abundance of pro-inflammatory compounds in the body is the precursor to a cascade of potential health problems. Research suggests that **bromelain**, and other **proteolytic enzymes** like **papain** and **actinidin**, **downregulates** the body's **pro-inflammatory immune response** and appear to be a promising alternative to common over the counter (OTC) counterparts without adverse side effects. In fact, individuals who frequently use NSAIDs (such as aspirin, ibuprofen, and naproxen) to alleviate common aches and pains are at greater risk of stomach irritation and ulcers, gastrointestinal bleeding, increased potential for bruising, kidney damage, as well as hypertension, heart attack, and stroke.

A review of clinical studies reported that **bromelain** may be effective in **relieving minor muscle pain, strain, or swelling** associated with degenerative joint conditions, sports injuries as well as postoperative. Like **bromelain**, **papain** and **actinidin** are **cysteine proteases**. Ongoing research on the therapeutic properties of papain and actinidin is **revealing similar inflammation potential**.

Enzyme supplementation is indicated for treating several **digestive conditions**. However, the mechanisms of enzyme therapy sharply contrast with those of anti-inflammatory drugs because the **natural healing process** of a **healthy inflammatory response** is not blocked, preventing the regenerative and remodeling phases of the inflammation cascade. When taken orally, **phyto-protease enzymes** have **systemic effects**, modulating immune function and engulfing autoantibodies that the immune system makes in degenerative joint conditions that have an autoimmune component which may help **support joint comfort**, and **improve quality of life**. To a large degree, enzymes can be seen as adaptogenic, seeking to restore a steady state to the body.

Beyond Protein Catabolism

Proteases act as sharp scissors, catalyzing highly specific reactions of proteolytic processing. **Cysteine proteases**, such as **bromelain**, **papain**, and **actinidin** not only improve protein digestion and assimilation, but they also **deliver inflammation-modulating effects** throughout the body. Phyto-proteases can **modulate** protein-to-protein interactions, **create new bioactive molecules**, as well as improve biophotonics, or the **processing of cell information and communication**.

Clinical uses for proteases have expanded beyond their protein-digesting capacity to provide the body with systemic benefits. The phyto-proteases contained in Inflammacin™ possess properties that assist with **regulating an overactive, pro-inflammatory immune response**, and **improve blood circulation**. As a result, proteases promote the breakdown of toxic metabolites that result from oxidative stress, thereby contributing substantially to the **detoxification of the body**.

This is a game changer for those dealing with persistent physical discomfort that results from an over-production of pro-inflammatory compounds! However, to utilize proteolytic enzymes for reducing physical discomfort, they **must be taken in between meals** to help 'eat up' and clear out inflammatory metabolites which are at the root cause of perpetuating physical discomfort. Same goes for acute allergic sinusitis. Studies indicate that phyto-proteases are **great mucolytics** and may **improve common allergic symptoms** including congestion, and sinus headaches.

Additionally, phyto-proteases can **activate or stimulate natural killer cells** and macrophages which play essential roles in the body's immunological defense and may also offer cardiovascular support via their **fibrinolytic activity** which inhibits platelet aggregation, improves blood flow, and supports microcirculation. With improved blood fluidity, pro-inflammatory metabolites can be eliminated more quickly, oxygenation is enhanced, and tissue tension decreases which helps reduce swelling.



Enzyme Activity Determines Appropriate Dose

As with any enzyme formulation, potency is the key factor in determining dosage. Enzyme potency is measured by enzymatic activity which is the most important measurement for enzymes. This activity is dependent on concentration, pH, temperature, and the substrate. The higher the activity, the faster the food is digested. When taken orally, most of the phyto-proteases are absorbed intact and thereafter can circulate their beneficial effects all over the body, post-digestion.

Calculating enzyme potency is quite complex and depends on the method being used that is generally determined by the type of enzyme. Enzyme units include Milk Clot Units (MCU), Casein Digestion Units (CDU), Gelatin Digesting Unit (GDU), USP units (USP), Food Chemical Code (FCC) Papain units (PU), and more.

Most research on bromelain discusses its potency in Gelatin Digesting Units (GDU), so it is helpful to have a sense of the conversion of GDUs to PUs. GDU can be converted into FCC PU by the following: 1 GDU = 15,000 FCC PU. For example, a bromelain sample that measures 2,000 GDU/g would be about equal to 30,000,000 FCC PU/g potency. For a mixture of phyto-proteases, such as papain, bromelain, and actinidin, PU is the required enzyme unit of measurement per the FCC PU methodology that helps determine the Total Protease Activity or total potency for all plant-derived enzyme blends.





Inflammacin™ - A Comprehensive Phyto- Protease Formula

Inflammacin™ offers comprehensive digestive support from the most extensively researched plant-derived enzymes; bromelain, papain and actinidin. Delivering 15 million PU's per dose, these phyto-protease enzymes work synergistically to support overall gastrointestinal health by improving protein digestion, enhancing nutrient absorption, and alleviating mild gastrointestinal stress associated with FGIDs.

It also features Inflammation-Support Blend which contains peppermint leaf (*Mentha x piperita*), fennel seed (*Foeniculum vulgare*), and ginger rhizome (*Zingiber officinale*), which are classic carminative herbs with a long history of use in Chinese and Ayurvedic medicine in managing digestive disorders.

Bioactive compounds in these aromatic herbs, specifically the volatile or essential oils they possess, soothe, and disinfect the digestive tract with their ability to inhibit microbes, protect from oxidative damage, and modulate inflammatory response.

Inflammacin™

Premier Ingredient Profiles

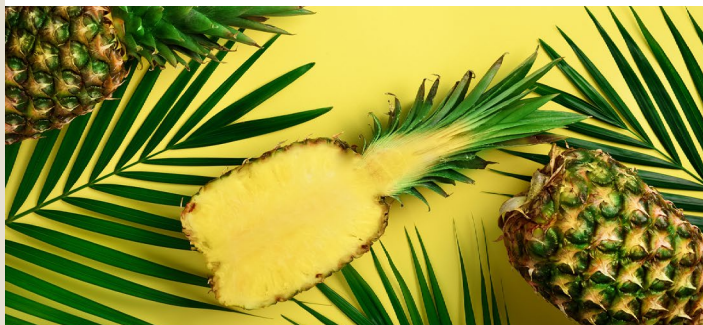
Bromelain from Pineapple

Native to Central and South America, the **pineapple (*Ananas cosmosus*)** plant has been utilized as both a food and medicine for centuries to balance digestive health. **The fruit is often used for nausea, morning sickness, and to stimulate appetite.** However, the pineapple stem contains concentrated amounts of the most extensively studied plant-derived, **proteolytic enzymes known as bromelain.** Bromelain is a mixture of protein-digesting enzymes, glycoproteins, carbohydrates and contains peroxidase, acid phosphatase and several protease inhibitors. When consumed with meals, bromelain's unique group of protease enzymes can support the digestion of protein in the stomach, including animal-derived proteins.

First introduced therapeutically in 1957, **bromelain** has been extensively studied for its extensive therapeutic properties which include **digestive support, inflammation-modulation, cardiovascular support, improving physical discomfort** due to chronic or acute injury. Bromelain's inflammation-modulating properties have received the most attention given the chronic overuse of over-the-counter NSAIDs (non-steroidal anti-inflammatory drugs) and their inherent adverse effects on the liver and digestive system. The clinical use of bromelain for promoting a healthy inflammatory response to normal wear and tear of the body spans three decades and has an excellent safety record. Not only have **clinical trials confirmed bromelain's efficacy** as a safer alternative to pain relieving over-the-counter medications, but bromelain has also been **used successfully** for its **analgesic** and **inflammation-modulating** properties to improve a variety of allergic, acute/traumatic, postsurgical, and chronic inflammatory conditions.

Bromelain promotes a healthy inflammatory response by reducing levels of pro-inflammatory, cyclooxygenase (COX)-mediated compounds, prostaglandin E2 (PGE2), and thromboxane A2 levels. Bromelain also modulates immune response by regulating specific immune cell surface adhesion molecules which are associated with acute injury. **Research confirms** that **bromelain** has **cardioprotective effects** including reducing blood viscosity and improving blood flow. It achieves this goal by increasing fibrinolytic activity and decreasing levels bradykinin and fibrinogen which also **helps regulate blood pressure**, as well as reduces pain and swelling. Bromelain's inflammation-modulating mechanisms include its effects on cytokines, platelet aggregation and fibrin formation.

Bromelain has been shown to be an adequate replacement for pepsin and trypsin in cases of deficiency. Unlike pancreatic enzymes, bromelain has a more stable pH (4.5 – 9.8) and can **provide proteolytic activity in the stomach as well as the small intestine**, and then circulate systemically, where it is able to exert beneficial physiological effects throughout the body. Other than allergy to pineapple, bromelain is well-tolerated and has potential for benefiting those with functional gastrointestinal disorders (FGIDs).





Papain from Papaya

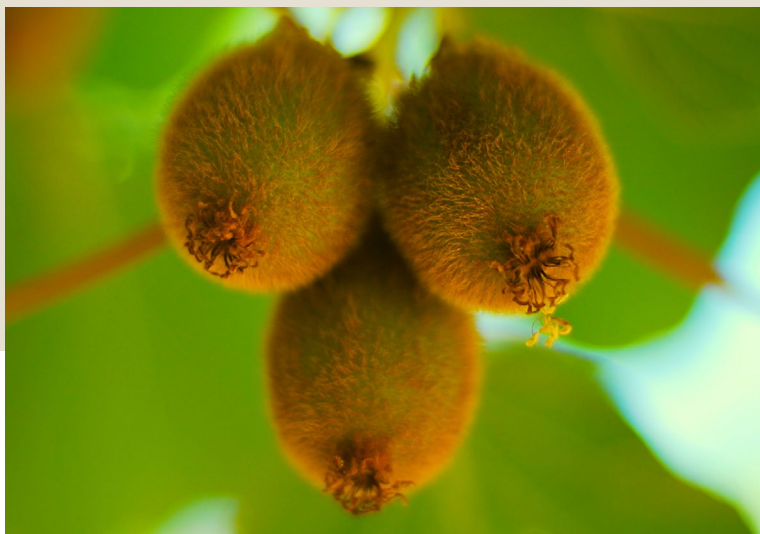
Papaya (*Carica papaya*) is an herbaceous, tropical tree-like plant that has a long history of use as a natural remedy as a digestive aid in tropical and subtropical regions of the world. When unripe, **papaya fruit contains papain**, a cysteine protease that is derived from the latex exuded from unripe papaya skins, which is collected, dried, then purified before using internally. Composed of a complex of several enzymes, papain possesses the power to **break apart proteins, starches, and fats** into their simpler components for **optimal absorption and utilization**.

Papain is used extensively in foods and medicines. Used commercially as a meat tenderizer, papain is excellent as a protein digestant. When used internally, papain's enzymes are used to soothe dyspepsia and other digestive disturbances of the GI tract. **Both papain and bromelain act similar to that of pepsin**, the stomach's enzyme that breaks down dietary proteins and alleviates mild gastrointestinal symptoms. Evidence suggests that both papain and bromelain may provide relief for functional gastrointestinal diseases (FGIDs), such as leaky gut, that results in malabsorption and loose stools. Papain also improves **hypochlorhydria**, and intestinal dysbiosis caused by **gluten intolerance**.

Papain has been shown to improve digestion and absorption of proteins, fats, and carbohydrates and may improve digestive symptoms in patients with chronic FGIDs of the lower GI. Beneficial effects were reported on flatulence, constipation, and painful bowel movements with a trend in the improvement of heartburn in participants with chronic indigestion and GI dysfunctions. This study concluded that **papain contributes** to the **maintenance of digestive tract physiology**.

In addition to providing digestive support, papain has a variety of clinical applications to **promote a healthy inflammatory response in the body**, which may improve physical discomfort. Clinical evidence indicates that papain may offer relief from postoperative pain, acute allergic sinusitis, and sports-related injuries and may **improve minor injuries faster** in comparison to placebo.





Actinidin from Kiwifruit

Native to southwestern China, *Actinidia* species produce some of the most nutrient and phytochemically dense fruits, commonly known as kiwifruit. As interest in plant-based enzymes continues to accelerate, so has research on **actinidin, a proteolytic enzyme** derived from the kiwifruit (*Actinidia deliciosa*). Evidence suggests that **actinidin improves protein digestion and digestive sensitivities**.

Belonging to the **same class of plant proteases as bromelain and papain**, actinidin has similar proteolytic activity to that of papain and bromelain **offering synergistic enzyme support** to improve digestion and reduce FGID-related symptoms. Additionally, while bromelain and papain are both active in a wide range of pH levels (pH 5.5 – 8.5 and 3.0 to 12.0, respectively), **actinidin has a broader, more active pH range** at (pH 3.0 to 10.0) and is available to work with in the stomach as well as the small intestine, to **improve digestion** and rate of gastric emptying. Actinidin-derived enzymes may be **especially helpful for elderly individuals** who have weaker digestion and lower HCl production.

In healthy adults, kiwi supplements have been shown to significantly increase daily bowel movements by more than 1 bowel movement per week and the supplements were well-tolerated. Research indicates that actinidin supplementation may improve protein digestion, **reduce symptoms of bloating, abdominal pain, gas, and constipation** in individuals with functional dyspepsia, a type of functional gastrointestinal disorder. Other than allergy to kiwifruit, actinidin is well-tolerated and has potential for benefiting those with functional gastrointestinal disorders (FGIDs).



Inflamma-Support Blend

Carminative Complex

Inflamacidin's ingredients make it not only **great for cooling the fire of inflammation** but also **aids/enhances digestion**. The Inflamma-Support Blend includes peppermint leaf (*Mentha x piperita*), fennel seed (*Foeniculum vulgare*), and ginger root (*Zingiber officinale*); classic carminative herbs in Chinese and Ayurvedic medicine and have been used to manage digestive disorders. Due to the high concentration of aromatic compounds known as volatile oils, **carminative herbs stimulate the gastrointestinal tract** and commonly possess anti-spasmodic, and antimicrobial properties. An article published in 2012 entitled "Functional foods with digestion-enhancing properties" reported that ginger, peppermint, and fennel were among the most important plants having digestive enhancing properties.

Peppermint (*Mentha x piperita*)

Likely the most widely used member of the mint family, (Lamiaceae) and is used as a beverage tea, a flavoring agent, and a medicine. Traditionally used as a **carminative, antispasmodic, antiemetic and digestive aid** around the world, peppermint leaves are abundant in **menthol**. This **cooling, a fat-soluble volatile oil** has been studied for its **beneficial** effects on **digestion** and its ability to promote smooth muscle relaxation as well as **enhance bile production** by stimulating Oddi's sphincter. Research suggests that menthol's ability to relax smooth muscle may be linked to its action as a calcium channel blocker.



Menthol's cooling properties help relieve abdominal cramping and intestinal spasms commonly experienced with irritable bowel syndrome (IBS) and functional dyspepsia (FD) some of the most common FGIDs.

Fennel (*Foeniculum vulgare*)

A seed that has a long history of traditional use as a warming, aromatic digestive herb used for dyspepsia, bloating flatulence, and poor appetite. It is also considered helpful for digestive problems such as indigestion, flatulence, and nausea. Both Eastern and Western herbal traditions look to **fennel seed for spleen, gall bladder, and liver support**. In Ayurveda, the medicine system of India, fennel seeds are used to **promote the digestive fire (agni)**, alleviate abdominal cramping and flatulence.



(ABC HC) Current research suggests **anethole**, a major **component of fennel seed oil**, is responsible for alleviating certain symptoms of **IBS**, including **intestinal spasms**, by mimicking dopamine's relaxant effects along the intestinal wall.

Ginger (*Zingiber officinale*)

This rhizome is one of the oldest domesticated spices in history. In Traditional Chinese Medicine and Ayurveda, **ginger is considered a warming**, pungent spice indicated for **relieving dyspepsia, flatulence, nausea and vomiting, diarrhea, smooth muscle spasms** and as an appetite stimulant appetite. Ginger rhizome **contains** potent, phenolic compounds known as **gingerols and shogaols**. Research indicates these compounds may inhibit microbes, reduce oxidative damage, and relieve smooth muscle spasms which may be beneficial for those with an over-reactive inflammatory response. The **mechanisms of ginger** that are associated with **promoting a healthy immune response** appear to be associated with the inhibition of NF-κB activation, and its ability to regulate the inflammatory response process.

In addition to alleviating mild digestive symptoms, such as nausea, other potential benefits include ginger's ability to decrease pressure on the lower esophageal sphincter, reduce intestinal cramping and bloating, improve gastric emptying, and can decrease bloating and abdominal pain associated with small intestinal bacterial overgrowth (SIBO).





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