

HistaGest-DAO™



Supports the Digestion of Histamine-containing Foods*

By David M. Brady, ND, DACBN, IFMCP, FACN and Caitlin H. Higgins, MS, CNS

This information is provided as a medical and scientific educational resource for the use of physicians and other licensed health-care practitioners ("Practitioners"). This information is intended for Practitioners to use as a basis for determining whether to recommend these products to their patients. All recommendations regarding protocols, dosing, prescribing, and/or usage instructions should be tailored to the individual needs of the patient considering their medical history and concomitant therapies. This information is not intended for use by consumers.

HistaGest-DAO™ provides exogenous diamine oxidase (the enzyme responsible for breaking down histamine) to help support normal and healthy histamine metabolism.* Each tablet provides 20,000 histamine-degrading units of diamine oxidase (DAO) from porcine kidney extract to promote the degradation of dietary histamines.* HistaGest-DAO™ is formulated with gastro-resistant coated tablets and delayed-release technology that allow the DAO enzyme to reach the small intestine where it helps break down histamine.*

Lower DAO activity may result in higher amounts of histamine being absorbed through the small intestine and accumulating in the blood. Taking one tablet before each meal provides an undenatured and clinically studied amount of DAO in the small intestine to help break down histamine in the digestive tract and help soothe digestive discomfort associated with sensitivity or intolerance to histamine-rich foods.* HistaGest-DAO™ may help support the dietary management of gastrointestinal, muscular, neurological, and dermatological concerns associated with DAO deficiency.* This formula is ideal for individuals with intolerance to histamine-producing foods or who have a known DAO deficiency.*

Highlights

- Provides 20,000 histamine degradation units (HDU) of diamine oxidase activity from 4.2 mg of porcine kidney extract per 1 tablet serving
- Gastro-resistant coated tablet with controlled-release allowing the DAO enzyme to reach the small intestine to help break down histamine*
- Small tablet delivery in a convenient travel dispenser for portability and ease of use when on-the-go or traveling
- Does not contain glucose, lactose, histamine, or sugars

Histamine is a vital aromatic biogenic amine synthesized by the L-histidine decarboxylase from the essential amino acid histidine. Histamine is produced endogenously and resides in various tissues, including the liver, lungs, intestine, heart, pancreas, and various other organs. Histamine is primarily stored and released by mast cells and basophils, but also by a variety of other cells, including histaminergic neurons and enterochromaffin cells.¹ Histamine is a mediator of many biological processes, including inflammatory responses, vasodilation, gastric acid secretions, neuromodulation, bronchospasm, and regulation of immune function.²

Histamines are also present in many types of foods, although the amount varies depending on ripeness, processing, and storage times. Common histamine-rich food sources include fermented foods such as sauerkraut, vinegar, and yogurt, alcoholic beverages, fish, cured meats and cheese, and certain fruits and vegetables (e.g., ripe bananas, citrus, spinach, tomatoes).³ Under normal physiological conditions, histamine is metabolized through two main pathways, the cyclooctyl action of histamine-N-methyltransferase (HMNT) and the oxidative deamination of diamine oxidase (DAO). Intracellular histamine is metabolized by HMNT while ingested, and extracellularly, histamine is broken down by the enzyme DAO in the small intestine.^{1,4}

DAO Deficiency and Histamine Intolerance

DAO is present in the gut and its main function is to metabolize ingested dietary histamines. DAO deficiency occurs when this enzyme is less active, reducing histamine degradation and allowing histamine to be absorbed through the intestinal epithelial cells and accumulate in the bloodstream. This accumulation may trigger a series of functional, nonspecific, non-allergic gastrointestinal (GI) and extraintestinal complaints, such as migraines, vertigo, flushing, rhinitis, constipation, diarrhea, bloating, indigestion, fatigue, muscular pains, urticaria, respiratory problems, and more.^{1,2,5-7}

Histamine intolerance (HIT) is a non-immune food intolerance that results from an imbalance between the capacity for histamine degradation and accumulated histamine in the body.^{6,8} There are several factors contributing to the reduced activity of histamine-metabolizing enzymes and, thus, elevated histamine levels; the primary etiology of HIT is related to DAO or HMNT genetic polymorphisms, intake of certain DAO-inhibiting drugs/medications, diseases associated with DAO deficiency, intestinal dysbiosis, and food-induced HIT.^{1,5} In vivo evidence suggests that alcohol and acetaldehyde competitively interacts with acetaldehyde dehydrogenase and can increase endogenous histamine release, reducing the rate of histamine metabolism.^{1,4,8}

Benefits*

- Promotes the degradation of food-derived histamines
- Supports diamine oxidase status in the gastrointestinal tract
- Promotes normal histamine metabolism
- May support individuals who are intolerant to histamine-rich foods

Supplement Facts

Serving Size 1 tablet

Amount Per Serving	% Daily Value
Porcine Kidney Extract (Diamine Oxidase Activity 20,000 HDU)	4.2 mg *

* Daily Value not established

Other Ingredients: Microcrystalline cellulose, hydroxypropylcellulose, ethylcellulose, potato starch, sodium alginate, magnesium salts of fatty acids, medium chain triglycerides, hydroxypropylmethylcellulose, oleic acid, vegetable stearate.

Malnutrition can also lead to an insufficiency of DAO enzyme nutrient cofactors, vitamin C, copper, and vitamin B6.² Considering there are 50 known single-nucleotide polymorphisms for the gene that codes for the histamine receptors and DAO, this may help explain the individual HIT-related symptom variability.⁵ Diagnosing HIT requires a complex multidisciplinary approach, including low basal serum DAO levels as a biomarker of HIT, eliminating disorders with similar symptom manifestations, and a positive response to a low-histamine diet, which is considered confirmation of HIT.^{2,9,10}

Histamine Intolerance and the Gut Microbiome

Increasing evidence suggests that HIT is primarily a GI disorder that originates in the gut and is associated with other GI disorders, such as irritable bowel syndrome-like disorders, inflammatory bowel diseases, non-celiac gluten sensitivity, food intolerance and malabsorption, disorders associated with mast cells (e.g., eosinophilic gastroenteritis, celiac, mast cell activation syndrome), and *H. pylori* infection.^{5,6,11} Gut microbial analysis in patients with HIT showed elevated levels of stool zonulin, increased levels of Proteobacteria and significantly reduced alpha diversity, Bifidobacteriaceae, Butyricimonas, and Hespellia compared with healthy controls, indicating gut dysbiosis and intestinal barrier dysfunction in HIT patients.¹² Further evidence demonstrates that HIT patients, when compared with the guts of healthy individuals, have a significantly higher abundance of histamine-secreting bacteria, which favor histamine accumulation in the gut and significantly reduced levels of bacteria related to gut health.¹³

Diamine Oxidase and Histamine Metabolism

In addition to implementing a low-histamine diet (the gold standard treatment), supplementation with exogenous DAO enzyme obtained from porcine kidneys has been shown to support dietary histamine degradation for individuals with intestinal DAO deficiency and HIT.^{2,4} In a double-blind, placebo-controlled crossover study (n = 39), supplementation with 0.5 mg gastric acid-resistant DAO resulted in significant symptom improvements compared with a placebo.¹⁴ A small, retrospective observational study showed that 0.3 mg of DAO administered twice daily resulted in improvements in at least one or more symptoms in 13 of 14 patients with HIT.¹⁵ A double-blind, placebo-controlled crossover study (n = 20) demonstrated that the group supplemented with 0.3 mg of DAO twice daily for 30 days experienced significant improvements in Urticaria Activity Score 7 (UAS7) in patients with unsatisfactorily controlled chronic spontaneous urticaria by antihistamines compared to a placebo, and subjects receiving supplementation were able to reduce their antihistamine dose.¹⁶ The level of UAS7 improvement was inversely associated with serum basal DAO levels.¹⁶

In episodic migraine patients with DAO deficiency, the group supplemented with 0.6 mg of DAO three times per day for 1 month experienced significant reductions in the number and duration of migraine episodes compared with baseline and a placebo, although a small nonsignificant reduction in the placebo group was observed.¹⁷ An open-label interventional study found that subjects who supplemented with 0.3 mg of DAO three times per day for 28 days experienced significantly reduced frequency and intensity of symptoms and 61% of patients demonstrated nonsignificant increases in serum DAO levels.¹⁸ During the follow-up period for 28 days without DAO supplementation, the symptom sum score increased and serum DAO levels slightly decreased.¹⁸ More robust clinical trials are needed to further confirm the significance of DAO enzyme supplementation.

Complementary strategies in the management of HIT may include dietary or supplemental intake of nutrient cofactors of DAO enzyme, including vitamins C and B6 and copper. Probiotic supplementation with strains that can degrade histamine and other biogenic amines or ones that do not produce L-histidine decarboxylase, such as members of the *Bifidobacterium* genus, may be supportive. However, clinical trials are warranted to confirm these potential strategies.²

Recommended Use: Take 1 tablet 20 minutes prior to the consumption of histamine-rich foods or as directed by your health-care practitioner.

It is recommended to not exceed three tablets per day. Should be swallowed whole; do not crush, break, or split the tablets.

For a list of references cited in this document, please visit:

<https://www.designsforhealth.com/api/library-assets/literature-reference---histagest-dao-tech-sheet-references>

Dosing recommendations are given for typical use based on an average 150 pound healthy adult. Healthcare practitioners are encouraged to use clinical judgement with case-specific dosing based on intended goals, subject body weight, medical history, and concomitant medication and supplement usage.

DAO Enzyme manufactured by Dr Healthcare Spain, S.L.U., for Designs for Health under Patents.

***These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.**

To contact Designs for Health, please call us at (860) 623-6314, or visit us on the web at www.designsforhealth.com.