

# **DIAMINE OXIDASE (DAO)**

Ingredients	<b>Qty Per Serving</b> (1 capsule)	Size	Servings	Code	Price
DAO	30,000 HDU	30 mini vcaps	30	DAO-3VC30	\$13.79
DAO	30,000 HDU	60 mini vcaps	60	DAO-3VC60	\$25.99
DAO	30,000 HDU	90 mini vcaps	90	DAO-3VC90	\$37.49

HDU = Histamine Degrading Units

Dosage: 1 capsule 1-3x daily 20 minutes before meals or as directed.

Contraindications: Caution in pregnancy and diabetes.

Safety Information: Generally well tolerated. Drug interactions may exist. Allergens: Does not contain corn, dairy, gluten, soy, wheat or yeast.

# The Ingredient

- Diamine oxidase (DAO) enzyme is the main intestinal enzyme involved in the metabolism of ingested histamine, and its deficiency is related to many chronic diseases.
- DAO is effective in managing symptoms associated with conditions related to DAO deficiency such as migraine and headaches, ADHD, digestive disorders, atopic dermatitis, fibromyalgia and muscle pain.
- It is mainly located in the intestinal lumen where it degrades dietary histamine.
- DAO is a flavoprotein/enzyme that catalyzes the aerobic oxidation of amines, mainly histamine, to the corresponding aldehyde and ammonia.
- Other histamine-degrading enzymes include HNMT (histamine N-methyltransferase), ALDH (aldehyde dehydrogenase), MAO (monoamine oxidase), UGTTA4 (UDP-glucuronosyltransferase I-4), ACAT (acetyl-CoA acetyltransferase), NAT (N-acetyltransferase), CYPTA2 (cytochrome p450 family I subfamily A member 2).
- Histamine is present in many foods and is rapidly degraded with normal DAO activity.
- Normally, histamine contained in food does not cause any health issues since it is quickly metabolized by DAO in the gut.
- DAO deficiency is a metabolic disorder that affects 16% of the global population and is a cause of a large variety of symptoms.
- DAO inhibits the transepithelial permeability of exogenous histamine, which prevents its passage into the systemic circulation.
- When histamine is not being degraded in the intestinal lumen, it is absorbed through the epithelium causing its accumulation in the blood and triggering several symptoms (i.e., migraine, intestinal and skin disorders, fibromyalgia, ADHD and more).
- Histamine intolerance (HIT) is also called food histaminosis or enteral histaminosis or DAO deficiency.
- With adequate DAO activity, the body should break down histamine into other compounds like imidazole acetaldehyde.
- Endogenous histamine is an essential molecule vital for human functioning.
- ♦ The main barrier against histamine in the intestine is the DAO enzyme.
- Conversely, exogenous or dietary histamine is naturally present in several foods and has no vital function known.
- DAO is unevenly distributed, being abundant in the small intestine, kidney, and placenta of humans and other mammals.
- Intestinal DAO is synthesized continuously by mature enterocytes localized in the upper intestinal villi and is mainly associated with the basolateral aspect of enterocytes.
- Taking DAO before each meal increases the amount of DAO in the gut, therefore boosting histamine degradation and overcoming the disabled metabolic condition.
- DAO is not absorbed and does not have systemic activity.
- DAO does not manage or address antibody-related or IgE-related food allergies.
- Our material is derived from pea (*Pisum sativum*) sprout dehydrated powder, and is suitable for vegans, whereas many other DAO supplements are derived from pig kidney. These pea sprouts have natural DAO content.
  - DAO is typically sensitive to stomach pH, necessitating the use of resistant delivery mechanisms.
  - DAO also interacts with other bioactive ingredients in a way that diminishes its benefits.
  - ABBiotek Health is a world leader in DAO technology with more than 100 Industrial Property patents worldwide.
  - ♠ adiDAO® is a microencapsulated DAO that provides two food-grade protective layers using a combination of coating technologies that are designed to protect the DAO, optimizing its delivery when it reaches the small intestine, and protects against undesirable interactions.
  - The delivery platform is compatible with probiotics or prebiotics, as well as in combination with other supplements.
  - It provides a controlled release and targeted delivery system that enhances bioavailability and enhanced compatibility and stability which works in synergy with other ingredients.

#### Histamine

- Histamine is an essential molecule, a transmitter that belongs to the group of biogenic amines and that is naturally present in many foods as well as inside of human cells.
- Normally, histamine contained in food does not cause any problem, since it is quickly processed and metabolized by the DAO enzyme.
- It is involved in a host of immunological and physiological mechanisms: stimulation of gastric secretion, muscle contraction, vasodilation, cell proliferation/differentiation, embryo development, healing processes, permeability or immunomodulation.
- Simultaneously, it acts as a neurotransmitter in the nervous system, regulating body functions such as temperature control, memory, wakefulness/sleep and sensation of pain.
- Histamine occurs in all tissues of the body, mainly in skin, connective tissue, lungs and the gastrointestinal tract.
- ♦ Histamine gets released from the cells as part of cell signaling and is considered a mediator.
- In general terms, histamine is found in two major types of immune cells in the body, the mast cell and the basophil.
- Mast cells typically are found in connective tissue and mucosal linings such as the lining of the nose, the mouth and the digestive tract.
- They are also located in the lungs, the brain and underneath our skin and are usually near nerve endings. Basophils circulate in the vascular system.
- Both types of cells and the chemicals they release, including histamine serve very important biological functions and are part of our primary defense against invaders.
- Histamine release can be triggered by foreign invaders (germs or parasites), allergens, and other chemicals in the body.
- ♦ The trigger cross links IgE and as a result, histamine is released.
- People usually think of the classical symptoms of allergies, red eyes, a runny nose, wheezing, coughing and chest congestion, hives and eczema.
- ♦ These are the classic symptoms, but histamine can cause other reactions.
- There are four types of histamine receptors, and they can cause different symptoms depending on many factors such as where the histamine is released, genetic differences, and the triggers or causes of excess histamine.
- ♠ Excess histamine can cause joint pain, musculoskeletal or connective tissue pain (fibromyalgia), chronic fatigue, bloating, constipation or diarrhea, estrogen dominance and painful menstruation, hypotension, tachycardia or rapid heart rate, dizziness, trouble regulating your body temperature, and trouble sleeping.
- It has also been linked to childhood ADHD.
- Adults will commonly complain of brain fog or trouble multitasking.

### Histamine Intolerance (HIT)

- Histamine intolerance results from an imbalance in the accumulation of histamine and its degradation capacity.
- ♦ This is not a food allergy even though it has some symptoms of allergic reactions.
- ♦ There aren't any proven ways to diagnose histamine intolerance, and not all providers recognize HIT as an official diagnosis.
- HIT is the term for that type of food intolerance which includes a set of undesirable reactions because of accumulated or ingested histamine.
- Manifestations may be caused by various pathophysiological mechanisms or a combination of them.
- Histamine Intolerance is often misdiagnosed as food allergies, eczema or Candida.
- It is, however, an IgG, as opposed to the IgE mediated response that occurs in allergies.
- The symptoms caused by histamine intolerance are dose-related; the amount of histamine present causes symptoms only when they're above a certain threshold. (This is another important difference between histamine intolerance and allergies.)

#### **DAO Deficiency**

- This refers to a deficiency in DAO metabolization activity or when there is an imbalance between the ingested histamine and the enzyme capacity to metabolize it.
- One source indicates that approximately 15% of the world population has a DAO deficiency without knowing it.
- As histamine has not been properly metabolized and degraded, it passes into the bloodstream triggering different symptoms.
- Supplementation before each meal increases the amount of DAO in the small bowel and therefore also boosts histamine degradation.
- This accelerates the processing of the histamine found in different foods in the digestive tract, which triggers the symptoms.
- Factors that may reduce DAO activity include the following:
  - Genetics: some people may be genetically programmed to produce less DAO enzyme
  - Intestinal damage: damage or inflammation to the inner lining of the digestive system may decrease DAO
  - Hormonal imbalances: estrogen dominance has been linked to histamine intolerance
  - Kidney and liver diseases
  - Nutrient deficiencies: such as B6, Copper, Zinc, Magnesium and Vitamin C
  - Mold toxicity

- Alcohol
- Foods with elevated diamine content
- High body histamine level: chronic histamine excess in the body (e.g., allergies, stress, mast cell disease, etc.) may reduce DAO production
- Gut Dysbiosis including SIBO, SIFO
- Leaky Gut

## Fibromyalgia

- Fibromyalgia is a chronic pathology due to the release of histamine molecules from mast cells.
- Fibromyalgia is characterized by chronic pain, fatigue, mood and sleep disorders, headaches, anxiety, depression and extreme sensitivity.
- Around 75% of fibromyalgia sufferers have a genetic DAO deficiency and it is estimated that about 2-4% of the population is affected by FM, with a higher prevalence in women than in men.
- Researchers have identified a connection between FM symptoms and specific changes in the AOCI gene that impact DAO enzyme activity.
- DAO supplementation has proven effective in alleviating symptoms.

## Migraine

- Migraine is the sixth largest disease worldwide, affecting between 5-8% of men and 15-20% of women, peaking in adulthood.
- Migraine is a complex and common neurological disorder characterised by attacks of moderate to severe, crippling, usually throbbing, single-sided headache (although it can be double-sided), accompanied by sensitivity to sensory stimuli, nausea and/or vomiting.
- ♦ A deficiency in DAO is one of the causes of this pathology.
- Headache is the main symptom of individuals with histamine intolerance.
- It can be induced by histamine both in healthy individuals and in individuals who already experience migraines.

### **Gastrointestinal Disorders**

- Followed by headache, gastrointestinal disorders, including diffuse stomach pain, cramps, flatulence and diarrhea, are the main symptoms of histamine intolerance.
- Élevated histamine concentrations and decreased DAO enzyme activity have been detected in various inflammatory and neoplastic diseases of the gastrointestinal tract, such as Crohn's disease, Ulcerative Colitis and colorectal neoplasms.

## **Skin Disorders**

- Elevated baseline plasma concentrations of histamine and increased release were seen in patients with severe atopic eczema when compared to patients without the condition.
- Reduced DAO enzyme activity has also been seen in patients with severe atopic eczema.

# **ADD and ADHD**

- Attention Deficit Hyperactivity Disorder (ADHD) is the most prevalent neurodevelopmental disorder, diagnosed in around 5% of children worldwide.
- DAO deficiency has been found to be highly prevalent in those diagnosed with ADHD (82%).
- Impaired histamine metabolism due to malfunctioning of the DAO enzyme has also been found to impact neuroinflammation and play a role in ADHD physiopathology.

## Mast Cell Activation Syndrome

- Mast Cell Activation Syndrome (MCAS) is a condition that causes intense episodes of swelling, shortness of breath, hives, diarrhea, vomiting and other symptoms and in severe cases, it may lead to life-threatening anaphylaxis.
- It's caused by mast cells mistakenly alerting the immune system that there's something harmful in the body.
- Because histamine intolerance involves the mast cells, it is often confused with mast cell activation.
- The difference, however, is that with MCAS, mast cells secrete multiple mediators in addition to histamine—whereas in histamine intolerance, the mast cells release only histamines and nothing else.
- A common cause of histamine intolerance and MCAS is a deficiency in DAO.

#### **Actions**

#### **Indications**

- Migraines and other headaches
- Fibromyalgia
- Joint and muscle pain
- Bloating, gas, stomach pain, fullness
- Diarrhea, constipation, heartburn, reflux
- Nausea, vomiting
- Asthma
- Sneezing, rhinitis, nasal congestion, cough

- Hives, dermatitis, psoriasis
- Chronic fatigue
- Hypotension, hypertension and arrythmias
- Mast Cell Activation Syndrome
- Genetic variants for DAO (ABPI/AOCI genes)
- Irregular menstrual cycle

# **High Histamine Foods**

- Fermented alcoholic beverages (beer, wine, champagne)
- Vinegars, sauerkraut, kimchi
- Dairy products (milk, yoghurt, ripened cheese, cream, sour cream)
- Avocado
- Nuts
- Fermented soy products
- Vegetables (spinach, tomatoes, eggplant, pumpkin, zucchini, sauerkraut)
- Oily fish

- Processed/Cured meats (salami, pepperoni, sausage, jerky)
- Shellfish
- Egg white
- Fruits (strawberries, pineapple, citrus fruits, bananas, kiwi)
- Coffee and tea
- Leftovers
- Artificial food additives