

NANOFORMULATED



# HISTA-AID®

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**Hista-Aid®** is a novel nanoformulated blend of vitamin C, quercetin, luteolin, and diindolylmethane (DIM), designed to support healthy immune function and balanced histamine levels. Appropriate for acute or preventative needs, a four pump dose can be taken multiple times daily for fast relief.

## EDUCATION

### HISTAMINE IS A UNIQUE AND QUINTESSENTIAL MEDIATOR

Allergic reactions to insect bites, dust, molds, foods, pollens and medications have been steadily rising for the last fifty years.<sup>1</sup> Inhalant allergies afflict 30% of adults and 40% of children in the US.<sup>2</sup> Ten percent of adults now suffer from food allergies, with nearly half having severe reactions.<sup>3</sup> Not surprisingly, antihistamine medications have been popular for over sixty years.<sup>4</sup>

Though histamine is best known for its impact on allergies and allergic symptoms such as rhinitis and urticaria, it is actually a broad and quintessential mediator that helps modulate the innate and adaptive immune response, systemic inflammation, gastric acid secretion, and a cascade of inflammatory molecules and cytokines in the body.<sup>5,6</sup> Histamine can function as a neurotransmitter with widespread influence on the CNS, modulating circadian rhythm and arousal.<sup>7</sup> It is a vasoactive amine, orchestrating vasodilation, vascular permeability and smooth muscle contraction.<sup>8</sup> Found primarily in mast cells and released upon mast cell degranulation, histamine binds to four different receptors in the body (H1-H4).<sup>9</sup>

Mast cells themselves have been called multifunctional master cells because they are intimately involved in the allergic response, bacterial and parasite elimination, cardiac and neurologic function and more.<sup>10</sup> Impaired degradation of histamine rich foods, due to reduced DAO activity, may cause many uncomfortable symptoms mimicking an allergic reaction.<sup>11,12</sup> At an extreme, excess mast cell activity and histamine can lead to mast cell activation syndrome, a multisystem disorder involving the skin, gastrointestinal, cardiovascular, respiratory, and neurologic systems.<sup>13</sup> Histamine, it is clear, is a molecule with far-reaching impact on the body, which may be one reason why allergies are often comorbid with other conditions, and why bringing histamine into balance treats not only allergies, but improves overall health.<sup>14,15</sup>

### QUERCETIN AND LUTEOLIN BALANCE HISTAMINE LEVELS

The phytonutrients quercetin and luteolin are natural flavonoids that modulate release of histamine from the body's mast cells.<sup>16,17,18</sup> Quercetin has been shown to modulate activity of NF- $\kappa$ B, cyclooxygenase (COX), lipo-oxygenase (LOX), proteins,



### Supplement Facts

Serving Size: 2 mL (4 Pumps)	Amount	% Daily
Servings Per Container: 25	Per Serving	Value
Vitamin C	170mg	189%
(as Sodium Ascorbate)		
Sodium	22mg	<1%
(as Sodium Ascorbate)		
Quercetin dihydrate	16mg	**
(Sophorae japonica L.) (Flower bud)		
Luteolin extract	20mg	**
(Sophorae japonica L.) (Flower bud)		
Proprietary Blend	120mg	**
Highly purified phospholipids, Diindolylmethane		

\*\*Daily Value not established

**Other Ingredients:** Water, glycerin, ethanol, tocopherol, medium-chain triglycerides, natural citrus oils, natural flavoring, natural mixed tocopherols

enzymes, cytokines and other potentially inflammatory molecules.<sup>19,20</sup> Quercetin also has the ability to inhibit IgE antibodies including allergens.<sup>21</sup>

Luteolin powerfully inhibits mast cell degranulation as well as the release of histamine from mast cells, lessens mucus production, reduces vascular permeability and diminishes gene activity that increases inflammation.<sup>22,23</sup> Luteolin may also curb inflammatory molecules including TNF, nitric oxide, inducible nitric oxygen synthase (iNOS), leukotrienes, numerous interleukins, and NF-κB. It scavenges reactive oxygen species (ROS) and activates antioxidant enzymes and interleukin-10, an anti-inflammatory molecule.<sup>24,25</sup>

## **VITAMIN C IS A BROAD-ACTING ANTIHISTAMINE AND ANTIOXIDANT**

Vitamin C (ascorbate) is widely known as a powerful aqueous-phase antioxidant. It protects against oxidative stress,<sup>26</sup> reduces histamine levels,<sup>27</sup> aids in the production of diamine oxidase (DAO), the body's key enzyme for breaking down histamine in food.<sup>28</sup> Allergic diseases are associated with lower blood levels of ascorbate and oxidative stress plays a significant role in the pathophysiology of asthma.<sup>29</sup> In fact, one gram of daily oral vitamin C for sixteen weeks allowed asthma patients to reduce their corticosteroid dose.<sup>30</sup> In a separate study, intravenous vitamin C resulted in a significant serum histamine reduction in individuals with allergies or upper respiratory infections.<sup>31,32</sup> Finally, vitamin C supports diamine oxidase (DAO), the enzyme that metabolizes and inactivates histamine ingested in foods. The ingestion of histamine-rich food can provoke diarrhea, headache, asthma, hypotension, urticarial, pruritus, and flushing. Adding vitamin C can lead to an increase in DAO activity.<sup>28</sup>

## **DIM ACTIVATES THE BODY'S MASTER ANTIOXIDANT SWITCH**

A key centerpiece of this novel formula is Nrf2 (Nuclear factor erythroid 2-related factor 2) activation, a cellular switch that orchestrates antioxidant, detoxification and cellular defenses.<sup>33</sup> It specifically activates over 200 genes involved in detoxification, encoding cytoprotective proteins that are associated with inflammation, including genes involved in histamine release.<sup>33,34</sup>

Diindolylmethane (DIM) activates our master antioxidant switch, Nrf2, and supports healthy hormone levels, leading to a more balanced histamine response as well.<sup>35,36,37,38</sup> By “turning on” the Nrf2 switch, DIM may increase the body's expression of enzymes, transporters, and anti-inflammatory molecules.<sup>39</sup> With oral intake, the highest amounts of DIM are found in the liver, followed by the lungs and kidneys.<sup>40</sup> The liver and kidneys are the organs most burdened by detoxification—and the liver has been shown to play a role in food allergies.<sup>41</sup>

## **NUTRACEUTICALS & LIPOSOMAL TECHNOLOGY**

Uptake and absorption of nutraceuticals, including flavonoids and vitamin C, can vary and be limited by breakdown in the digestive tract. Research indicates that liposomal delivery systems may enhance the bioavailability, uptake and action of quercetin, luteolin, and vitamin C.<sup>42,43,44</sup>

**Quicksilver Delivery Systems®** improve upon liposomal and emulsification technology with smaller, more stable particles made from the highest-grade ingredients available. In addition to exceptional absorption rates, these tiny liposomal and nanoemulsified particles increase diffusion across mucus membranes, enhance lymphatic circulation of nutrients and support cellular delivery.