Digestive

DAOgest: A premium diamine oxidase (DAO) enzyme ingredient

A scientific summary

Abstract

Histamine intolerance could be your next big opportunity in the digestive health space. *Why?* As a gastrointestinal condition that triggers allergy-like effects, it is thought to affect as much as 1-3% of the global population.[1] Not surprisingly, this number is expected to rise with the growing awareness of food intolerances, development of advanced detection tools and availability of health data. **Yet, histamine intolerance remains a largely unaddressed health issue.**

Introducing DAOgest

DAOgest is Bioiberica's science-backed solution for innovation in the digestive health market. A premium ingredient containing high-quality DAO enzyme and effective at a low dose of only 4.2 mg/serving/day, it can be taken before meals to help manage histamine degradation and the negative effects associated with histamine intolerance. Explore the science behind DAOgest and discover how you can play a part in **making histamine intolerance history.**

The role of DAO enzyme in histamine intolerance

DAO enzyme – also known as histaminase - is an important enzyme that is naturally produced in the body and involved in the metabolism and inactivation of histamine in the digestive tract. Histamine intolerance often develops as a result of diamine oxidase (DAO) deficiency in the body or impaired DAO activity, creating an imbalance between the intake of histamine and the body's ability to degrade it.

In individuals with the condition, the consumption of histamine-rich foods and beverages or histamine liberators can lead to an excess of histamine in the digestive tract. This triggers allergy-like effects, including gastrointestinal issues and abdominal pain, sneezing, runny nose or congestion, hives, asthma and more.[2,3,4]

Identification and management of histamine intolerance

1 Individual presents with effects

2 Clinical assessment by a healthcare professional

2.1 Medical Assessment

- ✓ Effects evaluation, including duration, frequency and occurrence to food intake
- ✓ Diet logged
- ✓ Medical conditions, emotional disruption, lifestyle and allergies identified

2.2 Situational evaluation

- ✓ Presence of food allergy, food sensitivity, celiac disease, vegetarian or vegan diet determined
- ✓ History of eating disorders checked
- ✓ Capacity to follow a diet, including time, skills and finances, confirmed
- ✓ Social factors, like school, work, family life and travel considered

3 Histamine intolerance levels determined (3-phase method)

Phase 1 (4 weeks)	Phase 2 (1-2 weeks)	Phase 3 (1-2 weeks)	Phase 4 (4 weeks +/-)
Dietary restriction of foods which can increase histamine levels in body	Small portions of high-histamine foods re-introduced	If phase 2 tolerated, larger histamine containing foods trialed	Continue tolerated histamine intake and add histamine liberators and blockers

3 Management approach recommended

Low histamine diet

DAO supplementation

Innovating with DAOgest

The growing awareness and prevalence of histamine intolerance is powering demand for enzyme-based solutions, like DAOgest, to address this common, yet unmet condition. It does so by increasing DAO enzyme levels in the gut, helping to:

1. Break down histamine from foods and beverages
2. Decrease histamine levels
3. Support the management of histamine intolerance.

Power-up your next digestive health innovation with DAOgest

Premium ingredient

Immediate effect

Complements low-histamine diets

Low dose (4.2 mg/serving/day)

100% biologically-derived ingredient

Extracted from porcine kidney

The science behind DAOgest

The efficacy of DAO supplementation is backed by years of science and research. Here, Bioiberica adds to this body of evidence through the exploration of its ingredient – DAOgest.

1. In vitro: Evaluation of DAOgest absorption and enzymatic activity

Objective

To assess the capability of DAOgest (4.2 mg) to degrade histamine and determine its absorption potential.

Methods

The enzymatic activity of DAOgest was evaluated using histamine as a substrate (15 and 30 mg/L) in an *in vitro* system in which DAOgest (4.2 mg) was incubated at 37°C for 5 h. Histamine reduction was determined by HPLC-PDA. The intestinal absorption of DAOgest was determined using the everted gut sac model.

Galvez-Martin P et al. In vitro characterization, evaluation of enzymatic activity and capacity of intestinal absorption of DAOgest (DAO extract from pig kidney), Clinical Nutrition ESPEN, 58 (512), 2023.

Results

The histamine-degrading capacity of DAOgest was shown to be higher with the lower histamine concentration (10.4% at 30 mg/L; 27.07% at 15 mg/L). The results of the everted gut sac model indicated that there is no absorption of DAOgest at intestinal level, as DAO activity was detected in the incubated medium but not in any of the intestinal segments studied - the duodenum, ileum and jejunum.

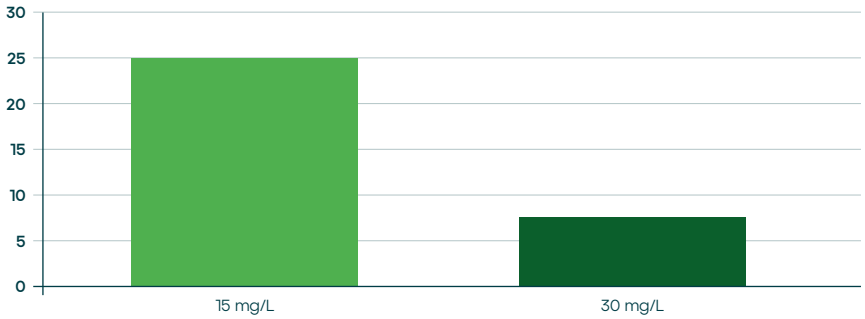

Figure 1: Percentage of histamine degraded by DAOgest (at histamine substrate concentrations of 15 and 30 mg/L).

Conclusion:

DAOgest has the capability to degrade histamine. These results suggest that exogenous administration with DAO from pig kidney as a food supplement might help in reducing the effects associated with histamine intolerance. The findings also confirmed that DAOgest is not absorbed in the intestine - this verifies that its activity is only at the intestinal level.

2. In vitro: DAO enzymatic activity in commercially-available nutritional supplements

Objective

To evaluate the enzymatic activity of marketed nutritional supplements containing DAO from animal or plant origin (alone or in combination).

Methods

Five products were selected: P1, P2, P3 with DAO of animal origin, P4 of vegetal origin and P5 with DAO and vitamin C. Enzymatic activity of the samples was evaluated using histamine (10 mg/L) as a substrate. Histamine reduction was determined by HPLC-PDA using an *in vitro* system (sodium phosphate buffer, 20 mM; pH 8.0) in which DAO extract was incubated at 37°C for 5 hours.

Gálvez-Martín P et al. Evaluation of the activity of the DAO enzyme in marketed nutritional supplements, Nutr Hosp, 40(1):95-96, 2023.

Results

The *in vitro* evaluation demonstrated that the finished dosage formulation combining DAO from porcine origin (DAOgest) and vitamin C had the highest percentage of histamine degradation – 93% at 10 mg/L.

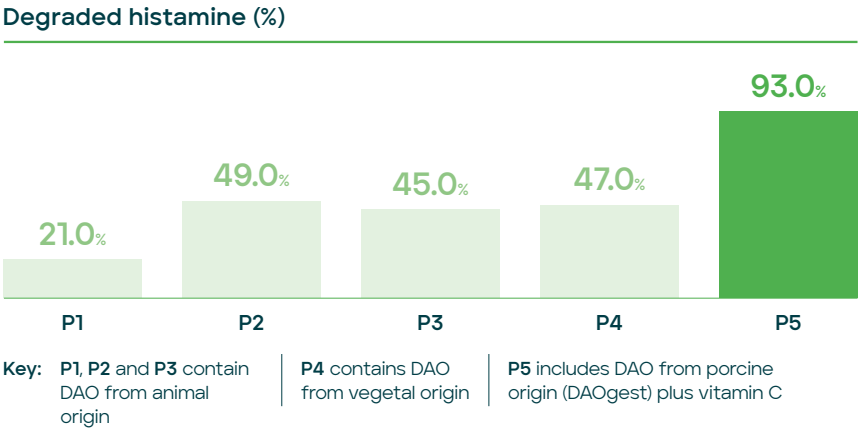

Figure 2: Percentage of histamine degraded by five DAO-based products. Enzymatic activity evaluated using histamine (10 mg/L) as a substrate.

Conclusion:

Compared to other DAO products on the market, the nutritional supplement containing DAOgest and vitamin C had the greatest histamine-degrading activity.

3. In vitro: Histamine-degrading capacity of DAO plus vitamin C

Objective

The activity of DAO enzyme is slowed down due to the hydrogen peroxide generated during histamine degradation. Vitamin C is a powerful antioxidant that is thought to remove the hydrogen peroxide. Therefore, the aim of the study was to evaluate the histamine degrading capacity of 4.2 mg DAO extract from pig kidney (DAOgest) when combined with 10 mg vitamin C.

Methods

Kinetic characterization of DAO extract (DAOgest) was determined using histamine as a substrate. Histamine concentrations ranging from 1.1 to 555 mg/L were incubated with DAO extract. Histamine reduction was determined by HPLC-PDA using an *in vitro* system (sodium phosphate buffer, 20 mM; pH 8.0) in which DAO extract was incubated at 37°C for 5 hours with histamine at a concentration ranging from 10 to 150 mg/L. In a subsequent experiment, vitamin C was added to the medium using 10 and 20 mg/L histamine.

Galvez-Martin, P. et al. In vitro characterization, evaluation of enzymatic activity and capacity of intestinal absorption of daogest (DAO extract from pig kidney). Clinical Nutrition ESPEN 58, 512 (2023).

Results

The *in vitro* study demonstrated that when using 4.2 mg of DAO extract, higher histamine reductions were obtained with the lower histamine concentrations (16% at 20 mg/L; 30% at 10 mg/L). The addition of vitamin C to the media increased histamine reduction by 77% at 20 mg/L histamine and 73% at 10 mg/L histamine.

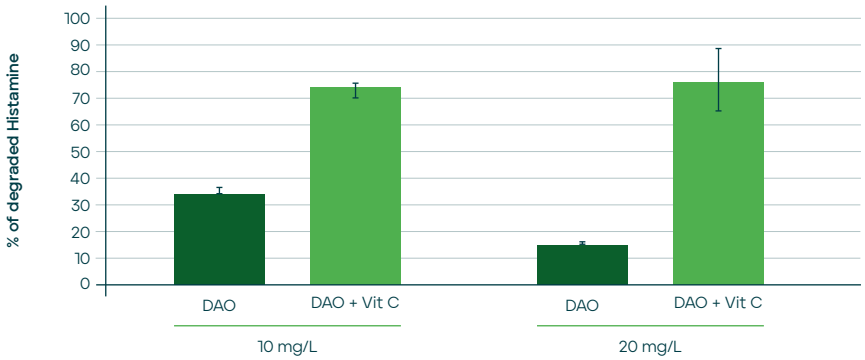

Figure 3: Histamine degradation after applying DAO extract and DAO extract plus vitamin C with histamine at 10 and 20 mg/L

Conclusion:

Pairing DAOgest with vitamin C boosted enzymatic activity. DAOgest plus vitamin C therefore increased the histamine degrading capacity of the formulation and consequent histamine breakdown.

4. Observational study:
Safety and efficacy of DAOgest

Objective

To assess the potential effect of oral DAO supplementation in improving allergy-like effects in individuals with histamine intolerance.

Methods

The observational study in 82 individuals with histamine intolerance investigated the effect of four weeks' DAO supplementation (Histamine Digest® containing 4.2 mg DAOgest) plus vitamin C and catalase on allergy-like effects. The supplement was taken daily before the main meal of the day and the effects of histamine intolerance were evaluated using a standardised questionnaire at baseline visit and every week for the duration of the study.

O'Connor ME, Terradillos-Guillén A, Gálvez-Martín P & Martínez-Puig D. Observational study to assess the efficacy and safety of diaminooxidase (DAO) supplementation in patients with histamine intolerance (HIT). Clinical Nutrition ESPEN, 58 (741), 2023.

Results

A significant improvement from baseline visit was detected for all histamine intolerance effect subcategories from week one: more than 90% in gastrointestinal and skin effects, more than 80% in nervous and respiratory and up to 38% in circulatory effects ($p<0.001$). These improvements were maintained throughout the study period. This correlated with the participants' perceived recovery (more than 50%) from week one. Additionally, no side effects associated with oral supplementation of the DAO product were recorded.

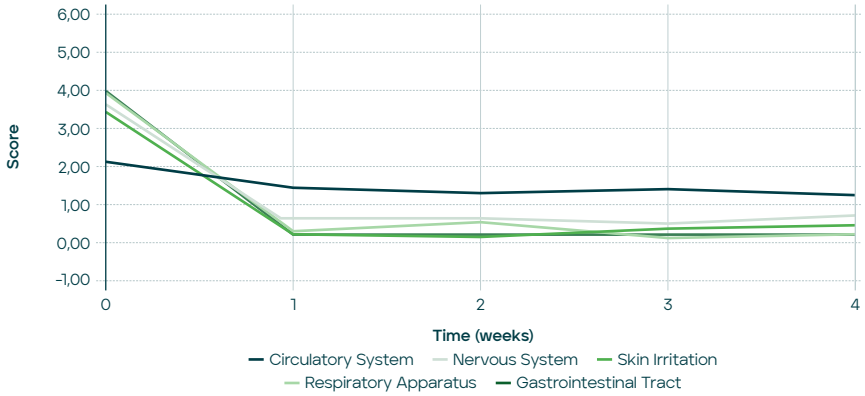

Figure 4: Histamine intolerance severity scores across the four-week study.

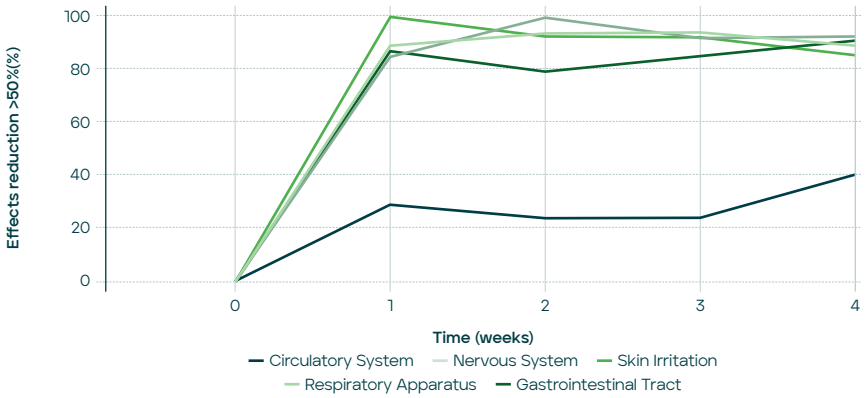

Figure 5: Percentage of individuals with >50% reduction in allergy-like effects during the four-week period.

Parameters	Symptoms	Percentage reduction in symptoms
Nervous system (NS)	Headache, dizziness	85%
Gastrointestinal tract (GI)	Bloating, flatulence, posprandial fullness, diarrhoea, abdominal pain, constipation, nausea and emesis	94%
Respiratory apparatus (RA)	Rhinorrhea, rhinitis, nasal congestion, sneezing and dyspnea	89%
Skin	Pruritus, flusk, urticaria, eczema and swelling	98%
Circular system (CS)	Tachycardia, hypotonia, collapse	36%

Conclusion:

Supplementation at a dose of 4.2 mg/serving/day in individuals with histamine intolerance is effective and safe at reducing the effects of histamine intolerance from the first week of intake.

References

1) Comas-Baste. Biomolecules, 2020;10:1181.
2) Maintz L. & Novak N. Am J Clin Nutr., 2007;85:1185-1196.
3) Comas-Basté O, Sánchez-Pérez S, Veciana-Nogués MT, Latorre-Moratalla M, & Vidal-Carou MDC. Biomolecules, 2020;10.
4) Schnedl WJ et al. Intest Res., 2019;17:427-433 (2019).

Notes

About Bioiberica

Bioiberica is a global Life Science company with more than 50 years' experience in the identification, extraction and development of biomolecules of high biological and therapeutic value for the pharmaceutical and nutraceutical industries. With a portfolio of scientifically-backed ingredients inspired by the latest consumer trends, Bioiberica Healthcare serves the mobility, digestive health and skin & beauty markets.

To innovate in the digestive health market with Bioiberica's science-backed DAOgest ingredient, contact us today.

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DAOgest
Diamine oxidase enzyme

Bioiberica