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Effects of Germination Parts of Seed Legumes on Histamine Levels in Rats

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Abstract
Diamine oxidase (DAO) is a major enzyme in the breakdown of dietary histamine. Histamine intolerance is caused by an imbalance of histamine scavenging mechanisms, which can be treated with small-histamine diet. The relevance of dietary supplements containing external DAO has lately grown especially that produced from low-cost sources to aid in the intestinal hydrolysis of histamine. As a result, this study aimed to test the sprouted sections of fenugreek and beans for histamine breakdown to determine their availability as nutritional supplements used to get rid of histamine and limit the harm caused by excessive concentrations which can lead to death. The impact of adding 10% lyophilised sprouted bean, 10% lyophilised sprouted fenugreek, and blends of them at 5% of each, on mice administrated orally histamine solution (200 mg/kg bw) was investigated. When compared to the positive control, the diet contain lyophilised legume sprouts (10% fenugreek, 10% bean, and their mixture at 5% from each of them) it found that histamine reduced by 29, 21, and 36 %, while glutathione increased by 129, 96, and 150 %, respectively. In addition, all liver function as well as malondialdehyde decreases, while the liver antioxidant enzymes were enhanced. Finally, the findings show that legume sprouts (fenugreek and beans) can be used to make functional enzymatic supplements that can help alleviate histamine intolerance symptoms.
Keywords: Histamine, Histamine Intolerance, Diamine Oxidase (DAO) Enzyme, Legumes, Sprouted Fenugreek and Beans
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1. Introduction

Histamine intolerance is a nutrition illness which has stimulated numerous researchers in recent decades due to its high predominance (Sánchez-Perez et al., 2018). Histamine intolerance is an unbalance produced by an unbalance in histamine decomposition that results in symptoms as allergy (Tuck and Biesiekierski, 2019). Diamine oxidase (DAO) and histamine-N-methyltransferase (HNMT) enzymes were necessary for the histamine removal mechanism, which destroyed it by removing its methyl group. DAO deficiency is one of the most main cause of histamine intolerance (Kaur et al., 2019), which caused by genetic background, a variety of disorders, drugs, or alcohol usage (Comas-Basté et al., 2020). According to (Manzotti et al., 2015), serum DAO activity less than 10 U/mL is a criteria indicating potential histamine intolerance. The most suggestion for symptom avoidance is by consumption a low-histamine meal (Tuck an Biesiekierski, 2019), which includes limiting foods that are high in histamine produced by bacteria (eg, fish and saved fishery commodities) or fermented products (eg, sauerkraut, sausage, cheese, beer, wine, and fermented soy products) (Comas-Basté et al., 2019a). Histamine amounts in aged cheese often surpass 2500 mg/kg, which is extremely harmful (Madejska et al., 2018). Histamine poisoning caused by body's immune responses can occur as soon as 24 hours after consuming contaminated food (Hungerford, 2010). Histamine poisoning is distinguished by a short incubation time, which can last 20–30 minutes after ingestion, with symptoms that are generally of low/moderate severity and remit in a few hours (Comas-Basté et al., 2019b). However, the more presence of histamine in foods leads to highly restrictive diets and makes it challenging to set well-based nutritional recommendations (Schnedl et al., 2019). The analysis of plasma histamine levels or the recognition of consumed food are the most common methods for detecting histamine poisoning (Elmore et al., 2002). DAO in the intestine serves as a barrier versus external histamine, especially of food origin (Kovacova et al., 2015), as a result of a DAO enzyme deficiency, normal levels of plasma histamine maybe increase between (0.3–1.0 ng/mL) and the subsequent symptoms of histamine intolerance (Maintz and Novak, 2007; Comas-Basté et al., 2017).The new DAO enzyme supplements from various sources are intended to improve the quality of life of histamine-intolerant patients by enhancing histamine breakdown. The European Commission recently approved pig kidney protein extract as a supplement helping to get rid of elevated histamine (EU 2018/1023). Plants are considered ideal sources of DAO that can be used to boost the production of the enzyme diamine oxidase (DAO) as shown in the study by (Comas-Basté et al., 2019b). Some legume sprouts, such as beans and fenugreek, are rich in bioactive compounds such as DAO and could be used for DAO production on an industrial scale. At pH values over 5, fenugreek sprouts'

endogenous diamine oxidases can breakdown exogenous histamine, putrescine, cadaverine, and tyramine (Cigi´c et al., 2020). The highest DAO activity to degrade histamine in vitro was obtained by germination of seed legumes in the dark for 6 days. Maximum DAO activity in freeze-dried legume sprouts kept intact for 12 months (Comas-Basté et al., 2020). As a result, this investigation aimed to determine whether or not legume sprouts (fenugreek and bean) might be used as a functional component source of enzymatic supplements for histamine intolerance when administered in vivo during a biological experiment on mice.

2. Materials and method

2.1. Materials and Chemicals

Sigma-Aldrich Chemical Co. (St. Louis, MO) supplied the histamine. Nimesh (Mumbai, India) Corporation provided the casein. SISCO Research Laboratories provided the AIN-76 mineral mix and AIN-76 vitamin mix (Mumbai, India). The analytical grade chemicals and solvents used in this study. Fenugreek and bean seeds were acquired locally, washed to remove any stones or contaminants, and then pulverized.

2.2. Preparing the fenugreek and bean germinated part:

The germination of fenugreek and bean seeds took 6 days in the dark, after which the sprouts were removed, freeze-dried, and then frozen until use.

2.3. Animal diets and treatments

The animals used in this study were treated according to guidelines of the Food Technology Research Institute's (FTRI) experiment animal house, follows ARC animal patronage commission assizes, which are in line with international care and use recommendations. Male Albino mice weighing 135-140 g were brought from the Food Technology Research Institute's Animal House at the Agriculture Research Center in Giza, Egypt. The animals were placed in well- aerated cages with a sieve down and continue supply for a basal diet (negative control) for 10 days for adaptation. Then, the mice were completely divided at random into five groups of six rats each. The mice were fed different experimental diet for 8 weeks. Group one (G1) fed on basal diet, the basal diet or control (G1) comprises 15% sugar, 21.7 % casein, 53.3 % corn starch, 5% corn oil, 1% vitamin mixture, 4% mineral mix, and 0.2% choline chloride as recommended by (Tebib et al., 1997). Salt mixture and vitamin mixture were prepared as recommended by the (AIN, 1977; Campbell, 1961). Group 2 (G2) fed on basal diet, oral administration of histamine solution (200 mg/kg bw), a dose 200 mg of dissolved in 0.5 ml (positive control). Group 3 (G3) included a positive control diet fortified with 10% lyophilised fenugreek sprouts, while (G4) was supplemented with 10% lyophilised bean sprouts (G4), finally (G5) included a positive control diet supplemented with 5% lyophilised fenugreek sprouts and 5% lyophilised bean sprouts. Temperature and humidity were maintained at 25±2ºC and 60%, respectively. Food and water were provided, ad libitum. After the experimental period (8 weeks), the rats were fasting overnight and then sacrificed.

2.4. Determination of plasma histamine level

The determination was performed according to (Sun et al., 2013). Blood were centrifuged at 3000 × g (10 min, 4°C). Histamine levels in plasma were then determined using (Diamond Co, Hannover, Germany) kit. Optical density in each well was measured at 450 nm.

2.5. Liver Function Enzymes in Serum

Serum markers such aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), were determined spectrophotometrically, using colorimetric enzymatic kits.

2.6. Biochemical parameters in tissues homogenates

Tissues from livers, were homogenized in phosphate buffer saline (KH_2PO_4/ K_2HPO_4, 50 mM, pH 7.4) using Potter-Elvehjem homogenizer. The homogenates were centrifuged at 10000 × g for 10 min (4° C) and the resulting supernatants were then used for the estimation of MDA, and antioxidant enzymes activity.

2.7. Lipid peroxidation

The extent of lipid peroxidation in different organs was evaluated in term of malondialdehyde (MDA) and measured according to the procedure method of (Draper and Hadley, 1990).

2.8. Glutathione

Glutathione was measured using the procedure given by (Beutler et al., 1963).

2.9. Antioxidant Enzymes in Liver

Catalase activity was measured in accordance with Aebi (1984). Glutathione reductase activity was determined according to Carlberg and Mannervik (1985). Glutathione peroxidase and superoxide dismutase activity were determined using the method published by Flohé and Günzler (1984).

2.10. Bilirubin

Total bilirubin was assayed according to procedure of (Bosma, 2003; Brito et al., 2008).

2.11. Statistical analyses

The Duncan test, included in the SPSS program (SPSS Inc., Chicago, IL), was employed for means comparison at a p-value of 0.05.

3. Results and Discussion

3.1. Hepatoprotective impact of sprouted powder of fenugreek and beans

Table 1. Effect of sprouted powder from fenugreek and beans on liver function enzymes in the serum of mice administered orally (200 mg histamine /kg bw).

	ALT (U/L)		AST (U/L)		LDH (U/L)		ALP (U/L)	
Treatment	**4 weeks**	**8 weeks**	**4 weeks**	**8 weeks**	**4 weeks**	**8 weeks**	**4 weeks**	**8 weeks**
G1	$28.6^{e}\pm0.31$	$30.4^{e}\pm0.61$	$50.9^{e}\pm0.62$	$45.3^{e}\pm2.4$	$1154.3^{e}\pm14.5$	$1076.6^{e}\pm33.2$	$112.7^{e}\pm1.46$	$105.2^{e}\pm0.43$
G2	$56.3^{a}\pm0.65$	$69.4^{a}\pm0.80$	$72.1^{a}\pm0.34$	$76.3^{a}\pm2.5$	$1840.3^{a}\pm18.1$	$1805.4^{a}\pm38.4$	$254.4^{a}\pm3.21$	$247.0^{a}\pm2.38$
G3	$36.9^{c}\pm0.88$	$37.8^{c}\pm0.41$	$52.7^{c}\pm0.53$	$55.4^{c}\pm1.7$	$1380.4^{c}\pm33.7$	$1430.7^{c}\pm16.4$	$122.1^{c}\pm1.30$	$128.3^{c}\pm2.20$
G4	$38.2^{b}\pm0.45$	$40.3^{b}\pm0.58$	$53.4^{b}\pm0.28$	$58.1^{b}\pm4.5$	$1405.5^{b}\pm34.9$	$1502.8^{b}\pm62.3$	$138.7^{b}\pm2.27$	$135.9^{b}\pm0.51$
G5	$30.6^{d}\pm0.47$	$32.4^{d}\pm0.33$	$51.4^{d}\pm0.17$	$48.7^{d}\pm5.8$	$1307.4^{d}\pm22.4$	$1276.8^{d}\pm44.1$	$116.4^{d}\pm0.62$	$108.4^{d}\pm1.80$

The diverse letters within the same column indicate considerable differences between the means of various treatments

Table 1 shows the activity of liver function enzymes in mice serum fed 8 weeks on diets containing sprouted powder of fenugreek and bean and administered orally (200 mg histamine /kg bw).

The remarkable increase of main serum biochemical parameters including ALT, AST, LDH, and ALP with extended administration orally high histamine dose, as seen when comparing control positive with control negative and these findings are consistent with those (Harri, 2005; Dey et al., 2015; Mejri et al., 2018). The feeding on diets containing sprouted powder from fenugreek and bean or a mixture of them tended to bring all the aforementioned parameters towards normal, due to its possible protective effect against histamine-induced injury in liver. The decrease being more pronounced in the group containing both sprouted powder from fenugreek and bean (G5), which recorded the most reduction, followed by G3 and G4. The reduction in alanine aminotransferase activity caused by dietary usage in G3, G4, and G5 after 8 weeks of feeding was 45.5, 41.9 and 53.3 % compared to the positive control, while the reduction in aspartate aminotransferase activity was 27.2, 23.8 and 36.1 % by the same groups. After 8 weeks, the activity of lactate dehydrogenase was reduced by 20.7, 16.7 and 29.2 % in the G3, G4, and G5 groups, respectively, while the activity of alkaline phosphatase was reduced by 48, 44 and 56 % in these groups compared to the control positive.

3.2. The effect of dietary sprouted fenugreek and beans on histamine and glutathione in the liver, malonaldehyde and bilirubin in mice administrated 200 mg histamine/kg orally.

Table 2. Effect of sprouted powder from fenugreek and beans on histamine and glutathione in the liver, malonaldehyde and bilirubin in mice administrated 200 mg histamine/kg orally.

	Histamine plasma		Glutathione**		Lipid peroxides**		Bilirubin (mg/dl)	
Treatment	**4weeks**	**8 weeks**	**4weeks**	**8 weeks**	**4weeks**	**8 weeks**	**4weeks**	**8 weeks**
G1	$73^{e}\pm0.06$	$74^{e}\pm0.12$	$45.7^{a}\pm0.54$	$43.9^{a}\pm0.14$	$5.18^{e}\pm0.17$	$5.57^{e}\pm0.05$	$0.33^{e}\pm0.04$	$0.29^{e}\pm0.01$
G2	$122^{a}\pm0.08$	$188^{a}\pm0.08$	$26.4^{e}\pm0.18$	$17.5^{e}\pm0.41$	$7.23^{a}\pm0.11$	$7.67^{a}\pm0.06$	$0.72^{a}\pm0.06$	$0.65^{a}\pm0.03$
G3	$86^{c}\pm0.11$	$90^{c}\pm0.06$	$39.4^{c}\pm0.44$	$37.4^{c}\pm0.18$	$6.32^{c}\pm0.12$	$6.68^{c}\pm0.07$	$0.54^{c}\pm0.06$	$0.48^{c}\pm0.04$
G4	$96^{b}\pm0.04$	$102^{b}\pm0.05$	$38.4^{d}\pm0.23$	$35.6^{d}\pm0.51$	$6.44^{b}\pm0.13$	$6.75^{b}\pm0.04$	$0.59^{b}\pm0.03$	$0.55^{b}\pm0.02$
G5	$78^{d}\pm0.09$	$80^{d}\pm0.14$	$43.1^{b}\pm0.38$	$40.1^{b}\pm0.33$	$5.98^{d}\pm0.07$	$6.04^{d}\pm0.04$	$0.42^{d}\pm0.05$	$0.36^{d}\pm0.02$

*** ng/ml, ** nmol/mg**

The diverse letters within the same column indicate considerable differences between the means of various treatments

Table 2 shows the effects of dietary sprouted powder from fenugreek and beans on histamine, the hepatic levels of glutathione and lipid peroxides or bilirubin in experimental mice after initially exposure to a high-histamine concentration orally.

According to DAO levels, patients of histamine intolerance were divided into three groups: under 3 U/mL

(more severity of symptoms), 3–10 U/mL (symptoms response to low histamine content in diet or DAO supplementation), and >10 U/mL (no or few symptoms). The intensity of histamine symptoms varies depending on the degree of DAO insufficiency (Cucca et al., 2022). The findings referred that addition supplements of sprouted powder from fenugreek and beans or their combination to the diet reduced the concentrations of histamine, lipid peroxides, and bilirubin compared to the control positive. Yacoub et al. (2018) found that supplementing DAO improved histamine-related cutaneous symptoms in patients with low basal serum DAO levels. At the conclusion of 8 weeks, hepatic reduced glutathione level increased by 129, 96, and 150 % in the G3, G4, and G5 groups, respectively, compared to the control positive group.

Malonaldehyde (MDA) was determined as a marker for lipid peroxidation. Hyper-histamine dose for mice exhibited high MDA content in the liver suggesting histamine-induced oxidative stress in this organ, similar results revealed by (Dey et al., 2015). Because oxygen-free radicals increased in rats administrated 200 mg histamine/kg orally, the highest MDA value was found in G2 rats given a high-histamine orally. The oxidative stress was further exacerbated by the decline of glutathione groups (The SH groups are essential components in maintaining the intracellular and membrane redox state of the secretory capacity of endocrine tissue). In contrast, treatment of the elevated histamine in mice with the natural supplements attenuates the extent of lipid peroxidation, restores the redox status, and alleviates the generation of free radicals as revealed for glutathione increasing. Similar results have been reported for other plant extract by (Murugan et al., 2015). Meanwhile, MDA levels were the lowest in G3 and G5. As a result of the presence of hyper-histamine levels, these data show that G2 rats have greater oxidation in their blood than G1. This discovery demonstrated the capacity of natural antioxidants, such as fenugreek sprouted powder and beans, to inhibit lipid oxidation.

Bilirubin levels over the normal range (1.2 mg/dl) can indicate a number of liver and gallbladder issues. An accelerated rate of red blood cell destruction can sometimes induce excessive levels of bilirubin (hemolysis). A bilirubin examination is typically used for checking jaundice (the skin and eyes tend to yellow) or hepatitis or liver disease, or anemia caused by breakdown red blood cells, determine the toxicity of drugs or chemicals ingested through the body. Lower-than-normal bilirubin levels are usually not a cause for worry. High levels, on the other hand, may suggest liver damage or disease.

3. 3. The effect of a dietary supplement of sprouted fenugreek and beans on antioxidant enzyme activity of liver mice administrated 200 mg histamine/kg orally.

Table 3. Effect of sprouted fenugreek and beans on antioxidant enzymes activities of liver mice administrated 200 mg histamine/kg orally.

	SOD*		CAT**		GSH-RED**		GPX**	
Treatment	**4weeks**	**8 weeks**	**4weeks**	**8 weeks**	**4weeks**	**8 weeks**	**4weeks**	**8 weeks**
G1	$21.15^{a}\pm0.16$	$19.47^{a}\pm0.27$	$693.6^{a}\pm3.2$	$684.1^{a}\pm1.3$	$52.8^{a}\pm2.1$	$56.4^{a}\pm2.4$	$8.38^{a}\pm0.09$	$8.54^{a}\pm0.72$
G2	$11.93^{e}\pm0.26$	$11.65^{e}\pm0.24$	$475.2^{e}\pm2.6$	$463.0^{e}\pm2.5$	$34.8^{e}\pm5.3$	$39.1^{e}\pm2.2$	$4.23^{e}\pm0.39$	$4.41^{e}\pm0.24$
G3	$13.08^{c}\pm0.27$	$13.75^{c}\pm0.63$	$569.7^{c}\pm4.2$	$555.3^{c}\pm3.8$	$42.7^{c}\pm3.6$	$45.8^{c}\pm1.4$	$5.95^{c}\pm0.41$	$6.05^{c}\pm0.31$
G4	$12.12^{d}\pm0.52$	$12.45^{d}\pm0.25$	$451.3^{d}\pm6.4$	$438.1^{d}\pm6.4$	$40.7^{d}\pm1.7$	$41.6^{d}\pm2.8$	$5.19^{d}\pm0.21$	$5.42^{d}\pm0.34$
G5	$14.52^{b}\pm0.14$	$15.35^{b}\pm0.37$	$633.7^{b}\pm2.8$	$632.7^{b}\pm4.1$	$45.5^{b}\pm1.8$	$47.7^{b}\pm1.1$	$6.93^{b}\pm0.41$	$7.25^{b}\pm0.21$

*** U/min/ mg protein, ** nmol/ min/ mg protein**

The diverse letters within the same column indicate considerable differences between the means of various treatments

The findings of Table 3 indicate that sprouted powder from fenugreek and beans and their mixture (G3, G4 and G5) treatment significantly enhanced the SOD, CAT, GSH-RED, and GPX, activities in liver compared with positive control. The observed alterations of the enzymatic antioxidant status were successfully restored confirming the potential antioxidant properties of natural supplements and supporting their hepatoprotective capacities. At this point, we can speculate that sprouted powder from fenugreek and beans and their mixture not only enhances the activity of the GSH, GPX, CAT and SOD, but it can directly prevent the oxidation of lipids that cause inflammation. Such antioxidant mediated alleviation of oxidative stress in histamine-induced animal was observed by (Gayathri et al., 2011) and confirmed later by (Dey et al., 2015).

4. Conclusions

Several strategies are employed to prevent the development of histamines in food, but inadequate techniques could lead to an increased risk of allergies and other health problems, especially for people had histamine intolerance. Another technique for histamine breakdown is DAO enzyme addition to the diet to overcome histamine intolerance or reduce the severity of symptoms. Because of the high costs of commercially producing DAO enzyme, the plant consider a good alternative source for producing greater quantities of DAO. This study focuses on histamine enzymatic breakdown by DAO during ingestion to avoid poisoning or death, by assessing the effect of fenugreek seed and bean sprouts on rats having higher dose of histamine orally. The current investigation on rats found that dietary supplementation with fenugreek seed and bean sprouts improved

hepatoprotective and liver antioxidants in mice given high doses of histamine orally. All tested indications show an improvement in liver function enzymes and antioxidant enzymes, with a significant drop in histamine compared to the positive control. The highest benefit was seen when fenugreek and bean sprouts were mixed, followed by 10% fenugreek sprouts incorporated in rat's diet, and finally 10% bean sprouts.

5. References

Aebi, H. (1984). Catalase in vitro. Methods Enzymol. 105, 121–126. Ambasta, S.P. 2000. Useful Plants of India. National Institute of Science Communication, New Delhi, India.

AIN (1977). American Institute Of Nutrition Recommended Dietary Allowances, Rev. Ed., 6, Washington, D.C.

Beutler, E. (1963). Improved method for the determination of blood glutathione. J. lab.clin. Med., 61, 882-888.

Bosma, P. J. (2003). Inherited disorders of bilirubin metabolism. Journal of Hepatology, vol. 38, no. 1, pp. 107–117.View at: Publisher Site | Google Scholar

Brito, M. A., Lima, S., & Fernandes, A. (2008). Bilirubin injury to neurons: contribution of oxidative stress and rescue by glycoursodeoxycholic acid. Neurotoxicology, vol. 29, no. 2, pp. 259–269, 2008.View at: Publisher Site | Google Scholar

Campbell, J. A. (1961). Methodology of protein evaluation. RAG. Nutr. Document R. 10, Adds. 37, June Meeting, New York.

Carlberg, I. & Mannervik, B. (1985). Glutathione reductase. Methods Enzymol. 113, 484–490.

Cigi´c, I. K., Rupnik, S., Rijavec, T., Ulrih, N. P. &Cigi´c B. (2020). Accumulation of Agmatine, Spermidine, and Spermine in Sprouts and Microgreens of Alfalfa, Fenugreek, Lentil, and Daikon Radish. Foods 2020, 9, 547; doi:10.3390/foods9050547.

Comas-Basté, O., Latorre-Moratalla, M. L., Bernacchia, R., VecianaNogués, M. T., & Vidal-Carou, M. C. (2017). New approach for the diagnosis of histamine intolerance based on the determination of histamine and methylhistamine in urine. J Pharm Biomed Anal. https://doi.org/10.1016/j.jpba.2017.06.029.

Comas-Basté, O., Latorre-Moratalla, M. L., Sánchez-Pérez, S., Veciana-Nogués, M. T., & Vidal- Carou, M. C. (2019a). Histamine and Other Biogenic Amines in Food. From Scombroid Poisoning to Histamine Intolerance. In C. Proestos (Ed.), Biogenic Amines. London: IntechOpen. https://doi.org/ 10.5772/intechopen.84333.

Comas-Basté, O., Latorre-Moratalla, M. L., Sánchez-Pérez, S., Veciana-Nogués, M. T., & Vidal- Carou, M. C. (2019b). In vitro determination of diamine oxidase activity in food matrices by an enzymatic assay coupled to UHPLC-FL. Analytical and Bioanalytical Chemistry, 411, 7595- 7602. https://doi.org/10.1007/s00216-019-02178-2.

Comas-Basté, O.; Latorre-Moratalla, M. L.; Rabell-González, J., Veciana-Nogués, M.T., & Vidal-Carou, M.C. (2020). Lyophilised legume sprouts as a functional ingredient for diamine oxidase enzyme supplementation inhistamine intolerance. LWT Food Sci. Technol., 125, 109201. [CrossRef].

Commission Implementing Regulation (EU) 2018/1023 of 23 July 2018 correcting 337 Implementing Regulation (EU) 2017/2470 establishing the Union list of novel foods. Official 338 Journal of the European Union, L 187, 1-133.

Cucca, V., Ramirez, G. A., Pignatti, P., Asperti, C., Russo, M., Della-Torre, E., Breda D., Burastero, S. E, Dagna L., & Yacoub, M. (2022). Basal Serum Diamine Oxidase Levels as a Biomarker of Histamine Intolerance: A Retrospective Cohort Study. Nutrients, 14, 1513. https://doi.org/10.3390/nu14071513.

Dey, P., Saha, M. R., Chowdhuri, S. R., Sen, A., Sarkar, M. P., Haldar, B., & Chaudhuri T. K, (2015). J. Ethnopharmacol., 161,128–137.

Draper, H. H., & Hadley, M. (1990). Malondialdehyde determination as index of lipid Peroxidation. In Methods in enzymology (Vol. 186, pp. 421-431).Academic press.

Flohé, L., & Günzler, W.A. (1984). Assays of glutathione peroxidase. Methods Enzymol., 105, 114–121.

Gayathri, V., Ananthi, S., Chandronitha, C., Ranakrishnan, G., Lakshmisundaram, R., & Vasathi, H. R. (2011). J. Cardio. Pharm. Therap., 16, 96-104.

Harri E. H. (2005). Clin. Diabetes., 23, 115–119.

Hungerford, J. M. (2010). Scombroid poisoning: A review. Toxicon, 56, 231–243. [CrossRef] [PubMed].

Kaur, S., Ali, A., Siahbalaei, Y., Ahmad, U., Nargis, F., Pandey, A. K., & Singh, B. (2019) Association of Diamine oxidase (DAO) variants with the risk for migraine from North Indian population. Meta Gene 2019. [CrossRef].

Kovacova-Hanuskova, E., Buday, T., Gavliakova, S., & Plevkova, J. (2015). Histamine, histamine intoxication and intolerance. Allergol Immunopathol. 2015. https://doi.org/10.1016/j.aller.2015.05.001.

Madejska, A., Michalski, M., Pawul-Gruba, M., & Osek, J. (2018).Histamine content in rennet ripening cheeses during storage at different temperatures and times. J Vet Res, 62(1), 65–69. https://doi.org/10.1515/jvetres-2018-0009.

Maintz, L., & Novak, N. (2007) Histamine and histamine intolerance. Am J Clin Nutr., 85:1185–96.

Mejri, F., Selmi, S., Martins, A. I., Khoud, H., Baati, T., Chaabene, H., Njim, L., Serralheiro, M. L., Rauter,A. P., & Hosni, K. (2018). Broad bean (Vicia faba L.) pods: a rich source of bioactive ingredients with antimicrobial, antioxidant, enzyme inhibitory, anti-diabetic and health-promoting properties. Food Funct., 2018, 9, 2051-2069. DOI: 10.1039/C8FO00055G (Paper).

Murugan, R., Prabu, J., Chandran, R., Sajeesh, T., Iniyavan, M., & Parimelazhagan T. (2016). Food Sci. Hum., Wellness., 5, 30–38.

Sánchez-Pérez, S., Comas-Basté, O., Rabell-González, J., Veciana-Nogués, M., Latorre-Moratalla, M., & Vidal-Carou, M. (2018). Biogenic Amines in Plant-Origin Foods: Are They Frequently Underestimated in Low-Histamine Diets? Foods, 7, 205. [CrossRef] [PubMed].

Schnedl, W. J., Schenk, M., Lackner, S., Enko, D., Mangge, H., & Forster, F. (2019). Diamine oxidase supplementation improves symptoms in patients with histamine intolerance. Food Science and Biotechnology, 28, 1779-1784. https://doi.org/10.1007/s10068-019-00627-3.

Sun, N., Zhou, C., Pu, Q., Wang, J., Huang, K., & Che, H. (2013), Allergic reactions compared between BN and Wistar ratsafter oral exposure to ovalbumin. Journal of Immunotoxicology, 10 (1): 67–74.

Tebib, K., Rouanet, J. M., Beasancon, P. (1997). Antioxidant effects of dietary polymeric grape seed tannins in tissues of rats fed a high cholesterol vitamin E deficient diet. Food Chemistry, 59: 135-141.

Tuck, C. J., Biesiekierski, J. R., Schmid-Grendelmeier, P., & Pohl, D. (2019). Food Intolerances. Nutrients, 11, 1684. [CrossRef].

Yacoub, M. R., Ramirez, G. A., Berti, A., Mercurio, G., Breda, D., & Saporiti, N. (2018). Diamine oxidase supplementation in chronic spontaneous urticaria: a randomized, double-blind placebo-controlled study. Int., Arch Allergy Immunol. https://doi.org/10.1159/000488142.