# Impact of the clinically approved Petasites hybridus extract Ze 339 on intestinal mechanisms involved in the handling of histamine.



**ID** 4642928
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**Year** 2022
**Title** Impact of the clinically approved Petasites hybridus extract Ze 339 on intestinal mechanisms involved in the handling of histamine.
**Journal** Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie
**Volume** 148
**Pages** / **Article-Number** 112698
**Keywords** Diamine oxidase; Histamine intolerance; Histamine transport; Intestinal histamine handling; OCT3 (SLC22A3); Petasites hybridus
In patients with histamine intolerance accumulated or ingested histamine causes a broad range of undesirable symptoms. Food-derived histamine is degraded by intestinal diamine oxidase (DAO) and histamine-N-methyltransferase (HNMT), while the organic cation transporter 3 (OCT3) contributes to the transcellular flux of histamine. Anecdotal evidence from patients with HIT suggests an improvement of symptoms related to histamine intolerance after intake of Ze 339, a lipophilic CO; 2; -extract prepared from the leaves of Petasites hybridus. Thus, it was the aim of this study to investigate the influence of Ze 339 on DAO, HNMT and OCT3 using Caco-2 and MDCKII cells. Even though Ze 339 reduced mRNA levels of HNMT and DAO, there was no change in protein expression. Ze 339 changed neither the basal release nor the enzymatic activity of DAO. Testing the interaction of Ze 339 with the transcellular histamine transport, we observed a significant increase in the basal to apical flux in presence of high Ze 339 concentrations at the early phases of the experiment. Testing the influence of Ze 339 on OCT3-mediated histamine uptake in overexpressing MDCKII cells revealed a dose-dependent inhibition with an estimated IC; 50; of 26.9ăug/mL for the extract. In conclusion, we report an effect of Ze 339 on transcellular histamine transport, where inhibition of OCT3 may contribute.

**ISSN/ISBN** 1950-6007
**Full Text on edoc** ;
**Digital Object Identifier DOI** 10.1016/j.biopha.2022.112698
**PubMed ID** http://www.ncbi.nlm.nih.gov/pubmed/35149385