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HPLC/HILIC determination of biogenic amines in wines produced by different winemaking technologies

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ABSTRACT

The present study evaluated the effect of winemaking technologies on the concentration of different biogenic amines in Chardonnay wines. Wines produced from sedimented, inoculated must with active dry yeast without malolactic fermentation were compared with wine produced from nonsedimented must spontaneously fermented with malolactic fermentation. Histamine and putrescine concentrations were not significantly different in either variant. The highest concentration of histamine was 0.055 mg L^{-1}, and the highest concentration of putrescine was 1.6 mg L^{-1} in both variants. Statistically significantly higher values of cadaverine (from 0.06 to 0.07 mg L^{-1}), spermidine (from 0.8 to 1.4 mg L^{-1}), spermine (from 0.15 to 0.25 mg L^{-1}), and isoamylamine (from 0.40 to 0.46 mg L^{-1}) were found in the variant made from nonsedimented must, in which spontaneous malolactic fermentation was performed. The higher concentration of biogenic amines in this variant may be due to the different composition of lactic bacteria during the spontaneous malolactic fermentation. A simplified, unpublished HILIC method of chromatographic separation of biogenic amines without prior deprivation with MS-MS detection was used to determine individual biogenic amines.

KEYWORDS

biogenic amines, HPLC/HILIC, wine, vinification, malolactic fermentation, lactic acid bacteria

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1. INTRODUCTION

Biogenic amines are organic bases naturally present in protein-rich food (fish, milk, and meat) and, generally at higher concentrations, in fermented foods (cheese, salami, beer, and wine) (Silla Santos, 1996). Biogenic amines can be formed in different stages of the winemaking process. The concentration of the biogenic amines can be affected by vineyard conditions during grape processing, in which nonsterile conditions may increase their formation as well as alcoholic and malolactic fermentation, and their concentration may also be affected by wine maturation and storage conditions (Guo et al., 2015). Histamine is not an additive but a natural biotechnological product during production, therefore the consumer packaging does not need to state "contains histamine" or "contains biogenic amines" (Ailer, 2016).

Biogenic amines occurring in wine at very low concentrations (range ng mL^{-1}) have similar structures, chemical and physical properties as other compounds in wine. Therefore, a suitable column is important for the proper separation of substances, which may increase the cost of analytical determination. Pretreatment of samples is also important due to the presence of interfering compounds such as polyphenols, lipids, and proteins. Many studies have been conducted on the determination of biogenic amines in wine. Most of these HPLC assays require derivatisation of the samples. For example, *o*-phthaldialdehyde, dansyl chloride, dabsyl chloride, and ethoxy methylene malonate are used for the derivatisation of wine samples that are determined by HPLC coupled to fluorescence, PDA, or UV detector (Caruso et al., 2002; Martín-Álvarez et al., 2006). In wines, a reversed phase (RP)-HPLC method that used o-phthaldialdehyde (OPA) for pre-column derivatisation and detection by fluorescence was adopted by the International Organization of Vine and Wine (OIV), allowing the simultaneous quantification of 18 biogenic amines (OIV, 2009).

In reverse phase LC (RP-HPLC), an apolar stationary phase and a polar mobile phase are used, leading to increased retention when the polarity of the analysed compounds and/or the stationary phase decreases, and/or when the polarity of the mobile phase increases (Doyle and Dorsey, 1998; Rizzi, 1998). Its main disadvantage is that very polar and hydrophilic compounds are not or insufficiently retained.

In normal phase LC (NPLC), contrary to RP-HPLC, the stationary phase is polar, and apolar solvents are used as mobile phase, resulting in increased retention when the polarity of the analysed compounds and/or the SP stationary phase increases, and/or when the polarity of the mobile phase decreases (Caude and Jardy, 1998). However, the nonpolar mobile phase solvents are quite expensive, often toxic, and environmentally unfriendly. Moreover, polar and hydrophilic compounds are not well soluble in these solvents.

Hydrophilic interaction LC (HILIC), first introduced by Alpert (1990), can be used as an alternative for NPLC. In HILIC, a hydrophilic stationary phase and an aqueous-organic solvent of mobile phase with high organic-solvent content that has an increased solubility for the polar and hydrophilic compounds, are used. HILIC has similarities with NPLC in the sense that there is also increased retention when the polarity/hydrophilicity of the analysed compounds and/or the stationary phase increases.

Only a few studies have been performed to determine biogenic amines without prior derivatisation of the samples. An HILIC-PI APCI MS/MS method has been developed for the determination of seven biogenic amines (cadaverine, histamine, putrescine, spermidine, spermine, tryptamine, and tyramine) in cheese (Gianotti et al., 2008), and ultra-performance liquid

chromatography (UPLC) coupled to triple quadruple mass spectrometry (TQ/MS) has been used to determine biogenic amines in Macedonian red and white wines (Tashev et al., 2017). The present study investigated the effect of wine-producing technologies on the concentration of different biogenic amines. The novelty of the study is the use of a simplified, unpublished HPLC/HILIC method with ESI for the determination of biogenic amines in wine without prior deprivation with MS-MS detection.

2. MATERIALS AND METHODS

2.1. Design of the experiment

The experiment was performed at the Mendel University in the Czech Republic using the Chardonnay variety from Mendeleum, Lednice. The grapes were handpicked at the optimal ripening stage (pH 3.25, total acidity of 7.7 g L^{-1}, °NM of 21.5, and yeast assimilable nitrogen concentration of 184 mg L^{-1}). The destemmed and crushed grapes were pressed in a WOTTLE 1200 (Wottle, Austria) pneumatic press.

Variant 1 was processed in a stainless-steel tank, and bentonite (Bentogran, AEB) (40 g hL^{-1}) and 10 mg L^{-1} SO_2 were added. After 24 h of bentonite treatment, the must was divided into three demijohns (20 L) as repetitions 1A, 1B, and 1C. Variant 2 was directly divided into three demijohns as three repetitions (2A, 2B, and 2C) without any intervention. The sedimented must from Variant 1 had approximately 320 NTU, and the nonsedimented must from Variant 2 had approximately 1700 NTU.

In Variant 1, active dry wine yeasts (Siha cryaroma, Lipera: EATON Technologies GmbH, Germany) at a dose of 20 g hL^{-1} were used for inoculation. After fermentation, SO_2 was added at a dose of 40 mg L^{-1}, and the final wine was racked. In Variant 2, spontaneous alcoholic and malolactic fermentation was performed.

2.2. Determination of biogenic amines

2.2.1. Chemicals. Acetonitrile (ACN), formic acid (HCOOH), and ammonium formate ($HCOONH_4$) were purchased from Sigma Chemical Co. (St. Louis, MO, USA). The other chemicals used were p.a. quality from a local supplier (Lachema, Penta). Standards of biogenic amines (histamine, phenylethylamine, tyramine, tryptamine, putrescine, cadaverine, spermidime, spermine, isoamylamine, and 1,6-diaminohexane) were purchased from Sigma Chemical Co. (St. Louis, MO, USA).

2.2.2. Wine sample preparation. After centrifugation of the wines (3,000×*g*; 6 min), 20 µL of 0.1 mM (11.62 mg L^{-1}) internal standard (hexamethylenediamine) and 930 µL of 80% ACN with 3 mM $HCOONH_4$ were added to 50 µL of wine. The pH was then adjusted to 2.7 with formic acid.

2.2.3. HPLC-MS/MS analysis. Biogenic amine analyses were performed on an ExionLC high-pressure binary gradient HPLC system coupled to a 3200QTrap LC-MSMS/MS detector (AB Sciex, Concord, Canada). The ion source was a Turbo V interface equipped with an

electrospray ionisation (ESI) probe. The data were processed using Analyst 1.5.1 software (AB Sciex, Canada).

The mobile phase used consisted of solvent A (3 mM $HCOONH_4$ in water) and solvent B (3 mM $HCOONH_4$ in 95% can). The pH of both mobile phases was adjusted to 2.7 with HCOOH. The flow rate of the mobile phase was 0.5 mL min^{-1}. The gradient elution program was as follows: 0.00 min 100% B; 3.00 min 70% B; 7.00 min 0% B; and 7.10 min 100% B. The sample injection volume was 5 µL, and the separation temperature was 40 °C.

2.2.4. Detector settings. The ESI source was set in positive mode with an ionisation voltage of 3600 V, curtain gas of 30 psig, nebuliser gas GS1 of 40 psig, turbo gas GS2 of 60 psig, and desolvation temperature (TEM) of 720 °C. The 3200QTrap works was set to multiple reaction monitoring (MRM) mode with the settings summarised in Table 1.

The total time between two samples was 10 min. The mass detector recorded an analysis in the range of 0.3–8 min. The determination of the individual components was based on the calibration curves of the standards. HDA (1,6-diaminohexane) was used as an internal standard.

2.2.5. Calibration curves. Stock solutions (1 mg mL^{-1}) of each biogenic amine (tryptamine, 2-phenyethylamine, isoamylamine, putrescine, cadaverine, spermine, spermidine, tyramine, and histamine) were prepared in 0.1% (v/v) formic acid in water. For quantification, seven-point calibration curves were constructed in a range from 10 to 1,000 µg L^{-1} for all amines, except for spermine, for which a concentration range of 20–2000 µg L^{-1} was used (Table 2). To evaluate the effect of the wine matrix, the same series of standard solutions was prepared using a diluted mixed white wine sample (0.9 mL of white wine in 1 mL of standard solution). Calibration samples were prepared in the same way. Calibration and quantification were performed using an external standard. Substances were identified according to their retention times and MRM transitions.

Table 1. MRM transitions

Q1 (*m*/*z*)	Q3 (*m*/*z*)	RT (min)		DP (V)	EP (V)	CEP (V)	CE (V)	CXP (V)
112	95	4.24	Histamine	31	5.1	6.4	17.6	3.1
122	105	0.91	Phenylethylamine	36	4.0	7.7	16.0	2.7
138	121	1.53	Tyramine	33	4.0	8.8	14.5	2.8
161	144	1.21	Tryptamine	33	3.6	10.1	16.0	3.0
89	72	4.36	Putrescine	27	5.6	5.5	14.0	2.8
103	86	4.20	Cadaverine	30	5.4	7.5	14.0	2.6
146	129	5.13	Spermidine	40	4.2	9.9	16.0	2.9
203	129	5.59	Spermine	57	4.6	5.5	18.2	2.9
88	71	0.83	Isoamylamine	33	5.4	4.4	9.0	2.9
117	100	4.03	1,6-Diaminohexane	32	5.3	7.8	13.8	2.5

Q1 and Q3: precursor and product ions; RT: retention time; DP: potential declustering; EP: entrance potential; CEP: collision cell entrance potential; CE: collision energy; CX: collision cell exit potential; MRM transitions are monitored for each analyte.

Table 2. Results of HPLC/HILIC and results for repeatability and reproducibility of biogenic amines (μg L^{-1}) in white wine

BA	Range (μg L^{-1})	Slope	R^2	LOD (μg L^{-1})	LOQ (μg L^{-1})	Matrix Slope	Matrix R^2	SSE (%)
Histamine	10–1,000	523.0	0.9923	0.5	1.5	508.0	0.9874	97.1
Phenyethylamine	10–1,000	268.0	0.9937	1.0	3.0	271.0	0.9912	101.1
Tyramine	10–1,000	111.0	0.9879	2.5	7.5	119.0	0.9836	107.2
Tryptamine	10–1,000	51.4	0.9816	5.0	15.0	48.7	0.9754	94.7
Putrescine	10–1,000	192.0	0.9854	2.0	6.0	201.0	0.9817	104.7
Cadaverine	10–1,000	251.0	0.9895	1.0	3.0	265.0	0.9853	105.6
Spermidine	10–1,000	621.0	0.9968	0.5	1.5	609.0	0.9915	98.1
Spermine	20–2,000	79.4	0.9745	4.0	12.0	58.4	0.9637	73.6
Isoamylamine	10–1,000	498.0	0.9873	0.5	3.0	524.0	0.9812	105.2

Range: range of determination; slope: coefficients of the regression curves; R^2: correlation coefficient; LOD: limit of detection; LOQ: limit of quantification; Matrix Slope: coefficients of the regression curves in matrix; Matrix R^2: correlation coefficient in matrix; SSE: signal suppression enhancement.

2.3. Determination of biogenic amines

The HPLC/HILIC method with electrospray ionisation (ESI) was used for the separation and detection of biogenic amines (Table 2). The determination of the individual biogenic amines in wine samples was performed by comparison with the MS/MS data obtained for the standards and analysed under the same experimental conditions as in previous studies (Sagratini et al., 2012; Daniel et al., 2015). This method is simple, fast, and without sample derivatisation prior to HPLC analysis (Tashev et al., 2016). An InfinityLab Poroshell 120 (HILIC-Z, 2.1 × 150 mm, 2.7 μm) column was used for analysis.

Linearity was tested at seven concentration levels. The linearity data are presented in Table 2. The linearity was satisfactory in all cases with correlation coefficients ($R^2 > 0.97$) ranging from 0.9745 for spermine to 0.9968 for spermidine. The limit of detection (LOD) was determined as the concentration of the analyte that gives a signal equal to the average background (S_{blank}) plus three times the standard deviation of the blank (s_{blank}) as follows: $LOD = S_{blank} + 3 \times (s_{blank})$. The limit of quantification (LOQ) was determined using the following equation: $LOQ = 3 \times LOD$. The obtained values for LOD and LOQ ranged from 0.5 to 5 μg L^{-1} and from 1.50 to 15 μg L^{-1}, respectively.

The signal suppression enhancement (SSE) was calculated as the ratio of the slope of the standards in the wine matrix and the slope of the standards prepared without a matrix to evaluate the matrix effect (Sagratini et al., 2012). The wine matrix has a diverse influence on each biogenic amine. SSE >100% is caused by the signal enhancement and more efficient ionisation, whereas SSE <100% is caused by ionisation suppression in the presence of the matrix. A negative influence of the wine matrix was observed for spermine (SSE 73.6), tryptamine (SSE 94.7), histamine (SSE 97.1), and spermidine (SSE 98.1). A positive effect of the wine matrix was observed for phenylethylamine (SSE 101.1), putrescine (SSE 104.7), cadaverine (SSE 105.6), and tyramine (SSE 107.2). Based on these results, this method for the determination of biogenic amines in wine samples using a HILIC column can be successfully used for all studied

biogenic amines with a calibration curve standard in an aqueous solvent. None of the monitored biogenic amines had a signal suppression of more than 73.6%. Tashev et al. (2017) used an Agilent Zorbax C18 Plus (100 × 2.1 mm, 1.8 µm particle size) column and reported a higher signal suppression for spermine (SSE 39), resulting in a higher negative effect of the wine matrix. Chromatograms of standards and samples are in Attachment 1 – 6, available at the server of Publisher.

2.4. Statistical analysis

Statistical analysis and graphs were created using MS Excel 2010 (Microsoft Office, USA) and Statistica 10 (StatSoft, Czech Republic). A one-way analysis of variance (ANOVA) and Fischer's least significant difference (LSD) test were used to compare the means ($n = 3$) at the level of significance of $P = 0.05$.

3. RESULTS AND DISCUSSION

Figure 1 shows the results of the determination of individual biogenic amines, including histamine, isoamylamine, cadaverine, putrescine, spermidine, and spermine, in wines. Phenylethylamine, tyramine, tryptamine, and serotonin were also measured, but these amines were not detected in the wines tested in the present study.

The results of the present study showed that the concentrations of histamine and putrescine were not significantly different in Variants 1 and 2. Martínez-Pinilla et al. (2013) found no correlation between total amino acids and total biogenic amines after malolactic fermentation, suggesting that a higher initial concentration of amino acids in the medium does not affect the concentration of biogenic amines after malolactic fermentation. Martín-Álvarez et al. (2006) studied the effect of the amount of available amino acids as a consequence of several technological factors, including the length of skin maceration, and they reported that 2- or 4-fold lower concentrations of histamine and putrescine were detected in red wines produced with shorter skin maceration.

Variant 1 contained lower concentrations of isoamylamine, cadaverine, spermidine, and spermine compared to Variant 2. Yeasts generally present in wine are considered responsible for the formation of biogenic amines, such as histidine, tyramine, spermidine, ethanolamine, and cadaverine (Caruso et al., 2002; Torrea and Ancín, 2002; Landete et al., 2007; Wang et al., 2014). However, the contribution of yeast microflora and amino acid precursors to biogenic acid production in wine is controversial, and the results of different studies are inconsistent. Vidal-Carou et al. (1990a) reported formation of histamine and tyramine during alcoholic fermentation, but Lopéz-Rituerto et al. (2013) reported that the production of histamine in wine is the consequence of malolactic fermentation and not of alcoholic fermentation. However, in general, it is agreed that BAS formation by LAB during MLF is more significant than the contribution of yeast during alcoholic fermentation (Vidal-Carou et al., 1990b; Goñi and Azpilicueta, 2001; Smit et al., 2013). The more diverse bacterial microflora caused by spontaneous malolactic fermentation in Variant 2 should cause a significant increase in biogenic amines, which was not confirmed for histamine and putrescine. Lactic acid bacteria can produce biogenic amines simultaneously, and some strains may have more amino acid decarboxylase enzymes (Coton et al., 1998; Moreno-Arribas et al., 2000). Depending on environmental conditions, both *Oenococcus oeni* strains with histamine-forming capacity and strains without this capacity have been

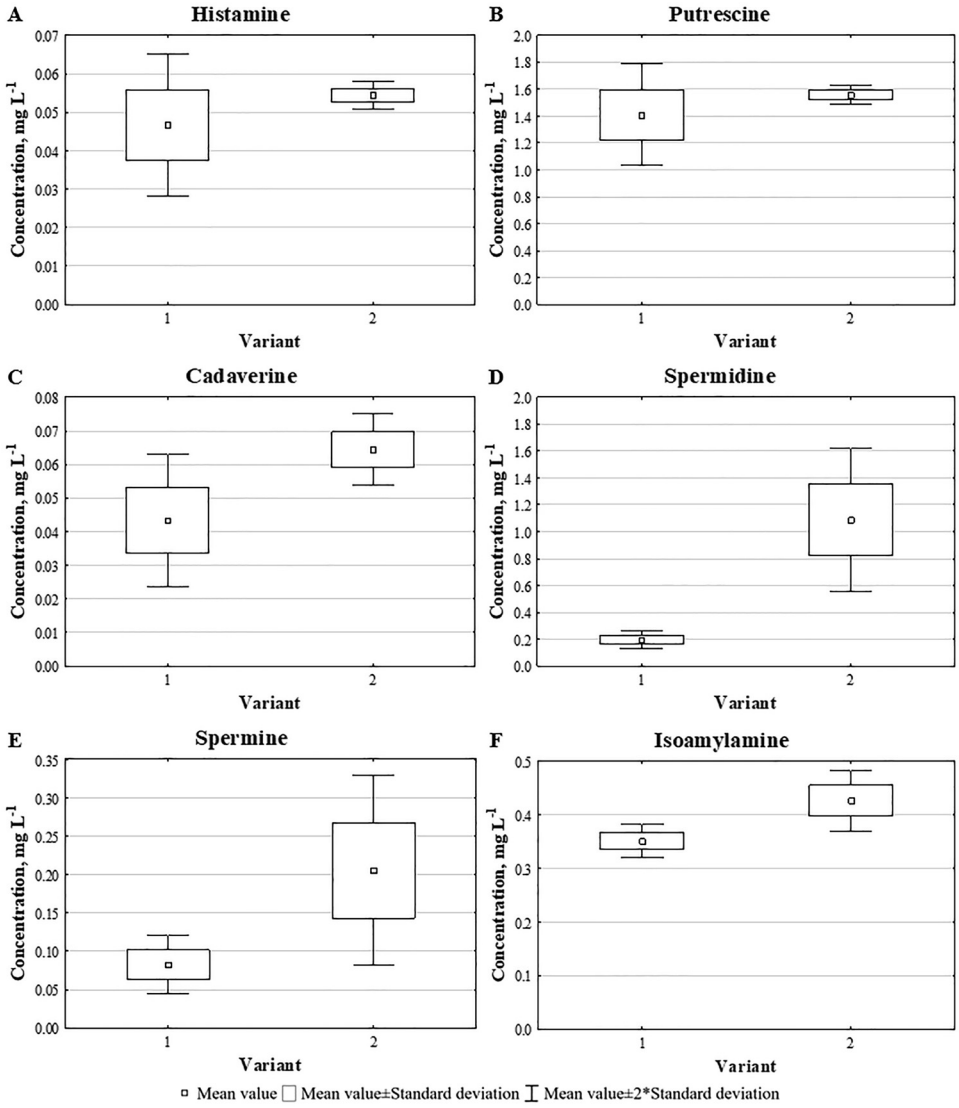

Fig. 1. Concentration of: A: histamine; B: putrescine; C: cadaverine; D: spermidine; E: spermine; F: isoamylamine (1: sedimented must, inoculated alcoholic fermentation without malolactic fermentation; 2- non-sedimented must, spontaneous fermentation with spontaneous malolactic fermentation)

isolated from wine (Coton et al., 1998; Moreno-Arribas et al., 2000; Landete et al., 2005; Garai et al., 2007).

Conflicting results have been explained in a review by Garcia-Moruno and Muñoz (2012), who suggested that the following factors attribute to the contradictory results: absence of validated controls, such as histamine-producing *O. oeni* strains; analytical errors affecting the published results; very low reported HIS concentration produced by *O. oeni* strains; and the

presence of contradictory data for the same strain or method, i.e., *Lactobacillus* with reference to *L. buchneri, L. brevis, L. hilgardii, L. mali, Leuconostoc* spp., and *L. mesenteroides*, which are frequently linked with BA production in wine.

The higher values of several biogenic amines, namely, cadaverine, spermidine, spermine, and isoamylamine, in Variant 2 can be explained by spontaneous malolactic fermentation when there is a different population of lactic bacteria in the wine. Henríquez-Aedo et al. (2016) isolated *Lactobacillus rhamnosus* as the predominant species in Chilean Cabernet Sauvignon, in which spontaneous malolactic fermentation is performed during the wine-making process, and they suggested that *L. rhamnosus,* with the highest aminogenic capacity, is the principal species responsible for biogenic amine formation in their study. Other species of bacteria, such as *Pediococcus*, also often occur during spontaneous malolactic fermentation and affect not only the formation of biogenic amines but also the further spoilage of wine. Lonvaud-Funel (2001) and Landete et al. (2007) suggested that *P. damnosus* and *P. parvulus* are responsible for histamine production. Additionally, some uncommon strains of *Enterococcus faecium*, *Gluconobacter oxydans*, *Asaia siamensis*, *Serratia* sp., and *Enterobacter* sp. have been reported in wine, grape, and musts, and these strains can produce histamine (Ruiz et al., 2010; Capozzi et al., 2011; Garcia-Moruno and Muñoz, 2012; Pérez-Martín et al., 2014).

There are currently no uniform limits in the EU for the content of biogenic amines in wines. The literature has reported that different countries have established upper limits of histamine in wine: 2 mg L^{-1} in Germany, 5 mg L^{-1} in Finland, 10 mg L^{-1} in Australia and Switzerland, 8 mg L^{-1} in France, 3.5 mg L^{-1} in Netherlands, and 6 mg L^{-1} in Belgium (Smit et al., 2008). In this study, the average concentration of histamine in Variant 1 and 2 was 0.05 mg L^{-1}. OIV with regard to Resolution OENO 4/97, in view of the actions K.4 of the 2009–2012 strategic plan of the OIV, which intends in particular to propose the means to detect and limit the presence of contaminants in vine-based products; and taking into account the principles provided for in Resolution CST 1/2004 on the development of a sustainable viticulture and resolution CST 1/2008, decides to adopt, as follows, the code of good vitivinicultural practices in order to minimise the presence of biogenic amines in wines, establishing the actions to be carried out in vineyards and wineries to help reduce the risks related to the presence of biogenic amines in wines (OIV, 2011).

4. CONCLUSIONS

The HPLC/HILIC method with ESI was used for separation and detection of biogenic compounds without sample derivatisation prior to HPLC analysis. This method was successfully used to determine the most abundant biogenic amines in wine samples. None of the monitored biogenic amines had a signal suppression of more than 73.6%.

Statistically significant differences were found in the concentrations of cadaverine, isoamylamine, spermine, and spermidine. The highest values were found in Variant 2, which was made from nonsedimented must fermented spontaneously and with malolactic fermentation.

SUPPLEMENTARY MATERIALS

Supplementary data to this article can be found online at https://doi.org/10.1556/066.2022.00247.

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REFERENCES

Ailer, Š. (2016). *Vinárstvo & somelierstvo*. Agriprint, Olomouc. ISBN 978-80-87091-63-0.

Alpert, A.J. (1990). Hydrophilic-interaction chromatography for the separation of peptides, nucleic acids and other polar compounds. *Journal of Chromatography A*, 499: 177–196. https://doi.org/10.1016/S0021-9673(00)96972-3.

Capozzi, V., Ladero, V., Beneduce, L., Fernández, M., Alvarez, M.A., Benoit, B., Laurent, B., Grieco, F., and Spano, G. (2011). Isolation and characterization of tyramine-producing *Enterococcus faecium* strains from red wine. *Food Microbiology*, 28(3): 434–439. https://doi.org/10.1016/j.fm.2010.10.005.

Caruso, M., Fiore, C., Contursi, M., Salzano, G., Papaprella, A., and Romano, P. (2002). Formation of biogenic amines as criteria for the selection of wine yeasts. *World Journal of Microbiology and Biotechnology*, 18: 159–163. https://doi.org/10.1023/A:1014451728868.

Caude, M.J. and Jardy, A. (1998). Normal-phase liquid chromatography. In: Katz, E., Eksteen, R., Schoenmakers, P., and Miller, N. (Eds.), *Handbook of HPLC*. New York; Marcel Dekker, pp. 325–363.

Coton, E., Rollan, G., Bertrand, A., and Lonvaud-Funel, A. (1998). Histamine-producing lactic acid bacteria in wines: early detection, frequency, and distribution. *American Journal of Enology and Viticulture*, 49: 199–204. https://doi.org/10.5344/ajev.1998.49.2.199.

Daniel, D., dos Santos, V.B., Vidal, D.T.R., and do Lago, C.L. (2015). Determination of biogenic amines in beer and wine by capillary electrophoresis–tandem mass spectrometry. *Journal of Chromatography A*, 1416: 121–128. https://doi.org/10.1016/j.chroma.2015.08.065.

Doyle, C.A., and Dorsey, J.G. (1998): Reversed-phase HPLC: preparation and characterization of reversed-phase stationary phases. In: Katz, E., Eksteen, R., Schoenmakers, P., and Miller, N. (Eds.), Handbook of HPLC. New York; Marcel Dekker, pp. 293–323.

Garcia-Moruno, E. and Muñoz, R. (2012). Does *Oenococcus oeni* produce histamine? *International Journal of Food Microbiology*, 157(2): 121–129. https://doi.org/10.1016/j.ijfoodmicro.2012.05.013.

Garai, G., Dueñas, M.T., Irastorza, A., and Moreno-Arribas, M.V. (2007). Biogenic amine production by lactic acid bacteria isolated from cider. *Letters in Applied Microbiology*, 45(5): 473–478. https://doi.org/10.1111/j.1472-765X.2007.02207.x.

Gianotti, V., Chiuminatto, U., Mazzucco, E., Gosetti, F., Bottaro, M., Frascarolo, P., and Gennaro, M.C. (2008). A new hydrophilic interaction liquid chromatography tandem mass spectrometry method for the simultaneous determination of seven biogenic amines in cheese. *Journal of Chromatography A*, 1185: 296–300. https://doi.org/10.1016/j.chroma.2008.02.038.

Goñi, D.T. and Azpilicueta, C.A. (2001). Influence of yeast strain on biogenic amines content in wines: relationship with the utilization of amino acids during fermentation. *American Journal of Enology and Viticulture*, 52: 185–190. https://doi.org/10.5344/ajev.2001.52.3.185.

Guo, Y.-Y., Yang, Y.-P., Peng, Q., and Han, Y. (2015). Biogenic amines in wine: a review. *International Journal of Food Science & Technology*, 50(7): 1523–1532. https://doi.org/10.1111/ijfs.12833.

Henríquez-Aedo, K., Durán, D., Garcia, A., Hengst, M.B., and Aranda, M. (2016). Identification of biogenic amines-producing lactic acid bacteria isolated from spontaneous malolactic fermentation of Chilean red wines. *LWT - Food Science and Technology*, 68: 183–189. https://doi.org/10.1016/j.lwt.2015.12.003.

Landete, J.M., Ferrer, S., Polo, L., and Pardo, I. (2005). Biogenic amines in wines from three Spanish regions. *Journal of Agricultural and Food Chemistry*, 53(4): 1119–1124. https://doi.org/10.1021/jf049340k.

Landete, J.M., Ferrer, S., and Pardo, I. (2007). Biogenic amine production by lactic acid bacteria, acetic bacteria and yeast isolated from wine. *Food Control*, 18(12): 1569–1574. https://doi.org/10.1016/j.foodcont.2006.12.008.

Lonvaud-Funel, A. (2001). Biogenic amines in wines: role of lactic acid bacteria. *FEMS Microbiology Letters*, 199(1): 9–13. https://doi.org/10.1111/j.1574-6968.2001.tb10643.x.

Lopéz-Rituerto, E., Avenoza, A., Busto, J.H., and Peregrina, J.M. (2013). NMR Study of histidine metabolism during alcoholic and malolactic fermentations of wine and their influence on histamine production. *Journal of Agricultural and Food Chemistry*, 64(39): 9464–9469. https://doi.org/10.1021/jf402489g.

Martín-Álvarez, P.J., Marcobal, Á., Polo, C., and Moreno-Arribas, M.V. (2006). Influence of technological practices on biogenic amine contents in red wines. *European Food Research and Technology*, 222: 420–424. https://doi.org/10.1007/s00217-005-0142-7.

Martínez-Pinilla, O., Guadalupe, Z., Hernández, Z., Ayestarán, B. (2013). Amino acids and biogenic amines in red varietal wines: the role of grape variety, malolactic fermentation and vintage. *European Food Research and Technology*, 237: 887–895. https://doi.org/10.1007/s00217-013-2059-x.

Moreno-Arribas, V., Torlois, S., Joyeux, A., Bertrand, A., and Lonvaud-Funel, A. (2000). Isolation, properties and behaviour of tyramine-producing lactic acid bacteria from wine. *Journal of Applied Microbiology*, 88(4): 584–593. https://doi.org/10.1046/j.1365-2672.2000.00997.x.

OIV (2009). Analysis of biogenic amines in musts and wines using HPLC. Resolution OIV/OENO 346/2009.

OIV (2011). OIV Code of good vitivinicultural practices in order to minimise the presence of biogenic amines in vine-based products. Resolution OIV-CST 369-2011.

Pérez-Martín, F., Seseña, S., Izquierdo, P.M., and Palop, M.L. (2014). Are *Enterococcus* populations present during malolactic fermentation of red wine safe? *Food Microbiology*, 42: 95–101. https://doi.org/10.1016/j.fm.2014.03.001.

Rizzi, A. (1998). Retention and selectivity. In: Katz, E., Eksteen, R., Schoenmakers, P., and Miller, N. (Eds.), Handbook of HPLC. New York; Marcel Dekker, pp. 1–54.

Ruiz, P., Seseña, S., Izquierdo, P.M., and Palop, M.L. (2010). Bacterial biodiversity and dynamics during malolactic fermentation of Tempranillo wines as determined by a culture-independent method (PCR-DGGE). *Applied Microbiology and Biotechnology*, 86: 1555–1562. https://doi.org/10.1007/s00253-010-2492-8.

Sagratini, G., Fernández-Franzón, M., de Berardinis, F., Font, G., Vittori, S., and Mañes, J. (2012). Simultaneous determination of eight underivatised biogenic amines in fish by solid phase extraction and liquid chromatography–tandem mass spectrometry. *Food Chemistry*, 132(1): 537–543. https://doi.org/10.1016/j.foodchem.2011.10.054.

Silla Santos, M.H. (1996). Biogenic amines: their importance in foods. *International Journal of Food Microbiology*, 29(2–3): 213–231. https://doi.org/10.1016/0168–1605(95)00032-1.

Smit, A.Y., du Toit, W., and du Toit, M. (2008). Biogenic amines in wine: understanding the headache. *South African Journal for Enology and Viticulture*, 29: 109–127. https://doi.org/10.21548/29-2-1444.

Smit, A.Y., du Toit, W., Stander, M.A., and du Toit, M. (2013). Evaluating the influence of maceration practices on biogenic amine formation in wine. *LWT – Food Science and Technology*, 53(1): 297–307. https://doi.org/10.1016/j.lwt.2013.01.006.

Tashev, K., Ivanova-Petropulos, V., and Stefova, M. (2016). Optimization and validation of a derivatization method for analysis of biogenic amines in wines using RP-HPLC-DAD. *Macedonian Journal of Chemistry and Chemical Engineering*, 35: 19–28. https://doi.org/10.20450/mjcce.2016.884.

Tashev, K., Ivanova-Petropulos, V., and Stefova, M. (2017). Ultra-performance liquid chromatography-triple quadruple mass spectrometry (UPLC-TQ/MS) for evaluation of biogenic amines in wine. *Food Analytical Methods*, 10: 4038–4048. https://doi.org/10.1007/s12161-017-0936-9.

Torrea, D. and Ancín, C. (2002). Content of biogenic amines in a Chardonnay wine obtained through spontaneous and inoculated fermentations. *Journal of Agricultural and Food Chemistry*, 50(17): 4895–4899. https://doi.org/10.1021/jf011653h.

Vidal-Carou, M.C., Ambatlle-Espunyes, A., Ulla-Ulla, M.C., and Marine-Font, A. (1990a). Histamine and tyramine in Spanish wines: their formation during the winemaking process. *American Journal of Enology and Viticulture,* 41: 160–167. https://doi.org/10.5344/ajev.1990.41.2.160.

Vidal-Carou, M.C., Codony-Salcedo, R., and Mariné-Font, A. (1990b). Histamine and tyramine in Spanish wines: relationships with total sulfur dioxide level, volatile acidity and malo-lactic fermentation intensity. *Food Chemistry*, 35: 217–227. https://doi.org/10.1016/0308-8146(90)90035-3.

Wang, Y.-Q., Ye, D.-Q., Zhu, B.-Q., Wu, G.-F., and Duan, C.-Q. (2014). Rapid HPLC analysis of amino acids and biogenic amines in wines during fermentation and evaluation of matrix effect. *Food Chemistry*, 163: 6–15. https://doi.org/10.1016/j.foodchem.2014.04.064.