Effects of Low-Altitude and High-Altitude Meteorological Factors on Berry Quality and Metabolome of 'Merlot' Grapes (Postprint)

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Abstract

To elucidate the differences and underlying causes in berry metabolome and quality between low-altitude (41 m) and high-altitude (2,343 m) 'Merlot' grape growing regions, this study employed GPRS-Base system weather stations to monitor meteorological factors in both regions, utilized gas chromatography/time-of-flight mass spectrometry (GC/TOF-MS) to parse the metabolomic differences in 'Merlot' berries, and determined the contents of soluble solids, pH, total acidity, reducing sugars, anthocyanins, total phenolics, tannins, flavones, flavonoids, and proteins in 'Merlot'grape berries at different altitudes. The results demonstrated that meteorological factors including average sunshine hours, total radiation during the growth period, daily average radiation, daily average temperature difference, daily average temperature, and effective accumulated temperature during the growth period were all higher in the high-altitude 'Merlot' grape region compared to the low-altitude region. Compared with the low-altitude region, 'Merlot' grape berries from the high-altitude region exhibited increased contents of soluble solids, tannins, and reducing sugars, while total phenolics and anthocyanins decreased. Metabolic pathway analysis revealed that grape berries in the high-altitude region accumulated greater amounts of amino acids, organic acids, alcohols, polyphenols, carbohydrates, and other substances. Metabolic pathway enrichment analysis indicated that the high-altitude region altered eight amino acid metabolism pathways, four carbohydrate metabolism pathways, three lipid metabolism pathways, and three nitrogen metabolism pathways in grape berries. Detrended Correspondence Analysis showed that meteorological factors in 'Merlot' vineyards, such as daily average sunshine hours, total radiation during the growth period, daily average radiation, temperature difference, daily average temperature, and effective accumulated temperature during the growth period, were the primary drivers of metabolite accumulation in 'Merlot' berries. The differences in meteorological factors between high- and

low-altitude regions constitute an important driving force for metabolite differences in 'Merlot' grape berries; 'Merlot' grape berries in high-altitude regions adapt to the high-altitude environment and enhance berry quality through a diversified strategy of metabolites and metabolic pathways.

Full Text

Preamble

Response of 'Merlot' grape berry quality and metabolome to meteorological factors at both low and high altitudes*

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Abstract
To elucidate the differences in berry metabolome and quality between low-altitude (41 m) and high-altitude (2,343 m) 'Merlot' grape production regions and their underlying causes, this study monitored meteorological factors in both regions using a GPRS-Base system weather station. GC/TOF-MS technology was employed to analyze metabolomic differences in 'Merlot' berries between altitudes, while berry quality parameters including soluble solids content, pH, total acidity, reducing sugars, anthocyanins, total phenols, tannins, flavonoids, and protein content were measured. Results showed that high-altitude 'Merlot' vineyards exhibited higher average sunshine duration, total radiation during the growth period, average daily radiation, average daily temperature difference, average daily temperature, and effective accumulated temperature compared to low-altitude regions. Compared with low-altitude regions, berries from high-altitude regions showed increased soluble solids, tannin, and reducing sugar contents, but decreased total phenol and anthocyanin contents. Metabolic pathway analysis revealed that high-altitude berries accumulated more amino acids, organic acids, alcohols, polyphenols, and sugars. Pathway enrichment analysis indicated that high-altitude conditions altered eight amino acid metabolic pathways, four carbohydrate pathways, three lipid pathways, and three nitrogen metabolism pathways in grape berries. Detrended Canonical Correspondence Analysis (DCCA) demonstrated that meteorological factors including average daily sunshine duration, total radiation during growth, average daily radiation, temperature difference, average daily temperature, and effective accumulated temperature were the primary drivers of metabolite accumulation in 'Merlot' berries. Differences in meteorological factors between altitudes constitute a major driving force for metabolite variation, with high-altitude 'Merlot' berries employing diverse metabolic strategies to adapt to high-elevation environments and enhance berry quality.

Keywords: 'Merlot' grape berry; Altitude gradient; Metabolite; Metabolome; Climatic factor; Metabolic pathway; Pathway enrichment

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'Merlot' grape (*Vitis vinifera* L. cv. Merlot), also known as 'Meiluo' or 'Meiluzhe' , is cultivated across more than 260,000 hectares worldwide (OIV) and ranks among the three major red grape varieties globally. It was originally used for producing premium wines in Saint-Émilion and Pomerol and is now widely planted in wine regions worldwide. Merlot exhibits good stress resistance, early maturity, and rich fruit flavors, enabling normal development even under unusual climatic conditions, and is often blended with other varieties in winemaking [1-5]. Research indicates that terroir factors—including soil, topography, altitude, slope, aspect, and cultivation management—significantly influence grape berry metabolite composition [6-8]. Metabolites such as amino acids, organic acids, higher alcohols, phenolic compounds, and sugars represent adaptive products of grapes to their environment, participating in multiple metabolic pathway regulations and serving as important nutrients for humans [1,5,9-18]. Among these factors, altitude gradient represents a primary constraint affecting wine grape quality and metabolome. In recent years, 'Merlot' has been extensively planted across Chinese wine regions, including Yantai in East China, Changli in Hebei (0-1,400 m altitude), Panxi in Southwest Plateau (1,200 m), Mile in Yunnan (1,500 m), and high-altitude dry-cold valley regions such as Deqin County in Yunnan (2,343 m) and Xiaojin County in Sichuan (2,500 m). However, research on quality characteristics and metabolite accumulation patterns of 'Merlot' berries in high-altitude regions remains limited, necessitating quantitative and qualitative studies of berry metabolites across altitude gradients.

Metabolomics technology has been increasingly applied to study organismal responses to environmental conditions [19], providing an effective analytical approach to explain metabolite and quality differences between high- and low-altitude grapes. This study employed gas chromatography/time-of-flight mass spectrometry (GC/TOF-MS) [20] to analyze metabolomic differences in 'Merlot' berries between high-altitude (2,343 m) and low-altitude (41 m) regions. UV spectrophotometry, widely used for grape and wine quality analysis [21-22], was applied to determine berry composition including soluble solids, pH, total acidity, reducing sugars, anthocyanins, total phenols, tannins, flavonoids, and soluble protein content. Integrated Pathway Analysis (IPA) was utilized to investigate metabolic pathway differences, Metabolite Pathway Enrichment Analysis (MEPA) to examine pathway enrichment [23-25], and Detrended Canonical Correspondence Analysis (DCCA) to correlate berry metabolites with meteorological factors across altitudes. These approaches aimed to elucidate the adaptability and quality characteristics of 'Merlot' grapes to high-altitude environments from a metabolomic perspective, understand the determinants of high-altitude grape quality, and provide a theoretical foundation for 'Merlot' grape and wine production in high-altitude regions.

1.1 Experimental Sites

From 2013 to 2014, two 'Merlot' vineyards at 41 m and 2,343 m altitude were selected for two consecutive years of study . Both vineyards contained six-year-old vines. The 2,343 m vineyard represents a low-latitude, high-altitude region located in the Lancang River valley on a shady slope with 10°–30° incline and 500 m elevation difference from the river surface. The 41 m vineyard is situated in a low-altitude region north of the Tropic of Cancer on flat plains, 10 km from the Bohai Sea/Yellow Sea junction, representing a classic Chinese wine region and the birthplace of modern Chinese viticulture.

1.3 Berry Sampling and Processing

In each vineyard, 60 vines were randomly selected with 16 fruiting shoots per vine. Two kilograms of mature berries were harvested at 120 days post-anthesis. One kilogram of berries was stored at 4°C and transported to the laboratory for subsequent processing according to reference [21], with prepared samples stored at -20°C for determination of soluble solids, pH, total acidity, reducing sugars, anthocyanins, total phenols, tannins, flavonoids, and soluble protein content. The remaining one kilogram of berries was randomly mixed, divided into 18 50 mL centrifuge tubes, and preserved in liquid nitrogen at -80°C for metabolomic analysis.

1.4 Berry Quality Analysis

Soluble solids content was measured using a temperature-compensated digital refractometer (Antago PAL-1, Japan) at 25°C following reference [21]. pH and total acidity were determined using a Ti-touch titrator (Metrohm, Switzerland) with pH 8.2 as the titration endpoint (OIV, 1990), with total acidity expressed as $g \cdot L^{1}$. Reducing sugars, anthocyanins, total phenols, tannins, flavonoids, and flavones were measured according to reference [22], while soluble protein content was determined using the Bradford method. All compound contents were expressed as $mg \cdot g^{1}$, except reducing sugars ($g \cdot L^{1}$).

1.5 Berry Metabolome Analysis

From each experimental site, berry flesh, skin, and seeds were collected using a cork borer. After mixing, 100 mg of grape sample was placed in a 2 mL centrifuge tube in triplicate for metabolite extraction [26] and metabolomic analysis [27].

1.6 Data Analysis

Variance analysis was used to examine differences in berry quality indices between altitudes, while Partial Least Squares Discriminant Analysis (PLS-DA) was applied to analyze quality variation distribution. Meteorological data from 2013–2014, including average temperature difference, maximum temperature difference, average daily temperature, effective accumulated temperature during growth, average daily relative humidity, rainfall, average daily sunshine duration, average daily radiation intensity, total radiation intensity, average daily UV radiation, and total UV radiation, were compiled. IPA was used to analyze metabolic pathway differences, and MEPA was employed for pathway enrichment analysis [23–25]. DCCA in Concoco 5.0 software correlated quality factors and differential metabolites with meteorological factors across altitudes.

2 Results and Analysis

Meteorological data were collected using a GPRS-Base system weather station at both altitude gradients, following agricultural meteorological monitoring standards. Light radiation, temperature, rainfall, and relative humidity were monitored continuously for two years, with data recorded every 15 minutes.

2.1 Meteorological Characteristics of 'Merlot' Vineyards at Different Altitudes

As shown in Table 2 , the high-altitude vineyard exhibited higher average daily temperature difference, effective accumulated temperature during growth, rainfall, sunshine radiation, and UV radiation compared to the low-altitude region. Conversely, relative humidity, average daily temperature, and atmospheric oxygen content were lower at high altitude.

2.2 Quality and Metabolite Characteristics of 'Merlot' Berries at Different Altitudes

High-altitude 'Merlot'berries showed significantly higher total phenol and soluble solids contents compared to low-altitude berries, while anthocyanin and tannin contents were significantly lower. No significant differences were observed in reducing sugars, protein, tartaric acid, flavonoids, flavones, or pH (Table 3).

PLS-DA analysis revealed highly significant quality differences between high- and low-altitude berries. PC1 and PC2 cumulatively explained 85.9% of variance, representing all quality factors (Figure 1A [Figure 1: see original paper]). High-altitude conditions positively correlated with pH, total acidity, tannins, total flavonoids, and reducing sugars, while negatively correlating with soluble protein, total phenols, flavones, soluble solids, and anthocyanins. PC1 and PC2 also captured altitude effects on metabolites (Figure 1B [Figure 1: see original paper]), showing positive correlations with -wheat germ phenol, maleamate, glycerol, phloretin, hesperetin, formononetin, coniferyl aldehyde, xylitol, N-methylglutamate, tartaric acid, fumaric acid, guanidinosuccinic acid, methylmalonic acid, threonic acid, glyceric acid, galactonic acid, shikimic acid, linoleic acid, oleic acid, mesaconic acid, gluconic acid, putrescine, xanthosine, proline, deoxyguanosine, 5-methoxytryptamine, N-formyl-L-methionine, S-carboxymethyl cysteine, glycine, thymidine, and other metabolites. Conversely, inositol, catechin, yeast sterol, mannitol, glycolic acid, succinate, diaminopimelic acid, stearic acid, mannose, ribose, ribitol, lactose, and resveratrol showed negative correlations with altitude.

2.3 Metabolic Pathways in 'Merlot' Berries at Different Altitudes

Higher alcohols and phenolic compounds are important berry constituents. Amino acid metabolic pathways (Figure 2 [Figure 2: see original paper]) showed that high-altitude conditions enhanced serine-to-glycine and cysteinylglycine pathways, pyruvate-to-5-methoxytryptamine, pyruvate-to-D-alanylalanine metabolism, oxaloacetate-to-N-formyl-L-methionine in the TCA cycle, 2-oxoglutarate-to-putrescine, 2-oxoglutarate-to-proline, guanine-to-deoxyguanosine, uric acid-to-thymidine, and inosinic acid-to-xanthosine metabolism.

Organic acid metabolic pathways (Figure 3 [Figure 3: see original paper]) revealed that high-altitude conditions enhanced glycerol-to-threonic acid, pyruvate-to-shikimic acid, acetyl-CoA-to-linoleic acid, acetyl-CoA-to-oleic acid, citrate-to-methylmalonic acid, succinate-to-guanidinosuccinic acid, tartaric acid, citrate-to-gluconic acid, urocanic acid, and galactitol-to-galactonic acid metabolism, while diminishing fumarate-to-succinate, citrate-to-diaminopimelic acid, pyruvate-to-glyceric acid, acetyl-CoA-to-stearic acid, and acetyl-CoA-to-malonic acid metabolism.

Higher alcohol and phenolic metabolic pathways (Figure 4 [Figure 4: see original paper]) demonstrated enhanced glyceraldehyde-to-glycerol, mannitol, pinoresinol-to-coniferyl aldehyde, tryptophan-to- -wheat germ phenol, glucose-to-N-methyl-glutamate, glucose-to-maleamate, malonyl-CoA-to-phloretin, glucitol-to-xylitol, glucoside-to-hesperetin and formononetin metabolism at high altitude, while suppressing glucose-to-ribitol, malonyl-CoA-to-catechin and resveratrol, 5-avenasterol-to-yeast sterol, and glucose-to-mannitol metabolism.

Sugar metabolic pathways (Figure 5 [Figure 5: see original paper]) showed enhanced 1-4 -galactosyl-fructose metabolism and reduced D-glucose-to-ribose and epimelibiose-to-mannose and galactose metabolism under high-altitude conditions.

2.4 Metabolic Pathway Enrichment in 'Merlot' Berries at Different Altitudes

Pathway enrichment analysis (Figure 6 [Figure 6: see original paper]) identified eight amino acid metabolic pathways, four carbohydrate pathways, three lipid pathways, and three nitrogen metabolism pathways. Amino acid metabolism represents crucial pathways for biosynthesis, degradation, and protein synthesis. High-altitude conditions enhanced valine, leucine, and isoleucine biosynthesis, as well as glycine, serine, and threonine metabolism. Additionally, galactose metabolism and fructose/mannose metabolism were enhanced, while starch and sucrose metabolism were reduced. High altitude also enhanced saturated fatty acid and glyceride biosynthesis while suppressing steroid and terpenoid backbone biosynthesis, and enhanced pyrimidine metabolism, amino sugar, and nucleotide sugar metabolism.

2.5 Relationship Between Environmental Meteorological Factors and 'Merlot' Berry Metabolites

DCCA analysis using Concoco 5.0 software (Figure 7 [Figure 7: see original paper]) revealed that average daily sunshine duration, total radiation during growth, average daily radiation, temperature difference, average daily temperature, and effective accumulated temperature were closely correlated with berry composition, metabolites enhanced at high altitude, and metabolites reduced at high altitude. Other factors such as atmospheric oxygen content, rainfall, humidity, growth-period sunshine duration, and UV radiation showed weak correlations. These results indicate that the primary meteorological drivers of metabolite differences between altitudes are sunshine duration, radiation parameters, temperature difference, average temperature, and effective accumulated temperature.

High-altitude 'Merlot' berries in this study achieved normal ripening with superior quality compared to low-altitude berries. High altitude increased multiple metabolites while decreasing others. Previous research suggested altitude limits grape yield and quality, reducing soluble solids and anthocyanins while increasing tartaric acid content [28]. This study demonstrates that at 2,343 m altitude, 'Merlot' berries can achieve high quality, indicating this elevation is suitable for premium 'Merlot' production.

Metabolic pathway analysis revealed that high altitude enhanced numerous pathways for amino acids, nucleotides, xanthosine, organic acids, glyceraldehyde, mannitol, coniferyl aldehyde, -wheat germ phenol, N-methylglutamate, maleamate, phloretin, xylitol, hesperetin, formononetin, and 1-4 -galactosyl-fructose metabolism, while suppressing ribose, galactose, succinate, diaminopimelic acid, glyceric acid, stearic acid, malonic acid, ribitol, catechin, resveratrol, and yeast sterol metabolism. Amino acids participate in various physiological functions, regulating berry ripening and abiotic stress resistance [16,29–32]. High-altitude conditions accelerate berry maturation, regulate postharvest physiology, enhance storage capacity and delayed harvest, and improve stress resistance and climate adaptation. Nucleotide and xanthosine metabolism, rarely reported in grape research, may contribute to biological functions not yet fully understood [30–31,33–40]. High altitude thus enhances berry quality and potential wine style. Organic acids regulate tannin concentration and lipid metabolism, modulate osmotic pressure and berry maturity, influence wine taste and style, and exhibit antioxidant, anticancer, and anti-apoptotic activities while regulating immune responses [7,11,15,37,29–36]. High-altitude environments thus improve grape quality and metabolite bioactivity. Higher alcohols and phenolics relate to wine taste, fungal resistance, abiotic stress tolerance, and anticancer properties [41–46], with high altitude enhancing taste, stress resistance, oxygen utilization efficiency, and health benefits. Sugars participate in diverse biological functions, including flavonoid and resveratrol synthesis, regulation of flavonoid pathways, cell wall and tartaric acid biosynthesis, and nutritional fiber provision [5,47–48], with high altitude enhancing these metabolic processes to improve grape quality.

Previous studies suggest metabolites achieve biological functions through feedback and negative feedback regulation of metabolic networks [24]. This study demonstrates that high-altitude 'Merlot' berries adjust metabolic pathways to accumulate quality factors and adapt to physical environments, with pathway differences between altitudes representing the fundamental cause of quality and flavor variation. Most metabolic pathways were enhanced under high-altitude conditions, leading to greater accumulation of flavor compounds compared to low-altitude regions.

Pathway enrichment analysis revealed that high altitude altered amino acid, carbohydrate, and lipid metabolism while suppressing steroid, terpenoid backbone, and nitrogen metabolism. Most metabolic pathways were enhanced in high-altitude berries, though glycine/serine/threonine metabolism, starch/sucrose metabolism, steroid biosynthesis, and terpenoid backbone biosynthesis were reduced. While pathway enrichment methods have been applied in metabolomics [23–25], their use in environmental studies on wine grapes remains limited. This study demonstrates that pathway enrichment effectively reveals altitude effects on grape berry metabolism, identifying key differential pathways that guide understanding of high-altitude wine grape quality determinants.

This study confirms that average sunshine duration, total radiation during growth, average daily radiation, temperature difference, average daily temperature, and effective accumulated temperature are the primary drivers regulating 'Merlot' berry quality and metabolites, validating previous research. Terroir conditions significantly affect grape quality [29], with factors such as sunshine duration, temperature variation, and UV radiation influencing berry composition [9,15,30–41]. Unlike other studies, this research employed DCCA, currently the most effective tool, to correlate vineyard meteorological factors with berry quality and metabolites, confirming the reliability of previous findings.

Meteorological factors at the 2,343 m vineyard constitute the primary reason for superior 'Merlot' berry quality compared to low-altitude regions. These factors drive metabolite accumulation through diverse metabolic pathways, enabling high-altitude 'Merlot' berries to accumulate more amino acids, organic acids, alcohols, polyphenols, and sugars. These metabolites adjust TCA cycle products and sugar, nucleotide, and phenolic metabolism through feedback regulation to adapt to high-altitude stress and enhance quality.

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