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Review

Bio-Dealcoholization of Wines: *Can Yeast Make Lighter Wines*?

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Abstract: The relationship between climate change and viticulture has become increasingly apparent in recent years. Rising temperatures have been a critical factor in early grape ripening. This, in turn, has led to wines with imbalanced acidity and, more importantly, higher alcohol content and pH values. Today, consumers demand high-quality and healthy products, and this trend has extended to wine consumption. Consumers prefer wines with reduced alcohol content due to the health risks associated with alcohol consumption. To meet this demand, researchers have developed modified yeast strains that reduce wine alcohol content during fermentation. These strains ferment less sugar or redirect carbon metabolism. However, their use may pose challenges, such as producing undesired secondary metabolites that can affect wine characteristics. Additionally, consumers are still divided on using genetically modified organisms (GMOs) in food and beverages. This review examines the impact of climate change on wine quality and consumer perception, taking into account new technologies used to reduce wine alcohol content or produce low-alcohol-content wines, such as low-cost techniques like bio-dealcoholization performed by non-GMO wine yeast, *Saccharomyces*, and non-*Saccharomyces*.

Keywords: climate change; post-fermentation; *Saccharomyces*; non-*Saccharomyces*; membrane separation; heat treatment

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1. Climate Change and Wine Quality

Climate change, primarily driven by anthropogenic influence, induces significant transformations in the Earth's system [1,2], including temperature extremes and modifications in precipitation patterns [3,4]. The latest Assessment Report of the Intergovernmental Panel on Climate Change (IPCC) [5] predicts a continued rise in global surface temperature and a decrease in annual precipitation across emission scenarios, with intensifying and more frequent extreme events globally [4,6]. The Mediterranean region is particularly vulnerable to global warming, with projected severe climate events affecting agriculture and leading to economic and food security challenges [7].

As indicated by Lamonaca et al. [8], detrimental outcomes, such as reductions in agricultural production and economic conditions associated with an increase in food insecurity, are anticipated to exacerbate, significantly affecting the agricultural sector [9,10]. This emphasizes the considerable vulnerability of agriculture to climate change, including viticulture. Despite being globally distributed, Europe hosts the world's largest vineyard area (approximately 40%), with a substantial portion in Mediterranean regions [11,12]. France, Italy, and Spain, the top wine-producing countries (Table 1), contribute significantly to the global wine sector [13].

Table 1. Top 5 wine-producing countries in 2022 (with respective rate of change from 2021 and % of global wine production in 2022). The table is based on wine production, defined by OIV, 2022 [13].

Country	Wine Production (Mhl)	Rate of Change	% of Global Wine Production
Italy	49.8	−1%	19.3%
France	45.6	21%	17.7%
Spain	35.7	1%	13.8%
USA	22.4	−7%	8.7%
Australia	12.7	−14%	4.9%

In 2022, wine exports from these three European countries amounted to around EUR 23 billion, emphasizing the economic importance of viticulture in Europe and globally, highlighting wine grapes as one of the most valuable fruit crops worldwide [2,14,15]. Additionally, global wine production in 2022 reached 258 million hectoliters, slightly lower than the previous year's output of 261 million hectoliters. Nevertheless, the vineyard area has decreased by approximately 1.18% over the past five years (from 2018 to 2022) due to extreme weather changes [13], underscoring that climate factors, particularly temperature, exert a more significant influence on vine development and berry composition relative to other factors such as soil or variety [16,17]. However, it is essential to acknowledge the multifaceted nature of these interactions, and the impact can vary based on specific vineyard locations [17].

This demonstrates that, as stated earlier, due to the strong relationship between viticulture and climate, fluctuations in temperature and frost events (early or late frosts) can directly impact grape production and the quality of the wine produced [3,6,18]. Increasing temperatures lead to premature grape ripening, culminating in an undesirable rise in sugar levels and a decrease in organic acids and phenolic compounds. This results in higher alcohol content, reduced acidity, and modified sensory profiles [18–20], ultimately altering wine quality and typicity [2,21,22]. Given the potential compromise of crop yields and viticulture productivity under future climatic conditions, the urgent adoption of cultivation approaches and strategies is crucial to mitigate the effects of climate change on wine production and quality.

Moreover, recent data indicate a growing consumer preference for low-alcohol wines (9% to 13%). This preference is associated with increased social awareness of the harmful effects of alcohol on human health (calorific intake and possibility of alcohol-related diseases) as consumers seek a healthier lifestyle [23–26]. This has led to an increase in the volume of no and low-alcohol beverages of over 7% across the 10 major global markets in 2022. This upward trajectory is projected to outpace the growth observed in the past four years, with a forecasted Compound Annual Growth Rate (CAGR) of over 7% from 2022 to 2026. This forecasted rate represents an increase compared to the 5% CAGR recorded from 2018 to 2022 (Figure 1). In this context, wine producers are innovatively lowering alcohol content to meet consumer demands and address challenges posed by high grape sugar concentration during winemaking. Musts with high sugar content usually present difficulty in performing alcoholic fermentation, causing stuck or sluggish fermentation, leading to prolonged and intricate processes or even complete stoppage [24,25,27,28]. These issues arise from the osmotically stressful environment of high sugar concentrations, hindering water absorption and slowing yeast metabolic activity. The resulting alcohol production can reach toxic levels for the yeast, and the must's nutritional conditions and the potential presence of fermentation inhibitors further contribute to the complications [29]. Furthermore, in some countries, such as the USA, Finland, Sweden, Ireland, and the United Kingdom, exceeding 14.5% (v/v) alcohol content results in higher taxes [24,30,31].

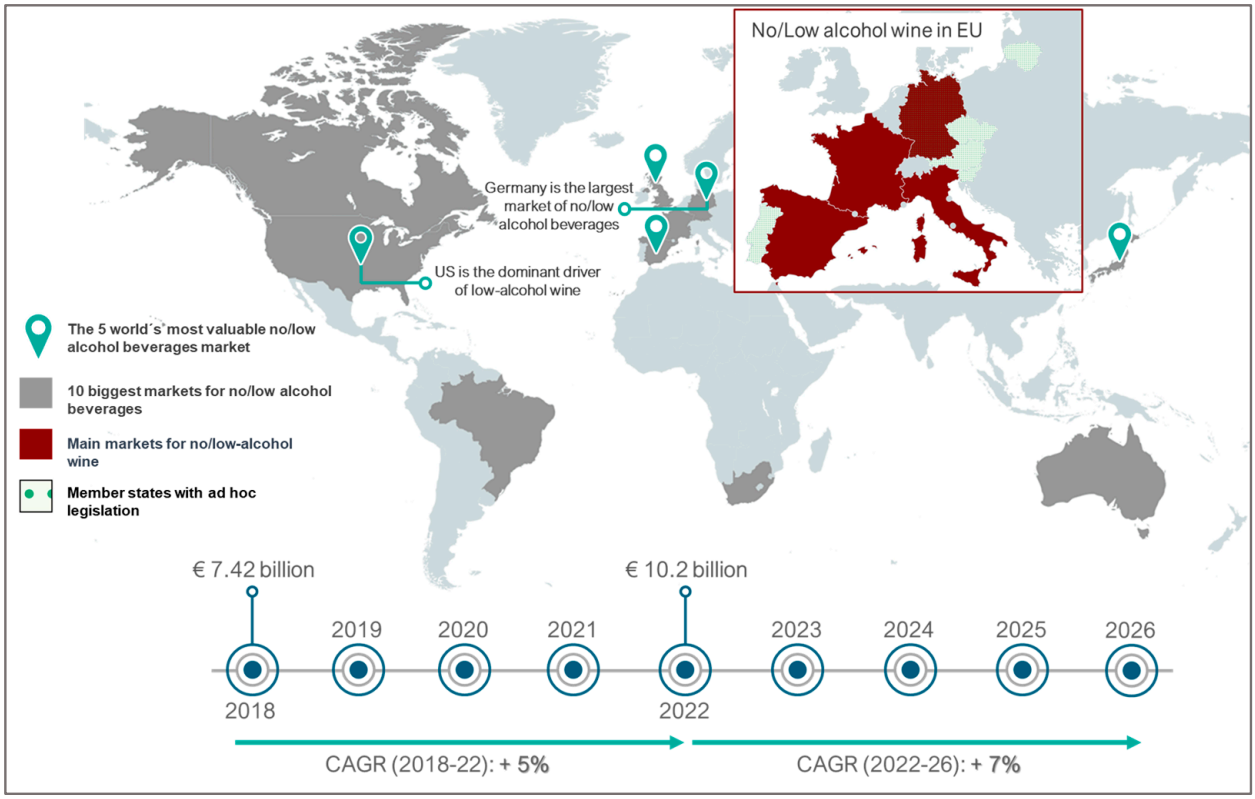

Figure 1. Overview of global market trends for no-alcohol and low-alcohol beverages, including wine. Sources: [32,33].

This review aims to overview the problem of climate change and its impact on wine quality, typicity, and composition, namely increased alcohol content, and link it to traditional and new technologies used to reduce that content. The overviewed strategies include pre-fermentation approaches, like early-harvest of grapes, fermentation modifications, for instance, using non-*Saccharomyces* yeasts, or post-fermentation prospects, namely bio-dealcoholization performed by *Saccharomyces* and non-*Saccharomyces* yeasts. Finally, consumers' perspective on low-alcohol wines is also addressed, as they are a critical factor in the wine industry.

1.1. Impact of Climate Changes on Wine Sensory Perception

1.1.1. Influence of the Higher Alcohol Content

The close link between climate change and viticulture is evident, with temperature playing a decisive role. While other atmospheric factors influence vine growth, researchers emphasize temperature as central [12,34,35]. Rising temperatures notably lead to earlier grape ripening, observed across diverse wine-producing regions. The stages of vine development, such as budding, flowering, and veraison, happen earlier than usual. This results in grapes ripening faster than expected and accumulating sugars at an accelerated rate, owing to the increased speed of the metabolic processes involved in grape maturation [16,19,36,37]. Higher temperatures lead to higher evapotranspiration rates, exacerbating the impact on grape maturation [2,35,38].

The high sugar content in these grapes at harvest plays a crucial role, as, during the fermentation process, the yeast converts these natural sugars into alcohol [19,39,40]. This transformation, in turn, produces wines with a high alcohol content [24,41]. However, in this particular scenario, the early harvest of grapes can be employed to mitigate these effects. On the other hand, excessive humidity during ripening is unfavorable to maturation due to the promotion of sugar dilution. However, this effect is minor compared to bunch rot's more rapid and devasting spread [22,42].

Grapes accumulate sugar naturally as they ripen on the vine. Several studies have shown that glucose and fructose are the predominant sugars in grape berries. Sucrose is present in trace amounts in most cultivars; however, this amount is higher in some interspecific hybrids involving *Vitis labrusca* and *Vitis rotundifolia* [43,44].

Bock et al. [45] studied data from 1805 to 2010 in the Franconia wine-growing region, Germany, finding that higher temperatures correlated with an increased vine yield (hl/ha) and must sugar content (°Oe). Temperature changes contributed to a 15% yield increase and a 38% rise in sugar content. Another study by Alston et al. [46] highlighted a significant sugar level increase in California wine grapes, leading to higher alcohol levels in wines produced over the last two decades. Other researchers [37] studied the impact that hail, a phenomenon likely to increase due to climate change, may have on Thompson seedless grapevines. While the damage caused by hail did not affect certain factors, it notably reduced the overall leaf area. Importantly, this damage revealed potential implications for cluster quality, as it coincided with an increase in the sugar content of the grapes. Additionally, Bigard et al. [39] studied 12 vine varieties, finding that rising temperatures led to significant changes in grape composition and significantly increased sugars. Navrátilová et al. [47] observed similar trends in the Czech Republic's central wine regions from 2000 to 2019. Over six decades, evaluations of Bordeaux and Napa Valley also linked higher temperatures to increased grape sugar content [48].

Therefore, we can assess that the sugar composition of grapes plays a vital role in the quality of wine, encompassing factors such as flavor complexity, balance, and overall sensory appeal. Late-season accumulation of aroma compounds and specific phenolics further contributes to the wine's distinctive character. Furthermore, the sugar content influences the alcohol level, contributing to variations in wine styles and sensory profiles [49–58]. Several studies corroborate this statement. In a prior 13-year study, a rise in sugar concentration at harvest corresponded to a yearly 0.17% increase in potential alcohol content in Australian wines [53]. Recent research by Van Leeuwen et al. [6] revealed a 35-year trend in the Languedoc region of France, with wine alcohol content increasing from 11% to 14%.

It is essential to highlight that the increase in alcohol content, in which ethanol is the main component of wine alcohol, can significantly impact the sensory characteristics of wine [28,54,55]. Indeed, a term encapsulates this concept—the "alcohol sweetspot"—which, although still debated, signifies the optimal alcohol content of a wine that enhances its sensory characteristics [56]. Wines with high alcohol contents, close to or above 14% to 16% (v/v), are often perceived by consumers as unbalanced. This perception is not exclusively attributed to a masking effect but also involves a reduction in volatility. Ethanol, the dominating element, tends to overshadow the perception of other flavors, thus affecting the wine's complexity and elegance [24,28,56–59]. In addition, ethanol is responsible for increasing bitterness [60], the burning sensation (at certain levels) [24,61], and the metallic mouthfeel of wines [18,62], changing the perception of sweet [63] and sour [64], as well as reducing the perceived astringency [65].

Escudero et al. [66] discovered that wines with alcoholic contents surpassing 14.5% (v/v) lose their fruity aroma, as ethanol can suppress fruitiness by masking ester perception [67,68]. This observation aligns with findings from King et al. [28], indicating a negative correlation between alcohol levels and fresh fruity and floral aromas. Interestingly, the study found that high alcohol concentrations had minimal to no significant impact on wine viscosity or body, essential aspects of wine quality. However, negative impacts on the sensorial perception of reducing alcohol in wines have been shown, namely reduced fruity aromas and increased vegetative and musty aromas [67].

1.1.2. Imbalance Acidity and Perceived Sourness

Another notable effect of climate change, in addition to the increase in sugar concentrations, is the significant reduction in the acidity of wines, directly impacting wine quality. The lack of acidity results in wines with changes at the sensory level, as well as being more

predisposed to spoilage by harmful microorganisms (bacterial genera *Lactobacillus* (e.g., *L. hilgardii*), *Leuconostoc* (e.g., *L. mesenteroides*), *Pediococcus* (e.g., *P. damnosus* and *P. pentosaceus*), *Acetobacter* (e.g., *A. aceti* and *A. pasteurianus*), or *Gluconobacter* (e.g., *G. oxydans*), reducing their chemical and microbial stability [6,22,41,69,70]. The tartaric, malic, lactic, and citric acids are the primary acids that determine the total acidity of the wine, with tartaric and malic acids representing approximately 90% of the whole berry acidity and contributing to the pH of the juice, must, and wine [70,71]. The relationship between acidity and pH depends on complementary factors, such as potassium accumulation. Potassium is influenced by temperature, and in the context of climate change, with increasing temperature during maturation, the accumulation of potassium ions increases (potassium enters berry cells in direct exchange for protons), reacting with organic acids, affecting the acid-base balance acidity and pH balance [72].

Several studies confirm tartaric acid's stability with temperature changes, while malic acid decreases at higher temperatures due to respiratory substrate consumption [73]. Generally, lower acidity levels correlate with higher grape pH [19]. Ganichot's 22-year study in southern France showed a decline in total acidity from 6 to 4 g/L (expressed as H_2SO_4) and an increase in pH from 3 to 3.3 [74]. Similarly, a 35-year study in Languedoc, France, noted reduced total acidity from 6.0 to 4.5 g/L and an increased pH from 3.5 to 3.75 [6]. Global studies reveal consistent trends of decreasing acidity and rising pH, indicating the impact of climate change on grapes in various wine-producing regions [19]. These studies highlight the trend in decreasing acidity and increasing the pH of grapes in the most varied wine-producing regions of the world, and these trends are intrinsically linked to climate change. These changes challenge the wine industry since acidity and pH are preponderant in consumers' perceived quality, taste, flavor, and color [75].

1.1.3. Phenolic Compounds and Health-Promoting Compounds Deficiency

Phenolic compounds are widely present in plants, encompassing a diverse category of secondary metabolites produced through various branches of the phenylpropanoid pathway [76]. These compounds perform several vital plant functions, including antioxidant action, chemical communication, and pigmentation [35,77]. Moreover, they protect plants from biotic and abiotic stresses [35,78].

Phenolic compounds, encompassing non-flavonoids and flavonoids, play crucial roles in wine. Non-flavonoids, including hydroxycinnamic acids prevalent in wine grapes, contribute to oxidative browning processes [79]. Phenolic compounds, especially flavonoids, significantly influence a wine's sensory profile, quality, and market value [78,80]. Notably, flavonoids can be categorized into three subclasses: flavonols, anthocyanins, and polymeric proanthocyanidin forms, commonly known as tannins [35,78]. Their presence and concentration in grapes and wines are pivotal for determining color and shaping the wine's flavor, aroma profile, bitterness, astringency, and aging potential [6,19].

In a climate change scenario, in which an increase in average temperature and extreme events' frequency, intensity, and duration, the synthesis and concentration of flavonoids in grapes are expected to be affected. For instance, anthocyanins, the pigments responsible for the red color in grapes and wines, are highly sensitive to temperature fluctuations, especially during the intermediate maturation of grapes when all genes are highly expressed, contrary to what is observed in the pre-veraison stage [55,78,81]. Their accumulation occurs in the skin of red berries during maturation and is present as glycosidic derivatives of delphinidin, cyanidin, petunidin, peonidin, and malvidin [82].

Keller (2010) [83] established that the optimal temperature for synthesizing anthocyanins is around 30 °C. Therefore, an increase in temperature above this limit can be significant in the phenolic composition of grapes, resulting in the degradation of anthocyanins or, more importantly, leading to irreversible inhibition of their synthesis. This process, in turn, can lead to color changes in wines [84]. In a study conducted by Tarara et al. [85], it was found that high temperatures were associated with reductions of anthocyanins based on delphinidin, cyanidin, petunidin, and peonidin in sun-exposed Merlot

berries. However, no changes were observed in malvidin derivatives in the same study. The synergistic interaction among anthocyanidins, such as malvidin, and other phenolic compounds is crucial for the diversity of colors in red wines.

Consequently, exposure to high temperatures affects the production of anthocyanins in the grapes, leading to a discoloration of the berry skin. However, this phenomenon occurs not only due to the suppression of anthocyanin genes but also due to more complex phenomena, such as changes in gene expression and enzymatic activity of anthocyanins [86]. Petoumenou et al. [37] also report a decrease in phenolic compound content resulting from other abiotic constraints, such as the impact of hail, which might have inhibited phenolic biosynthesis and promoted phenolic degradation.

Throughout the grape maturation process, climatic variables play an essential role in forming volatile compounds responsible for the aromatic quality of wines [87]. This complex interaction can affect the perception of aromas, as it is directly correlated with phenolic compounds' antioxidant power and reactivity. In climate change, primary flavors are mainly the most affected. For example, high temperatures or U.V. radiation reduce the aromatic expression of grape varieties such as Sauvignon Blanc and are associated with undesirable high concentrations of TDN (1,1,6-trimethyl-1,2-dihydronapthalene) in wines [80,88]. TDN contributes to petrol or kerosene aromas in wines, masking desired fruity aromas [89]. In addition, nutty aromas or premature aging in wines may result from climate change [80]. Climate change is thus creating changes in the aromatic profiles of wines. This influence results from interaction with phenolic compounds and environmental conditions, such as sun exposure and high temperatures.

Therefore, it is imperative to understand how phenolic compounds respond to temperature changes since their decrease due to extreme events can have, in addition to damages in terms of wine quality, significant implications for consumers' health. Even considering the presence of alcohol, bioactive compounds in wine are linked to health benefits [90]. The positive effects of phenolic compounds on health promotion are widely recognized [91]. They possess antioxidant capacity as they can protect cells from oxidative stress, thereby reducing the effects of neurodegenerative diseases and helping to prevent cardiovascular disease [79]. Other studies potentiate phenolic compounds' anti-inflammatory activity and anticancer capacity [92,93]. Resveratrol is one of the most studied non-flavonoid phenolic compounds in wine, which has cardioprotective, anti-inflammatory, and anticancer properties [94]. Furthermore, Doshi et al. [95] have demonstrated the anti-diabetic activity of flavonols.

2. Techniques to Decrease Alcohol Content in Wines

In recent years, consumer preferences have evolved substantially as they have become increasingly demanding, conscious of the characteristics of the goods they choose, and focused on products that promote a healthier lifestyle. This trend extends to the consumption of wine, where consumers are more attentive and concerned about the health risks associated with alcohol consumption. As a result, there is an increasing demand for wines with reduced alcohol content [24–26], thus driving the production and sale of such wines. In this regard, winemakers have been actively seeking technological strategies to decrease or eliminate the alcohol content of wines. Furthermore, given the context of climate change, which has significantly contributed to the production of grapes with higher sugar levels and, consequently, an increase in the alcohol content of wines, the search for innovative methods to meet this demand becomes imperative.

These strategies for winemakers to produce wines with reduced alcohol levels can be categorized in several approaches. Still, more commonly, they are separated depending on when they are applied in the wine production process. Some authors [96–98] indicate four different categories, while other authors [99,100] divide these strategies into three, as will be discussed in this document (Figure 2).

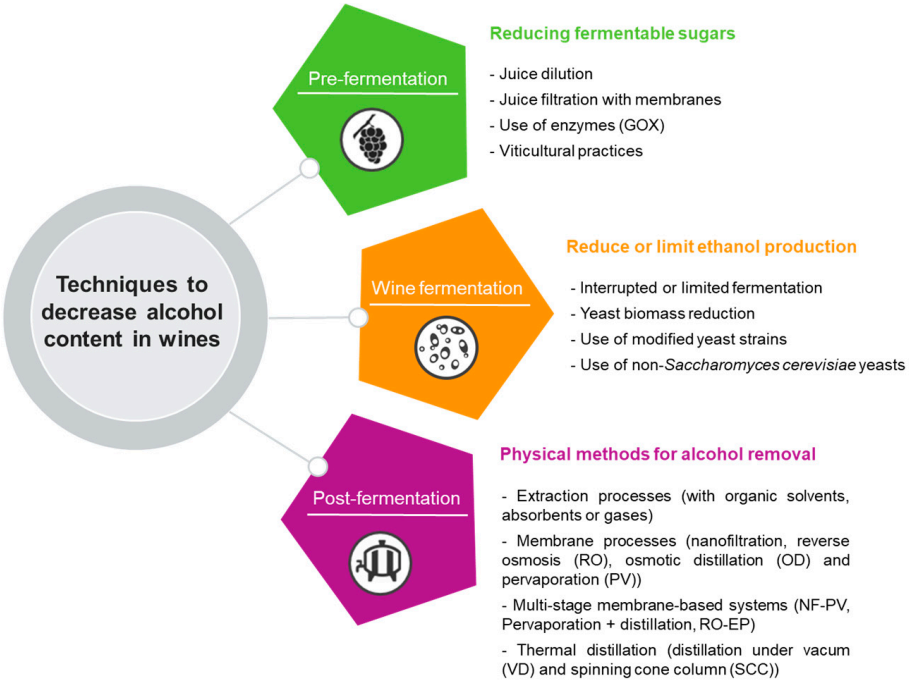

Figure 2. Techniques to decrease alcohol content in wines and fermented beverages.

2.1. Non-Microbial Alcohol Reduction in Wines

2.1.1. Reducing Fermentable Sugars in the Grapes

The first category, used during the pre-fermentation stage, focuses on reducing fermentable sugars. This limits the amount of alcohol produced during fermentation, resulting in wines with lower alcohol content right from the start [100]. It is one of the most common methods for producing wines with lower or reduced alcohol content. Techniques such as juice dilution and juice filtration with membranes or enzymes are employed at this stage. Additionally, viticultural practices such as early harvesting, growth regulators, reducing leaf area to limit photosynthetic rate, and pre-harvest irrigation are cited by Schelezki et al. [101]. Specific viticultural methods can produce a wine with lower alcohol content and higher acidity, which can then be blended with a more mature fermented juice. Although these methods are known to decrease ethanol concentration by 3% (v/v), the resulting wines may have unpleasant, acidic, and unripe flavors [102,103].

In Table 2, a summary of non-microbial techniques applied during the pre-fermentation phase for the reduction in alcohol content in wine is provided.

Table 2. Non-microbial techniques employed in the pre-fermentation phase for alcohol content reduction in wine.

Method Used		Type of Wine	Alcohol Reduction		Advantages	Disadvantages	Ref.
			Original Alcohol Content (% *v*/*v*)	Final Alcohol Contente (% *v*/*v*)			
Juice dilution		Shiraz red wine	Fresh Fruits: 13.6 Mature Fruits: 15.5	9.6 to 14.5	Within legal limits, the addition of water may have relatively limited effects on the chemical composition of the wine, preserving many of its characteristics. Wines produced from mature grapes tended to exhibit sensory characteristics closer to the expectations of producers and consumers.	Sensory analyses suggest that dilution can lead to a diminished perception of attributes such as 'flavor intensity' and 'body,' which could impact the wine's overall acceptance.	[101]
Juice filtration with membranes	Nanofiltration	Garnacha red wines and Verdejo white wines	Garnacha red wines: 12.40 Verdejo white wines: 13.88	Garnacha red wines: 11 Verdejo white wines: 11.95	The two-stage NF process without backflush is the most effective, minimizing sugar content while promoting higher recovery of polyphenolic compounds. Red wines are favorite for odor and color.	Sensory evaluation revealed no consumer preference for wine samples, although white wines present lower persistence, possibly related to their lower alcohol degree.	[104]
	Reverse Osmosis	The red wine blends Tinta Roriz, Syrah, and Alicante Bouschet.	15.2	5.4 to 13.8	Production of beverages with lower alcohol content without excessively compromising sensory quality.	Beverages with lower alcohol content were perceived by tasters to have diminished color, reduced aromatic intensity, and increased detection of defects like oxidation and hydrogen sulfite, negatively affecting sensory persistence.	[105]
Use of enzymes (GOX)		Verdejo white wine	13.8	11.1 to 11.7	Enzymatic treatment led to more balanced wines, reducing alcohol content and pH. The chromatic properties of GOX wines remained unchanged compared to control wines, indicating color stability. GOX wines had lower concentrations of C6-alcohols associated with green-herbaceous notes, contributing to improved aroma.	GOX treatment resulted in lower concentrations of certain wine alcohols with floral notes. The technique did not uniformly affect all volatile compounds, influencing the sensory characteristics differently.	[106]

Table 2. *Cont.*

Method Used		Type of Wine	Alcohol Reduction		Advantages	Disadvantages	Ref.
			Original Alcohol Content (% *v*/*v*)	Final Alcohol Contente (% *v*/*v*)			
Viticultural practices	Early grape harvesting	Tempranillo red wine	14.8	10.61 to 10.63	The early harvesting of grapes, including the use of must or wine obtained from green pruning (green harvest), may lead to producing wines with reduced alcohol content. No significant changes in color intensity and phenolic compounds were observed. Early harvesting can contribute to fresher and less mature wines, although the outcomes may vary depending on the specific conditions of each vintage.	The resulting wines were perceived as more acidic and less full-bodied.	[107]
		Pinot Noir and Tannat red wines	Pinot Noir: 14.3 Tannat: 14.7	11.5 for both Pinot Noir and Tannat	Substituting ripe must with less ripe must result in wines with lower alcohol content (reduction of 14% to 21%) and lower pH. Wines exhibited greater color intensity, concentration of phenolic compounds, total anthocyanins, proanthocyanidins, and polysaccharide concentration.	Possible losses of anthocyanins may occur. Results may vary depending on the specific conditions of each harvest.	[108]
	Growth regulators (Auxin treatment)	Shiraz red wine	14.3	13.9	No significant differences were observed in the sensory properties of the wine.	Potential alterations in the chemical composition of the wine, particularly in volatile compounds. Understanding the long-term effects of synthetic auxin application is crucial before implementing it on a large scale. The effects of NAA application may vary with climatic conditions and the environment.	[109]

Table 2. *Cont.*

Method Used		Type of Wine	Alcohol Reduction		Advantages	Disadvantages	Ref.
			Original Alcohol Content (% *v*/*v*)	**Final Alcohol Contente (% *v*/*v*)**			
Viticultural practices	Grapevine canopy management	Shiraz red wine	2010/2011: 12.40 2015/2016: 13.27 (Apical leaves removal at veraison)	2010/2011: 11.72 2015/2016: 12.94	Reduction in alcohol content in wine, especially with apical defoliation. Moderation of wine aromatic properties. Potential mitigation of the effects of global warming on the increase in alcohol content of wine.	Variations in response to the technique among different cultivars and clones. Consider factors such as timing, defoliation method, and location for consistent results. Limited influence of apical defoliation on wine characteristics compared to basal defoliation.	[110]
		Aglianico red wine	2012: 14.1 2013: 13.1 2014: 13.3 (post-veraison pruning techniques, such as leaf removal and shoot trimming)	2012: 13.2 to 13.8 2013: 11.8 to 12.2 2014: 2.2 to 12.5	The post-veraison pruning techniques, such as leaf removal and shoot trimming, have shown a significant decrease in alcohol concentration in the wine. Both leaf removal and moderate shoot trimming resulted in improvements in the overall sensory score of the wine.	Results may vary based on climate and vine characteristics. Intensive pruning, whether leaf removal or shoot trimming, may negatively impact wine sensory scores in specific years. The concentration of compounds like anthocyanins and phenolic substances in the berries fluctuated based on pruning intensity and the year.	[111]

Juice Dilution

The addition of water to the must to reduce the concentration of fermentable sugars effectively reduced the characteristics of Cabernet Sauvignon and Shiraz wines. However, it is necessary to find a limit to avoid changes in the sensory profile of wines, as demonstrated in other studies [112].

Juice Filtration with Membranes

Nanofiltration, ultrafiltration, or reverse osmosis membranes retain sugar from the must before fermentation. The filtered juice is then fermented to produce wine with reduced alcohol content. Several studies have investigated this technology's use and reported positive results that do not affect essential compounds such as polyphenols, malic acid, and tartaric acid, with no significant changes in the sensory profile of the wines [104,105,113–115].

Use of Enzymes

The use of enzymes, specifically glucose oxidase (GOX), has shown to be an effective technique in reducing the alcohol content of wines by reducing glucose in grape juice before the fermentation process and has been the subject of numerous studies [106,116–119]. Derived from the fungus *Aspergillus niger*, the GOX enzyme promotes the conversion of β-D-glucose into D-glucono-lactone, releasing H_2O_2, and subsequently catalyzes the conversion of D-glucono-lactone into gluconic acid, producing gluconic acid [116]. These reactions are responsible for the oxidation of fermentable sugars in the juice, thus preventing ethanol formation during fermentation. Applying the GOX enzyme has been shown in assays to decrease alcohol content by approximately 2% v/v [117] to 4.3% v/v [118]. Petkova et al. [119] found a 28% reduction in glucose after enzyme application, preserving some glucose and fructose for yeast fermentation in a second treatment. Additional studies observed not only reduced alcohol content but also decreases in heptyl acetate concentration, certain alcohols with floral notes, and ketones with floral and fruity notes in the wines [106].

Viticultural Practices

Early grape harvesting is another widely used pre-fermentation method to reduce alcohol in wines, involving either early harvesting or blending mature grapes with early-harvested ones. This approach has shown promise, achieving about a 3% v/v decrease in ethanol content [107,120]. In studies with Pinot Noir and Tannat grape varieties, this technique not only lowered alcohol content but also decreased pH and total acidity without affecting other wine constituents [108].

Therefore, regarding viticultural practices, it is essential to carefully consider early harvest to maximize grape flavor compounds for the final wine style. However, this approach may not be appropriate for all wine styles. Early harvest can be beneficial when there is a rapid onset of berry shrivel. Still, options for color enhancement in red wines should be considered depending on how early the harvest is conducted [121,122].

Using growth regulators also appears to be a viable option, as they can reduce the sugar concentration in the berries, resulting in lower wine alcohol content [123–125]. Naphthaleneacetic acid, used as an antitranspirant on Syrah grapes during pre-veraison, led to delayed berry ripening. This delay allowed better management of sugar accumulation and resulted in wines with no significant changes in sensory profiles [109].

Grapevine canopy management, a crucial viticultural practice for vineyard balance, significantly influences sugar accumulation in grapes [126]. Reducing leaf area through severe pruning or leaf removal at various growth stages minimizes fermentable sugar accumulation, lowering ethanol content in the resulting wine [99]. Zhang et al. [110] compared basal and apical defoliation, observing lower alcohol content in Shiraz grapes and wines with minimal impact on aromatic properties. Similar outcomes were reported by Poni et al. [127], achieving significantly reduced total soluble solids and alcohol concentration

without affecting phenolic composition through leaf removal above the grape cluster zone in Sangiovese after veraison. Other studies have aimed to reduce the alcohol content in wine through leaf area reduction [111,128–130]. However, shoot thinning in Carot Noir grapes (a red interspecific hybrid of Vitis) increased soluble solids and alcohol content [131], as it did in Cabernet Sauvignon grapes [132]. Demonstration that the effects of shoot thinning practices are unclear and depend on the grape variety. A previous study on shoot thinning found that shoot-thinned Marechal Foch (a red interspecific hybrid of Vitis) vines showed higher total soluble solids (°Brix) and berry anthocyanin concentrations compared to un-thinned vines [133]. However, the increase in berry anthocyanin did not result in higher anthocyanin concentration in the final wine. Furthermore, shoot thinning did not affect the sensory perception of the "fruitiness" of the wines [133]. In contrast, a study focused on Corot noir and the implementation of shoot thinning provided inconsistent results in grape and wine quality across a two-year evaluation (2008–2009). The evaluation was determined by soluble sugars (°Brix), pH, titratable acidity (TA), wine anthocyanin, berry, and wine tannin content. The study found that shoot thinning increased berry °Brix, wine alcohol concentration, and anthocyanin concentration only in the second year [131].

2.1.2. Reduce or Limit Ethanol after Winemaking

The following category relates to post-fermentation procedures. In this phase, physical methods for alcohol removal, including extraction, membrane separation, or distillation, are applied. In Table 3, a summary of non-microbial techniques applied during the post-fermentation phase for the reduction in alcohol content in wine is provided.

Table 3. Non-microbial techniques employed in the post-fermentation phase for alcohol content reduction in wine.

Method Used		Type of Wine	Alcohol Reduction		Advantages	Disadvantages	Ref.
			Original Alcohol Content (%, *v*/*v*)	Final Alcohol Contente (%, *v*/*v*)			
Extraction processes	CO_2	Rose wine	11.3	1.1	Wine retained several aromatic compounds from the original wine. Slight modification in antioxidant activity, with values similar to the original wine.	Extremely expensive, and their application in the food industry for nonalcoholic wine production is becoming rare.	[134]
Membrane processes	Nanofiltration	Cabernet Sauvignon	13.62	7.38 to 11.01	Retention of desirable compounds, including polyphenols and aromas, preserving wine's sensorial quality. The technical capability to permeabilize acetic acid can be explored to correct this component in wine, providing sensory improvements.	High energy consumption requirements, especially when dealing with low molecular weight compounds, may lead to increased membrane fouling. Cooling is necessary, adding complexity to the process and potentially increasing operational costs.	[115]
		Red wine	12	7 to 8	Nanofiltration produces dealcoholized wine with preserved aromatic compounds, enhancing the gustatory experience.	The membrane selection is crucial, and different membranes exhibit distinct performances in terms of ethanol rejection, aromatic compound rejection, and organoleptic properties.	[135]
	RO	Sauvignon blanc	13.6	10.5 to 12.2	Reducing alcohol can enhance specific flavors and aromas, providing a unique sensory experience.	Professionals included terms such as "less persistent" and "less balanced", suggesting a potential loss of desirable characteristics.	[67]
		Syrah	13.4	7.9 to 11.4	The reduction in alcohol-induced an increase in the perception of familiarity, harmony, and balance, reaching an optimum of −4%. The reduction in alcohol is noticeable but not apparent to consumers.	Reverse osmosis can impact the overall sensory experience of wine by decreasing complexity, persistence, and the number of aromas and influencing texture and viscosity. However, it may not be suitable for wines that are sensitive to adjustments in alcohol content.	[136]

Table 3. *Cont.*

Method Used		Type of Wine	Alcohol Reduction		Advantages	Disadvantages	Ref.
			Original Alcohol Content (%, *v*/*v*)	Final Alcohol Contente (%, *v*/*v*)			
Membrane processes	RO	Red wine	16	14.1	No adverse effects on the treated wines' color, aroma, and taste were observed, suggesting the preservation of sensory quality.	A reduction in total phenols and anthocyanins was noted, along with a decrease in both total and volatile acidity, concurrent with the reduction in alcohol content.	[137]
	OD	Montepulciano d'Abruzzo red wine	13.23	2.67 to 8.31	Preservation of satisfactory sensory characteristics. The color and flavor characteristics, assessed by flavonoids and phenolic compounds, remained virtually unchanged in all dealcoholized samples.	The taste of dealcoholized wine is affected by acidity and pH variations. The decline in ethanol concentration affects the taste of red fruits, spices, sweetness, bitterness, and astringency. Samples with less than 5.4% *v*/*v* of alcohol are preferred.	[138]
		Aglianico red wine	13	0.19 to 6.52	Essential chemical and physical properties, such as pH and total acidity, remained unchanged from the control wine.	There was a pronounced reduction in volatile acidity. The technique requires constant monitoring throughout the process.	[139]
		Falanghina white wine	12.5	0.3	No significant changes were observed in the main quality parameters, such as total acidity, pH, organic acids, color, total phenols, and flavonols, during the dealcoholization process. Preservation of antioxidant compounds.	With increasing alcohol removal, the quantity of volatile compounds in the wine decreased significantly. The fully dealcoholized sample saw a total loss of 96% in these compounds. However, the completely dealcoholized sample was perceived as unbalanced in taste and globally unacceptable.	[140]
	PV	Cabernet Sauvignon red wine	12.5	<0.5	Enhanced smell and taste. Effective separation of ethanol and aroma substances. Production of high-quality, alcohol-free wine. Stable membrane performance over extended operation.	High investment and operating costs for pilot-scale equipment. Need for membrane cleaning after red wine batches—potential quality issues at higher operating temperatures.	[141]
Multi-stage membrane-based systems	NF–PV	Verdejo white wine	11.90	10.25	Wines resulting from the NF–PV process exhibited aromatic profiles similar to the original wine.	Nanofiltration and pervaporation equipment can be costly for winemakers, and outcomes may vary based on grape variety and other factors.	[142]
	RO–EP	5 Cabernet Sauvignon red wines	Wine A: 17.0 Wine B: 15.5 Wine C: 14.9 Wine D: 14.5 Wine E: 16.0	Wine A: 14.5 Wine B: 13.3 Wine C: 13.3 Wine D: 13.2 Wine E: 14.2	Applied in industrial volumes of wine, the technique is suitable for large-scale operations. Preservation of specific volatile and aromatic compounds in the wine contributes to the retention of desirable sensory characteristics, with minor decreases observed in the intensity of specific flavors, such as "dark fruit", "sweet spice", and "chocolate".	Modifications in "body", "acidity", "bitterness", and "astringency" are particularly evident in Wine A following a 2.5% ABV reduction. Installing and maintaining RO–EP equipment may constitute a substantial investment for wine producers.	[143]
Thermal distillation	VD	Langhe Rose Verduno Pelaverga red wine Barbera red wine	Langhe Rose: 13.2 Verduno Pelaverga red wine: 15.2 Barbera red wine: 14.6	5 for all wines	Maintained a wine-like physicochemical composition. Richer aromatic profile, particularly in ethyl esters and isoamyl acetate.	Higher losses of alcohol were observed.	[144]
	SCC	Shiraz Sangiovese red wine Petit Verdot Sangiovese red wine	Shiraz Sangiovese red wine: 15.1 Petit Verdot Sangiovese red wine: 14.2	0.3 to 14.5 0.3 to 13.8	It selectively amplifies key non-volatile elements like organic acids, anthocyanins, and tannins, heightening the sensory intricacy of the wine.	Loss of desirable volatile compounds responsible for fruity and floral aromas compromises the wine's varietal expression.	[145]

RO (Reverse Osmosis); OD (Osmotic Distillation); PV (Pervaporation); NF–PV (Nanofiltration–Pervaporation); RO–EP (Reverse Osmosis–Evaporative Perstraction); SCC (Spinning Cone Column).

Alcohol Removal via Extraction Methods

Extraction can be carried out using gases, organic solvents (not for wine used commercially), or adsorbents.

The unique properties of carbon dioxide (CO_2), including its ability to transform into a supercritical fluid under specific temperature and pressure conditions, make it an effective compound for extracting organic compounds, such as ethanol in wine. In its liquid state within the wine, CO_2 has an affinity for the carbon chain of ethanol, facilitating its dissolution. As it transitions back to a gaseous state, it carries the dissolved ethanol, reducing the ethanol content in the wine [146]. According to Ruiz-Rodríguez et al. [134], extraction carried out with supercritical CO_2 in white, red, and rosé wines has proven to be an advantageous alternative. Besides removing ethanol from beverages, it leaves no residues in the wines and does not alter their aromatic profile or antioxidant activity. Furthermore, it is an economical, safe, and easy-to-handle solvent [100]. Other organic solvents like pentane and hexane are also used to remove ethanol from wines but may remove other aromatic compounds, affecting the final taste of the wines [147]. Hydrophobic adsorbents like zeolites are used in the production of dealcoholized wine. Nikolaou et al. [148] reported a conversion rate of 69.2% of malic acid content and the production of wines with low ethanol content. According to Akyereko et al. [149], this method enables the production of wines with an ethanol content of 0.5% v/v.

Alcohol Removal through Membrane-Based Processes

The separation through the use of membranes refers to physical separation techniques aimed at reducing or eliminating the alcohol content of wine through a semipermeable membrane. In this method, a natural osmotic pressure occurs due to the difference in concentration between two solutions flowing through the semipermeable membrane (tangentially, in parallel, or circularly). As a result, alcohol and water from the wine move from the more concentrated solution to the less concentrated one, reducing or eliminating ethanol from the wine [105,150,151]. The most commonly used membrane separation techniques include nanofiltration, reverse osmosis (RO), osmotic distillation (OD), and pervaporation (PV).

Besides its application in pre-fermentation to lower the sugar content in the must, nanofiltration can also be employed for alcohol removal from finished wines [105,152,153]. The semipermeable membrane has a size ranging from 1 to 10 nm, allowing the rejection of smaller molecules (such as sugars and proteins) at a pressure of about 75 bar, surpassing ultrafiltration membranes [154]. Some studies demonstrate the advantages and effectiveness of this technique compared to the reverse osmosis technique, which, in addition to reducing the alcohol content of wine, preserves its organoleptic characteristics with fewer losses in anthocyanins at lower pressures, making the process more cost-effective [115,135,137,155].

On the other hand, the RO process involves the application of high pressures, in the range of 60 to 80 bar, under which water and ethanol molecules are forced through the semi-permeable membrane, leaving behind a retentate with the remaining compounds. Simultaneously, a permeate flow is generated, containing higher amounts of water and ethanol due to their smaller molecular size [25,156]. However, adding water to the retentate is necessary to achieve efficient dealcoholization, which becomes a disadvantage of this process since it is generally illegal or restricted in many wine-producing countries. Additionally, this technique has other challenges related to dilution due to potential alterations in the sensory properties of wines and the operation at high pressures [136,137,157].

Another membrane separation technique for producing low-alcohol wine is osmotic distillation (OD), also referred to as evaporative perstraction (EP) or isothermal membrane distillation [100]. This technique is based on two aqueous phases: the wine containing volatile compounds and the water acting as the stripping liquid. Both circulate in countercurrent on opposite sides of a hydrophobic hollow fiber membrane module. The mechanism of ethanol removal in this technique involves the initial evaporation of ethanol due to increased temperature and the difference in partial pressure between ethanol in the wine and

the space inside the membrane pores. Subsequently, the ethanol vapor diffuses through the membrane pores and, upon emerging from these pores, mixes with the stripping water solution. When the ethanol vapor comes into contact with the stripping water, it condenses into a liquid state [113,151]. This evaporation, diffusion, and condensation process allows ethanol removal from wine, with values ranging from 1.3% to 10.5% v/v, while preserving some essential components [138–140]. Reducing alcohol in wine can negatively affect its quality, causing loss of aroma, oxidation, and spoilage due to microorganisms. Therefore, it is crucial to follow the manufacturer's recommendations and perform the alcohol reduction with care [140,158,159].

In contrast to OD, vapor permeation (PV) is a separation technique that employs dense and non-porous membranes to separate components from liquid mixtures based on partial evaporation. In this technique, the liquid mixture comes into direct contact with the selective side of the membrane (chemical affinity). In contrast, the permeate is collected in vapor form on the opposite side of the membrane. Separation occurs due to a driving force, a vacuum, a sweep of inert gas (such as nitrogen), or a temperature difference. This technique has three main steps: adsorption of the target component onto the membrane, diffusion of this component through the membrane, and desorption on the permeate side [141,160]. This technique has been explored as a promising method for reducing the alcohol content in wines due to several advantages applied in this context: it allows for the selective removal of ethanol from wine while preserving its aromatic profile, thus avoiding significant losses in sensory quality; it is more energy-efficient compared to traditional distillation; there is a lower possibility of contamination of the final product; it operates at lower temperatures than other dealcoholization methods; it is a "clean" technique as it produces water and ethanol as byproducts that can be reused [141,161,162]. Nevertheless, this technique faces limitations, such as high investment costs, a limited membrane market, low permeation rates at low temperatures, and the need to optimize operating conditions to achieve desired results [99,151,162].

Alcohol Removal: Thermal Processes in Winemaking

Thermal processes are widely employed to reduce the alcohol content in wines. Vacuum distillation (VD) and spinning cone column (SCC) are methods based on the fundamental principle of heating and evaporation.

Vacuum distillation (VD) is another process for producing low-alcohol wines. It is a thermal process that, under vacuum conditions, concerns evaporation, distillation, and condensation [144]. VD entails heating the wine to relatively low temperatures (typically between 15 °C and 20 °C) compared to traditional distillation. Heating is essential for evaporating volatile compounds, particularly ethanol, from the wine. The alcohol vapor is then separated under vacuum conditions and condensed into liquid form, yielding a distillate containing the extracted alcohol. After alcohol removal, the remaining wine has a significantly lower alcohol content, and retention of the aromas and flavors present in the original wine can occur under certain conditions [99]. Furthermore, it allows for flexible adjustment of wine alcohol content based on producer and consumer preferences. The recovered distillate can be added to the dealcoholized portion [99,141]. Nevertheless, studies indicate that while VD enhances volatile compounds, it may significantly reduce esters, alcohols, and terpenes, impacting the wine's aromatic complexity and sensory profile [100,163].

The SCC technique, widely used in the beverage industry for producing low-alcohol beverages, efficiently preserves aromatic compounds [164]. It involves rotating vertically stacked cones within a column [124]. The alcohol removal occurs in two phases: first, the wine undergoes SCC at a moderate temperature (26–28 °C) and reduced vacuum pressure (0.04 atm) to extract aromatic compounds. In the second phase, at higher pressure and temperature (38 °C), the alcohol content is reduced, resulting in a low-alcohol or non-alcoholic wine, depending on the remaining ethanol. Aromas recovered in the first phase enhance the final wine's aroma [165,166]. Studies highlight the effectiveness of SCC in

reducing wine alcohol content and recovering aromatic compounds from red, white, and rosé wines [151,164–167]. Furthermore, a study conducted by Puglisi et al. [145] suggests SCC, combined with adsorbents, as a profitable strategy for remediating "smoke taint" in wines from grapes affected by wildfires. However, SCC technology is costly and involves expense management [100].

Multi-Stage Membrane-Based Systems

Recently, an innovative approach has emerged for producing low-alcohol beverages, aiming to prevent the loss of desirable aromatic compounds associated with single-membrane dealcoholization methods (such as NF, PV, RO, and OD) and thermal separation processes [25,138,139,144,151]. This approach uses an integrated membrane and distillation system called a multi-stage membrane-based system [151]. This technique combines two or more alcohol removal methods to remove ethanol from wines and beers. Commonly used multi-stage membrane-based systems include nanofiltration and pervaporation (NF–PV) systems [142], pervaporation units combined with distillation [135], and reverse osmosis-evaporative pertraction (RO–EP) systems [143], with the RO–EP system being the most widely used. These combined systems have proven highly efficient for producing low-alcohol wine, as they not only maintain aroma characteristics similar to the original wine but often achieve improved versions compared to the original product [142,168,169]. Despite some losses of desirable aromatic compounds such as ethyl esters, acetate esters, and monoterpenes [143,170], the ability of these systems to preserve the wine's aroma and volatiles constitutes a promising strategy in the production of low-alcohol or alcohol-free beverages, meeting the growing consumer demand for healthier and high-quality products.

2.2. Microbial Strategies for Producing Low-Alcohol Wines

The increasing trend of alcohol content in wines, linked to climate change, might result in changes in flavor and complexity and, given the current consumer preferences, might negatively impact commercialization. Therefore, strategies limiting alcohol production or its reduction must be defined. These techniques can be categorized into three fundamental approaches, as mentioned earlier: pre-fermentation, fermentation processes, and post-fermentation techniques [171]. Focusing on microbial strategies, emphasis must be placed on the selection of fermentation microorganisms, their proportion or time of inoculation on grape must, and the conditions during fermentation. The goal is to reduce or restrict ethanol production during the fermentation phase. Specific yeast strains (genetically modified or non-*Saccharomyces* yeasts) can also be used to reduce yeast biomass (keeping the fermentation rate of fermentable sugars as low as possible) [100], or techniques such as interrupted fermentation are employed for this purpose. Table 4 briefly overviews the microbiological techniques employed to reduce wine alcohol content during grape-must fermentation.

Table 4. Overview of microbiological techniques employed to reduce wine alcohol content during fermentation.

Approaches	Used Approach or Microorganism	Approximate Decrease in Ethanol Content (%)	Inoculation Regime	Scale of Fermentation	Grape Variety or Media	Ref.
GMO-based approaches	Over-expressed GPD1	35	Unspecified	Unspecified	YEPD	[172]
		3	Single	Laboratory	MS	[173]
		10.5–17.5	Single	Laboratory	MS	[174]
	Over-expressed GPD2	24	Single	Laboratory	Synthetic Leu-free	[174]
	PDC2 deletion mutant	28–45	Unspecified	Unspecified	YEPD	[172]
		2	Single	Laboratory	Diluted white must	[175]
	Alcohol dehydrogenase (*ADH*) mutants	63	Single	Laboratory	YEPD	[176]
	Triose phosphate isomerase (*TPI*) mutants	Undetermined	Single	Laboratory	YEPD	[177]
	NADH oxidase (*NOX*) mutants	7	Single	Laboratory	Synthetic MS medium	[178]
	Glycerol transporter (*FPS*) mutants	10	Single	Laboratory	Synthetic MS medium	[173]
	Glucose oxidase (*GOX*) mutants	2	Single	Laboratory	Chardonnay grape juice	[179]
	Hexose transporter (*HXT*) mutants	Undetermined	Single	Laboratory	5× defined minimal medium	[180]
non-*Saccharomyces* (NS) yeasts	*C. stellata*	19	Single	Laboratory	Grape juice	[181]
	C. zemplinina	57	Single	Laboratory	Grape juice	
	H. uvarum	33	Single	Laboratory	Grape juice	[182]
	Z. sapae	14	Single	Laboratory	Grape juice	
	Z. bailii	4	Single	Laboratory	Grape juice	
	Z. bisporus	7	Single	Laboratory	grape juice	
	M. pulcherrima	0.9	Sequential fermentations with *S. cerevisiae*	Laboratory	Chardonnay	[183]
		1.6	Sequential fermentations with *S. cerevisiae*	Laboratory	Shiraz	

Table 4. *Cont.*

Approaches	Used Approach or Microorganism	Approximate Decrease in Ethanol Content (%)	Inoculation Regime	Scale of Fermentation	Grape Variety or Media	Ref.
non-*Saccharomyces* (NS) yeasts	*M. pulcherrima*	0.9	Sequential fermentations with *Saccharomyce bayanus*, and *S. cerevisiae*	Laboratory	Sila	[184]
	P. kudriavzevii	52	Sequential inoculation	Laboratory	CDGJ medium	[185]
	Z. bailii	16	Sequential inoculation	Laboratory	CDGJ medium	
	S. pombe	4.9	Single	Laboratory	Airen	[186]
	S. pombe	3.1	Sequential fermentations with *S. cerevisiae*	Laboratory	Airen	[186]
	H. uvarum	1	Sequential fermentations with *S. cerevisiae*	Laboratory	Synthetic grape juice and natural grape juice	[187]
	H. uvarum	1.3	Sequential fermentations with *S. cerevisiae*	Laboratory	Pinotage	[188]
	H. uvarum	0.8	Sequential fermentations with *S. cerevisiae*	Laboratory	Sauvignon Blanc	[188]
	H. uvarum	3.3	Sequential fermentations with *S. cerevisiae*	Laboratory	Negroamaro	[189]
	H. osmophila	1.2	Sequential fermentations with *S. cerevisiae*	Laboratory	synthetic grape juice and natural grape juice	[187]
	H. opuntiae	2	Sequential fermentations with *S. cerevisiae*	Laboratory	Pinotage	[188]
	H. opuntiae	11	Sequential fermentations with *S. cerevisiae*	Laboratory	Sauvignon Blanc	[188]
	M. pulcherrima	67	Single	Laboratory	Tinta Roriz	[190]
	M. pulcherrima	7	Co-fermentations with *S. cerevisiae*	Laboratory	Tinta Roriz	[190]
	M. pulcherrima	8	Co-fermentations with *S. cerevisiae*	Laboratory	Malvasia and Viura	[191]

Table 4. *Cont.*

Approaches	Used Approach or Microorganism	Approximate Decrease in Ethanol Content (%)	Inoculation Regime	Scale of Fermentation	Grape Variety or Media	Ref.
non-*Saccharomyces* (NS) yeasts	*M. pulcherrima* and *S. uvarum* mixed inoculum	1.6	Sequential fermentations with *S. cerevisiae*	Laboratory	CDGJ medium	[192]
	M. pulcherrima	1.3	Sequential fermentations with *S. cerevisiae*	Laboratory	Synthetic grape juice and natural grape juice	[187]
	M. pulcherrima	7	Single	pilot-scale	Viura-Malvasía	[193]
	T. delbruekii	4	Single	pilot-scale	Viura-Malvasía	[193]
	L. thermotolerans	1	Sequential fermentations with *S. cerevisiae*	Laboratory	Riesling	[186]
	P. kluyveri	1.8	Sequential fermentations with *S. cerevisiae*	Laboratory	Riesling	[186]
	M. pulcherrima	1	Sequential fermentations with *S. cerevisiae*	Laboratory	Riesling	[186]
	L. thermotolerans	1	Co- fermentations with *S. cerevisiae*	industrial	Sangiovese	[194]
	L. thermotolerans	5	Sequential fermentations with *S. cerevisiae*	industrial	Sangiovese	[194]
	L. thermotolerans	3	Sequential fermentations with *S. cerevisiae*	Pilot scale	Shiraz	[195]
	L. thermotolerans	0.5	Co- fermentations with *S. cerevisiae*	Laboratory	Airen	[196]
	L. thermotolerans	3	Sequential fermentations with *S. cerevisiae*	Laboratory	Airen	[196]
	L. thermotolerans	8	Sequential fermentations with *S. cerevisiae*	Laboratory	Tempranillo	[197]
	T. delbrueckii	3	Single	pilot-scale	Viura-Malvasía	[193]
	T. delbrueckii	2	Sequential fermentations with *S. cerevisiae*	pilot-scale	Airén	[198]

Table 4. *Cont.*

Approaches	Used Approach or Microorganism	Approximate Decrease in Ethanol Content (%)	Inoculation Regime	Scale of Fermentation	Grape Variety or Media	Ref.
non-*Saccharomyces* (NS) yeasts	*T. delbrueckii*	0.8	Co- fermentations with *S. cerevisiae*	pilot-scale	Amarone	[199]
	T. delbrueckii	3	Sequential fermentations with *S. cerevisiae*	pilot-scale	Amarone	[199]
	T. delbrueckii	4	Sequential fermentations with *S. cerevisiae*	Semi-industrial scale	Chardonnay	[200]
	T. delbrueckii	1	Sequential fermentations with *S. cerevisiae*	Semi-industrial scale	Palomino Fino	[200]
	T. delbrueckii	4	Sequential fermentations with *S. cerevisiae*	Laboratory	Verdejo	[201]
	C. stellata	54	Single	Laboratory	Chardonnay	[202]
	C. stellata	0.8	Co- fermentations with *S. cerevisiae*	Laboratory	Chardonnay	[202]
	C. stellata	6	Sequential fermentations with *S. cerevisiae*	Laboratory	Chardonnay	[202]
	C. stellata	6	Immobilized and sequential fermentations with *S. cerevisiae*	Semi-industrial scale	Grape must	[203]
Abiotic factors control			Controlled factor			
	M. pulcherrima	42	Controlled aeration	Laboratory	Synthetic grape must	[204]
	M. pulcherrima	14	Controlled aeration and Co- fermentations with *S. cerevisiae*	Laboratory	Natural white grape must	[191]
	M. pulcherrima	4	Controlled aeration	Laboratory	Riesling must	[205]
	S. cerevisiae	30	Controlled aeration	Laboratory	Natural white must	[206]
	S. cerevisiae	15	Controlled temperature	Laboratory	Concentrated white must	[207]
	S. cerevisiae	9	Controlled temperature	Laboratory	Modified MS300 medium	[208]
	S. cerevisiae	3	Controlled temperature	Laboratory	Carinyena	[209]

Table 4. *Cont.*

Approaches	Used Approach or Microorganism	Approximate Decrease in Ethanol Content (%)	Inoculation Regime	Scale of Fermentation	Grape Variety or Media	Ref.
Abiotic factors control	*M. pulcherrima*	6	Controlled temperature and sequential fermentations with *S. cerevisiae*	Semi-industrial scale	Merlot	[210]
	M. guilliermondii	3	Controlled temperature and sequential fermentations with *S. cerevisiae*	Semi-industrial scale	Merlot	[210]
	W. saturnus	3	Controlled temperature and Co-fermentations with *S. cerevisiae*	Laboratory	Emir	[211]
	Carbonic maceration	16	Unspecified	Laboratory	Carlos	[212]
	Carbonic maceration	5	Unspecified	Laboratory	Noble	[212]
	Carbonic maceration	1.5	*S. cerevisiae*	Laboratory	Muscat Hamburg	[213]
	Carbonic maceration	25	Several species	Semi-industrial scale	Tempranillo	[214]
	Carbonic maceration	24	Unspecified	Semi-industrial scale	Tempranillo and Graciano	[215]

YEPD (yeast extract, peptone, and dextrose); YNB (Yeast Nitrogen Base); MS (Standard defined medium); CDGJ (chemically defined grape juice medium.

2.2.1. GMO Microorganisms

Recently, genetic modifications or adaptive evolution and selection have developed modified yeast strains capable of reducing wine alcohol content during fermentation [134,135,216,217]. However, their use may pose challenges, such as producing undesired secondary metabolites, like acetaldehyde and acetoin, that can affect wine characteristics [184,218]. Another challenge in using such yeast strains is consumer acceptance of genetically modified organisms in food and beverages.

Given the relative simplicity of the yeast genome, its modification can be achieved. To obtain low-ethanol wine, the logical step would be to limit the expression of the enzyme alcohol dehydrogenase (ADH), Figure 3, which catalyzes the final step in ethanol production during alcoholic fermentation. However, this approach was deemed unpractical because strains with ADH deletion could not grow under anaerobic conditions and the production of higher levels of acetic acid and acetaldehyde [176,219]. Hence, novel targets had to be found to redirect the metabolism from ethanol production to other end-products [98]. However, these changes in the metabolic pathways must be carefully monitored, as other products can impact the overall quality of the wine [220].

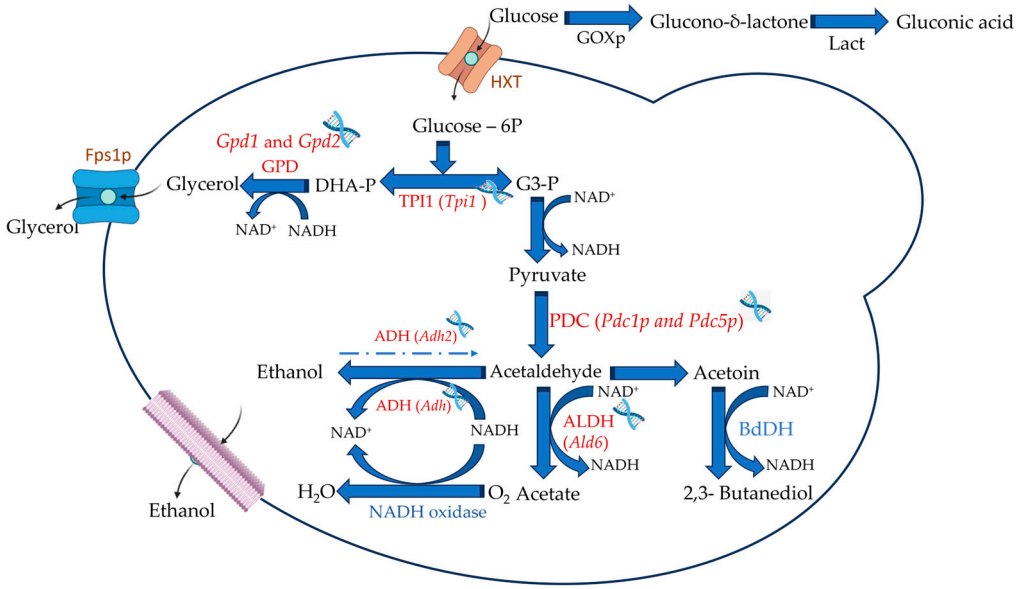

Figure 3. Main target specific enzymes and genes in yeast cells that may lead to lower ethanol yields. HXT—hexose transporter; Fps1p—aquaglyceroporin; GPD—glyceraldehyde-3-phosphate dehydrogenase; TPI1—triosephosphate isomerase; PDC—pyruvate decarboxylase; ADH—alcohol dehydrogenase and ALDH—Aldehyde dehydrogenase. GOXp—Glucose-oxidase—and Lact—lactonase—are expressions, in yeasts, of non-yeast genes.

One of the modifications that can be used to reduce ethanol production is linked to the overexpression of glycerol-3-phosphate dehydrogenase isozymes, namely through *Gpd1* and *Gpd2* genes [221], Figure 3. Glycerol production usually uses about 4% of grape juice carbon during fermentation by *S. cerevisiae*, generally in the initial stages of biomass formation [222]. Glycerol has two essential functions: to combat osmotic stress and to maintain the oxidation-reduction balance. The reaction behind glycerol formation is linked to the correction of redox balance within cells [223]. The overexpression of these genes increases glycerol synthesis while decreasing ethanol synthesis [224]. This increase in glycerol production can reach as much as 548%, while the reduction in ethanol can be of great significance, as shown in early works [172]. Other results indicate an increase in glycerol production ranging from 109 to 275% and a reduction in ethanol from 3 to 24%, depending on the experimental medium (yeast extract, peptone, dextrose medium, yeast nitrogen base medium, synthetic medium, grape juice or synthetic Leu-free) or the overexpressed gene

(*Gpd1* or *Gpd2*) [220]. However, other metabolites are also more produced and can cause changes in the quality of wine. Of those, succinate, acetate, acetaldehyde, acetoin, and 2,3-butanediol [174,225], Figure 3, must be referred to, as their presence above the sensory threshold may be detrimental to perceived wine quality [220,226]. Mutant yeasts with modifications of GPD need further genetic modifications to avoid excessive production of these metabolites. One modification is the deletion of aldehyde dehydrogenases, namely the *Ald6* gene, that contribute to the formation of acetic acid [227]. This modification decreased the formation of acetic acid, with increased glycerol production and lower ethanol yield [225]. However, a subsequent problem arose, as the deletion of *Ald6* increased acetoin production, negatively affecting wine aroma. Ehsani and collaborators [228] obtained a strain that produced lower ethanol levels (3%, *v*/*v* less) and higher glycerol production with a reduced impact on sensory parameters in the final wine.

Other changes in glycerol metabolism can be achieved by changing the expression of genes linked to Fps1p, an aquaglyceroporin channel that controls the intracellular glycerol concentration [229–231]. The production of glycerol is controlled by a regulatory domain located in the N-terminal extension of Fps1p. This domain regulates glycerol transport; when removed, the channel becomes hyperactive. As a result, glycerol continuously leaks out of the cell, and the cell compensates for the loss by producing more glycerol [173,230]. Varela et al. [218] observed that the increased glycerol production, due to deleting the regulatory domain of Fps1p, lowered ethanol formation considerably (Figure 3).

Another gene modification to reduce ethanol production can be deleting Pyruvate decarboxylase (PDC) genes. This enzyme catalyzes the decarboxylation of pyruvate to acetaldehyde and CO_2, being three genes known in *S. cerevisiae* (*Pdc1*, *Pdc5*, and *Pdc6*) up-regulated by the transcription factor *Pdc2p*; however, only *Pdc1p* and *Pdc5p* are known to be active in yeast during fermentation [232], Figure 3. Modifying the PDC genes resulted in diverse outcomes. Deleting *Pdc1* resulted in lower activity and increased pyruvate levels, which are undesirable, considering microbial stability and balance of sulfur dioxide. Still, no reduction in ethanol, while deleting *Pdc2*, led to a considerable decrease in ethanol levels and increased glycerol production while maintaining sufficient pyruvate decarboxylase activity to support glucose growth [172]. Further changes in this set of genes were performed by Cuello et al. [175], which resulted in a strain with reduced ethanol production without effect on other fermentation kinetics.

Another gene editing that can be used to reduce the production of ethanol is modifying the expression of triose-phosphate isomerase, encoded by the *Tpi1*, which is the enzyme catalyzing the interconversion between dihydroxyacetone phosphate and glyceraldehyde 3-phosphate, the two products following the breakdown of fructose 1,6-bisphosphate [219], Figure 3. The lack of this gene resulted in high amounts of glycerol, with a reduced ethanol yield [177]. However, the deletion of the *Tpi1* gene caused the inability of this strain to grow in a glucose medium, probably due to the reduced content of NADH, which is produced during the conversion of glyceraldehyde 3-phosphate into pyruvate [233,234]. A complete loss of activity of the TPI1 enzyme seems like it would be more feasible, as a reduction in yeast growth with attendant fermentation problems is likely to occur. Still, a partial reduction in its activity could provide an opportunity for low alcohol-producing yeast. This partial reduction can be achieved by changing regulatory genes, like *Gcr1* and *Gcr2* (transcription factor for glycolytic genes), that can reduce the expression of *Tpi1* [235], with mutations in other genes, like *Reb1* (an essential gene that maps on chromosome), *Rap1* (Repressor Activator Protein), and *Grc1* (component of the minus-end located γ-tubulin ring complex) also able to reduce TPI1 activity [236]. Avoiding glucose repression of respiration has also been a target for producing low-alcohol wines. This approach relied on the use of a chimeric glucose transporter, comprised of the amino-terminal part of HXT and the carboxy-terminal region of *Hxt7* (HXT1, 2, 3, 4, 6, and 7 are intramembrane transporter proteins known to be involved in the transport of glucose) [237]. Using a yeast strain with deleted *Hxt1*, 2, 3, 4, 6, and 7 resulted in a respiratory phenotype with low ethanol production [180], even though results were achieved using low sugar concentrations medium (5%, *w*/*v*)

compared to grape juice. This shifts the metabolism from the Pasteur effect (under low O_2 concentrations, yeasts conduct alcoholic fermentation forming ethanol and CO_2, or, under high O_2 concentrations, aerobic fermentation occurs with lower glucose consumption) to the Crabtree effect, where, in the presence of high sugar content (about 200 g/L), regardless of O_2 presence, fermentation can occur [238].

A different approach is the expression, in yeasts, of non-yeast genes. Reducing the content of sugars in grape juice before fermentation can be achieved by glucose oxidase (GOXp), an oxygen-dependent dehydrogenase that catalyzes the first step of a two-step process associated with converting glucose to gluconic acid [220]. Besides treating grape juice with GOX to reduce the sugar content, a strategy that has several limitations, even though it can reduce up to 40% of ethanol production [239], the introduction of the gene encoding this enzyme has already been performed in *S. cerevisiae* [179]. Microvinifications of Chardonnay juice samples resulted in wines containing 1.8–2.0% less alcohol, possibly due to the use of glucose to produce D-glucono-δ-lactone and gluconic acid by GOX (Figure 3). Other authors overexpressed the gene *noxE* from *Lactoccocus lactis*, encoding H_2O-forming NADH oxidase, *NoxEp*, that uses NADH, oxidizing it when oxygen is available [178]. The introduction of this NADH oxidase can decrease the available intracellular NADH pool, affecting alcohol dehydrogenase (ADH), hence resulting in reduced ethanol formation [98]. This resulted in using only half the available sugar but with paralleled changes in other metabolic pathways, increasing acetaldehyde production, impairing growth, and fermentation performance. All these genetic manipulation approaches to low ethanol-producing yeast, as well as others that might arise, will be dependent on the acceptability of both the industry and consumers of using such yeast, pushing current research on the search for non-GMO alternatives [97].

2.2.2. Yeast Selection for Low Alcohol Production

One alternative to avoid GMO yeasts, designed for low-ethanol production, is to isolate those that naturally present that trait. However, this effort for *S. cerevisiae* can be complex, as biochemical and physiological characteristics and the underlying genetics of this yeast have been pushed by natural selection to favor the yield of ethanol [97,240]. This has resulted in a slight variation in this phenotype [241], with currently available *S. cerevisiae* wine yeasts resulting in similar ethanol production when fermenting the same must [242]. Hence, the option would be selecting non-*Saccharomyces* (NS) yeasts that preferentially consume sugars by respiration rather than fermentation [238]. Therefore, evaluation of ethanol production variation among NS yeasts has been addressed. Using non-*Saccharomyces* yeasts has garnered significant interest from the scientific community and winemakers, as the available data state (e.g., [197,243,244]). These yeasts can divert carbon or sugar metabolism into other pathways, thus avoiding ethanol production during fermentation [183,197,243–245]. Several studies have shown significantly reduced wine ethanol levels when using these yeasts. For instance, Magyar and Toth [181] identified *Saccharomyces uvarum*, *Candida stellata,* and *C. zemplinina* strains with exciting properties. These strains produced, in laboratory fermentations, similar residual concentrations of sugars but with considerable chances in alcohol production, namely for *C. zemplinina*, with approximately half the alcohol content that was recorded for *S. cerevisiae*.

Another exciting work was performed by Gobbi et al. [182], using *Zygosaccharomyces bailii*, *Z. sapae*, *Z. bisporus*, *C. zemplinina*, *C. stellata*, *Hanseniaspora uvarum*, *Saccharomycodes ludwigii*, *Dekkera bruxellensis*, and *S. cerevisiae*, for fermentation tests with grape juices. Results showed significantly low ethanol production in *Z. bailii*, *Z. sapae*, *Z. bisporus*, and *C. zemplinina*, but more prominently when using *H. uvarum*, confirming data observed by other authors [246,247]. Low ethanol production has also been reported for strains of *Metschnikowia pulcherrima*, *Schizosaccharomyces malidevorans* and *C. stellata* [183], *Torulaspora delbrueckii* [246], *Pichia kudriavzevii* and *Z. bailii* [185]. *Schizosaccharomyces pombe* reduced 0.65% of ethanol in the fermentation of white Airén grapes [186], and some *Saccharomyces* species can also provide low ethanol-producing strains. A reduction of 0.7% was achieved

with the use of *S. uvarum* [248], with *S. kudriavzevii* also presenting interesting results [249]. However, some adverse effects have also been linked to the use of these alternative strains if partial aeration strategies during fermentation are applied to allow the use of sugar to be consumed via respiration rather than alcoholic fermentation, namely the formation of undesirable volatile compounds, including acetic acid [185,191,250], even though positive effects on sensory characteristics also occur [98].

Additionally, non-*Saccharomyces* yeasts play a multifaceted role in wine fermentation, potentially enhancing its sensory profile and aromas and contributing to wine stability and complexity [182,183,187,197,243–245,250–254]. Some non-*Saccharomyces* possess antimicrobial properties, including the production of Killer factors (mycocins), which inhibit the growth of undesirable yeasts (*Zygosaccharomyces* genus, *Brettanomyces bruxellensis*, among others), providing an additional advantage [255]. These "Killer factors", such as CpKT1 and CpKT2 produced by *Candida pyralidae*, have demonstrated effectiveness in controlling the population of undesired yeast strains, such as *B. bruxellensis*, in winemaking conditions, without adversely affecting the fermentation processes of *S. cerevisiae* or the tested lactic acid bacteria [256]. Other "Killer factors", such as KTCf20 and Pikt (produced by *Wickerhamomyces anomalus*), Kwkt (produced by *Kluyveromyces wickerhamii*), PMKT and PMKT2 (produced by *Pichia membranifaciens*), have also demonstrated potential in controlling unwanted yeast strains in vinification environments [257–260].

2.2.3. Co-Inoculations and Sequential Inoculations (Non-*Saccharomyces* and *S. cerevisiae*)

Considering some of the previously referred advantages and drawbacks of using different yeasts, two approaches to reducing the ethanol content in wine are co-inoculation of those yeasts or their sequential introduction in fermentation. The first approach (co-inoculation) involves concurrent inoculations of non-*Saccharomyces* or other *Saccharomyces* non-*cerevisiae* yeasts at high cell concentration with *S. cerevisiae,* and the second approach (sequential inoculation) consists of the start of fermentation with non-*Saccharomyces* or other *Saccharomyces* non-*cerevisiae* yeasts, occurring for a given duration and inoculating *S. cerevisiae* to take over and complete the fermentation [261].

The critical factors affecting fermentation and oenological outcomes of this approach are the time leading to the inoculation of *S. cerevisiae* (in sequential fermentations) and the ratio of *S. cerevisiae* and other yeast [252]. Besides ethanol changes, non-*Saccharomyces* or other *Saccharomyces* non-*cerevisiae* yeasts are essential due to their contribution to wine aroma and flavor, with several yeasts already described as contributors to that profile. Padilla et al. [252] and Ivit et al. [243] point out several yeasts as having great oenological interest and used in co- or sequential inoculations, which will be briefly reviewed here.

One of the most important genera is *Hanseniaspora*, which comprises at least ten species, *H. uvarum* and *H. guilliermondii* being the most common. Several *Hanseniaspora* species have been tested in sequential or co-inoculated fermentation with *S. cerevisiae*, with a recorded reduction in the ethanol content of wines. Reductions of around 1% were achieved using sequential inoculation of *H. uvarum* and *S. cerevisiae* in synthetic grape juice [187], and, in white (Sauvignon blanc) and red (Pinotage) musts, reductions in ethanol were also achieved of around 1.3% and 0.8%, for white and red musts, respectively [188]. Furthermore, three strains of *H. uvarum*, in sequential or co-inoculated fermentations with *S. cerevisiae*, resulted in lower ethanol concentration when compared to fermentations with the latter only [189]. Also, in synthetic grape juice, a reduction in alcohol was recorded with sequential inoculation of *H. osmophyla* and *S. cerevisiae* [187] and white (Sauvignon blanc) and red (Pinotage) musts; the use of *H. opuntiae* also resulted in less production of ethanol [188]. However, some studies point out the increase in acetic acid when fermentations are performed using *Hanseniaspora* yeast strains [189].

Another important yeast already known to have essential winemaking traits *is Schizosaccharomyces pombe*. Besides being able to moderate wine acidity by metabolizing malic acid, this strain enhances the color of red wine and reduces Ochratoxin A, biogenic amines, and ethyl carbamate [244]. In addition, some *S. pombe* strains used in sequential fermentation

resulted in lower ethanol content [186], even though a lack of reduction or even increase in alcohol has been reported when using *S. pombe*, or even the presence of unsuitable aroma produced by the fermentative metabolism of *S. pombe* [262].

An alternative non-*Saccharomyces* yeast of great importance is *Metschnikowia pulcherrima*. This non-*Saccharomyces* yeast is commercially available from many suppliers and is known to improve several organoleptic characteristics of wines [263]. Furthermore, the production of wines with lower ethanol in sequential fermentations with *S. cerevisiae* has been reported in several works, either with grape juice [190], synthetic grape must [204], Chardonnay and Shiraz musts [183], and in white grape must (mixture of Malvasia and Viura varieties) [191]. A reduction of up to 1.6% in ethanol was recorded in Shiraz wines [183], with a drop of alcohol further confirmed in later works [192]. The use of *M. pulcherrima* and *S. uvarum* mixed inoculum, sequentially used with *S. cerevisiae*, reduced 1.7% *v*/*v* of ethanol compared to wine fermented with *S. cerevisiae* [192]. When immobilized, the sequential inoculation of *M. pulcherrima* could also reduce ethanol content in synthetic or natural grape juice [187]. However, results are linked to several conditions, namely aeration regimes, that must be carefully monitored [191,193].

Lachancea thermotolerans (previously *Kluyveromyces thermotolerans*) is a commercially available yeast that positively influences wine's sensory profile and total acidity [253]. Besides organoleptic advantages, reduction in ethanol content has been achieved in sequential or co-inoculation. A fermentation started with *L. thermotolerans* and a sequential inoculation, after two days, with *S. cerevisiae*, led to a reduction in ethanol up to 0.7% *v*/*v* [194,195,251]. Mixed or sequential fermentation with *L. thermotolerans* and *S. cerevisiae* also reduced alcohol production [196]. Further works prove that sequential fermentations with *L. thermotolerans* and *S. cerevisiae* can reduce the ethanol content in must of Tempranillo grapes. Mixed fermentations of *S. pombe* and *L. thermotolerans* can lower the ethanol content in wine but may also increase the acetaldehyde content [197]. The sensory threshold for acetaldehyde ranges from 100–125 mg/L. Typically, table wines have acetaldehyde levels below 75 mg/L immediately after fermentation. However, if the levels exceed 125 mg/L, it can result in unpleasant odors such as 'over-ripe bruised apples', 'stuck ferment' character, or 'sherry' and 'nut-like' characters.

Torulaspora delbrueckii was one of the first commercially accessible non-*Saccharomyces* yeasts, as they had similar fermentation patterns as *S. cerevisiae* and were able to enhance aroma composition and positively impacting properties for traditional methods of sparkling wine [264]. Several studies have proven that its use in mixed or sequential fermentation resulted in reduced ethanol. Most of these studies refer to reductions of 0.5% or below [193,198–201,265]. Higher reductions of ethanol were recorded in other works, like 1% less alcohol using Chardonnay [254] or less than 1.5% using chemically defined grape juice [192]. However, to achieve higher levels of alcohol reduction, using *T. delbrueckii* in regular fermentations must be combined with high aeration processes [266].

Another yeast commonly studied due to positive contributions during fermentations is *Starmerella bombicola* (formerly known as *Candida stellata*). Early works by Soden et al. [202] with mixed and sequential fermentations with *C. stellata* and *S. cerevisiae* resulted in less alcohol than the mono-inoculated *S. cerevisiae* control. Further works with sequential fermentations using *Starmerella bombicola* and *S. cerevisiae* in Chardonnay juice yielded lower ethanol concentrations when compared to *S. cerevisiae* fermentations [202]. Immobilizing *Starmerella bombicola* is a practical approach to reducing the final ethanol content in grape must. Studies have shown that using this yeast species in the Trebbiano Toscano grape-must and the Verdicchio grape-must significantly reduce the final ethanol content [187,203].

2.2.4. Abiotic Factors Control during Fermentation

Control of abiotic factors can also be used to reduce alcohol levels in wines. One of those approaches is the use of aeration. This alternative uses the oxidative metabolism observed in some non-*Saccharomyces* species that can use oxygen for growth regardless of sugar concentration and, therefore, reduce those that would contribute to ethanol forma-

tion [219]. Under low sugar concentrations and with aeration, respiration is favored for *S. cerevisiae*, and this technique can be used for lowering ethanol content in wines. However, this approach can produce higher amounts of acetic acid, negatively affecting wine sensory characteristics [192,204]. For this approach to be successful, yeast strains that can withstand the conditions available for respiration within the grape must be found without negative impacts on the wine itself. Recently, Tronchoni et al. [206] identified strains with acceptable outcomes after aerobic fermentation, including low volatile acidity, acetic acid levels, and low ethanol production. Still, the most feasible approach is suggested to be the use of a non-*Saccharomyces* species yeast under aeration conditions for a defined amount of time, after which *S. cerevisiae* would be inoculated [245] or co-inoculation strategies. For instance, Morales et al. [191] identified one strain of *M. pulcherrima* and, in a co-inoculation with *S. cerevisiae* in laboratory-scale bioreactors, and depending on the condition, a reduction of 2.2% (*v*/*v*) in ethanol content was achieved, while maintaining acceptable volatile acidity levels. Using the same yeast, a decrease in ethanol of 1.5% was recorded, and, for certain aeration conditions (5 mL/min aeration, 0.025 volume of air per volume of culture per minute, for 72 h), changes in wine volatile profile were considerably acceptable and results similar to those observed using *Zygosaccharomyces bailii* [254]. On the other hand, other works using strains of *M. pulcherrima* show higher decreases in ethanol content but with a parallel increase in off-flavors (solvent-like notes, indications of oxidation, a reductive impression, a reduction in the overall purity and fruity characteristics, and the presence of undesirable aromas like "Maggi-flavour", "cheesy" and, "sweaty"), negatively impacting wine sensory analysis [205]. The same authors also recorded adverse effects on sensory analysis when *Candida zemplinina*, *Pichia guilliermondii*, and *P. kluyveri* conducted fermentation. Even though promising results might be found, the most common pattern is a decrease in sensory quality with the increase in aeration, pointing out the need for further studies that might convert this strategy into an industrial feasible solution.

Control of the temperature in which fermentation occurs is critical in the wine industry. Low temperatures during fermentations affect wine's final sensory attributes [267], changing several metabolic pathways of yeasts [268]. Still, it can result in sluggish fermentation, which is not a standard method. Even though there is widespread knowledge about the influence of temperature on the fermentation processes, the effect of this factor on the population dynamics of *S. cerevisiae* is still largely unknown. One critical work is from Torija et al. [207], which clearly shows the effect of temperature on the population of *S. cerevisiae* during fermentation. Different strains could be separated by their ability to perform better at higher or lower temperatures, even though the size of the population was the same, independently of the fermentation temperature. The wine composition reflected the population changes, with higher alcohol at low temperatures and secondary metabolites positively affected by temperature increase. However, correlations between temperature and secondary metabolites rely on intricate and dynamic metabolic pathways and do not always present the same trend [208]. Ethanol formation has been negatively correlated with temperature for *S. cerevisiae* [268], linked to higher growth rates, diverting carbon sources, and reduced ethanol production [269]. Rodrigues et al. [270] also observed the same pattern and recorded a reduction in ethanol yield with increasing temperature of *S. cerevisiae*. The use of preadapted inoculum (grown at a fermentation temperature of 13 or 17 °C) can be a helpful approach, as results showed a reduction in alcohol production, even though these results are dependent on the used strains [209]. Hence, using low-temperature fermentations to reduce the ethanol content of wines must rely on using non-*Saccharomyces* yeasts. The temperature at which fermentation occurs is a critical factor regarding non-*Saccharomyces*' growth [222] due to the increased tolerance to alcohol at reduced temperatures [271]. Indeed, even early data indicate that non-*Saccharomyces* yeast keeps their viability for extended periods at lower temperatures when compared to *S. cerevisiae* [272,273]. Further works have shown that ethanol concentration can be reduced in fermentations performed by *Metschnikowia pulcherrima* and *Meyerozyma guilliermondii* before inoculation of *S. cerevisiae*, using lower temperatures, without compromising the

sensory attributes of wine [210]. Similar results were observed using *Williopsis saturnus* var. *saturnus* or *Metschnikowia pulcherrima* [211,274]. Using non-*Saccharomyces* strains in low-temperature fermentations can be a feasible approach to reducing ethanol content in wines. Still, it must be combined with a carefully planned co- or sequential inoculation of traditional yeasts or fermentation times [275]. However, this short fermentation period cannot convert most must sugars, resulting in a wine with high residual sugar content. Preservation with sulfur dioxide or pasteurization is an additional and complementary procedure to ensure microbiological stability and wine storage [118,276]. Studies indicate that the short fermentation period also limits the production of monoterpenes, ethyl esters, and acetates, compounds responsible for desirable floral and fruity aromas in wines, leading to wines with poor aromatic profiles [276–279]. The study by Nikolaou and Kourkoutas [280] explored high-temperature effects on low-alcohol wine production with immobilized kefir cultures. Both wet and freeze-dried immobilization proved effective for simultaneous alcoholic and malolactic fermentation at over 30 °C, with operational stability for three months. Ethanol levels and daily productivity met industry standards. The research also examined using immobilized kefir cultures at 45 °C for low-alcohol wines with a sweet (liquored) character despite higher residual sugars, offering innovative approaches to sustainable production.

Carbonic maceration is a fermentation technique in which grape clusters are placed in a carbon dioxide-rich atmosphere inside a closed tank [281]. These conditions lead to a metabolic change in grapes, from a respiratory metabolism to an anaerobic fermentative metabolism called intracellular fermentation, without yeast intervention, with the formation of alcohol (1.5–2% alcohol) and reduced malic acid content. The resulting wines possess distinct characteristics, namely in flavor and color, but might not age well [282]. The effect of this practice on wine alcohol is variable, depending on several factors. Indeed, some early works recorded higher values of ethanol in wine from carbonic maceration [283], while other works found lower ethanol content [212] or no changes at all [284]. More recent works show that carbonic maceration increases the ethanol content in wine from Tempranillo red grapes [285], while a slight decrease (non-significant) was recorded in Muscat Hamburg vines [213]. Using carbonic maceration proves to be a practical alternative if the resulting wine is separated into two different fractions: one, the free liquid resulting from the fermentation, and, two, the liquid obtained after pressing the grapes [214,215]. Both these works show considerably lower ethanol content of the first fraction, the free liquid resulting after carbonic maceration, without significant variations on the oenological attributes of the wine. This strategy can be used to produce wines of low ethanol content, less affected by color and aromatic changes when compared to other methods used to reduce the alcohol content of wines.

Reducing yeast biomass during fermentation is another method to produce non-alcoholic or low-alcohol wines. This method involves periodically reducing the yeast population during the must fermentation to keep the fermentation rate of fermentable sugars as low as possible, thus preventing excessive ethanol formation [100,286–289]. However, this approach often leads to fermented beverages with substantial amounts of unfermented sugars, making them vulnerable to spoilage issues and potential deterioration [288], with negative off-flavors.

2.2.5. Wines Biological Dealcoholisation

Alcoholic fermentation is a biochemical process responsible for producing food products such as bread and various beverages, including wine, beer, and other alcoholic drinks [290–292]. In wine production, alcoholic fermentation is crucial in transforming grape must into wine, a time-honored tradition fundamental in creating a wide range of unique flavors and aromatic profiles [293].

This process is pivotal in the conversion of sugars into ethanol and carbon dioxide, along with other metabolites such as glycerol, acetate, succinate, pyruvate, higher alcohols, and esters, a process carried out by various yeast species, representing the primary

biotechnological process on a global scale [291]. Within the yeast species, *Saccharomyces cerevisiae* yeast dominates the wine fermentation process [245,294]. However, it is present on the surface of grapes and in vineyard soils in much lower numbers relative to other yeast species belonging to *Hanseniaspora* (the predominant) *Candida, Hansenula, Kluyveromyces, Metschnikowia, Pichia, Rhodotorula*, and *Torulaspora* genera [290]. The former is recognized to prevail during the initial stages of alcoholic fermentation [245,293].

Under anaerobic conditions, the yeast *S. cerevisiae* utilizes pyruvic acid generated from sugar catabolism as a sink for the reduced coenzyme NADH. Subsequently, pyruvic acid is converted via acetaldehyde into ethanol, enabling the regeneration of NAD^+ in a final step catalyzed by alcohol dehydrogenase to allow glycolysis and ATP production to proceed. In the fermentation process, and for the conversion of glucose into ethanol and CO_2, 12 enzymes are involved, with ten degrading glucose to pyruvate with ATP production for yeast growth and two enzymes for the conversion of pyruvate into the final fermentation products to preserve yeast redox balance. The pyruvate decarboxylase and alcohol dehydrogenase, the last enzymes in the yeast fermentative pathway, require magnesium and zinc ions to convert sugar into ethanol efficiently [295].

Saccharomyces cerevisiae is a yeast capable of fermenting pyruvate to ethanol when high glucose concentrations are present. However, when these carbon sources are depleted, *S. cerevisiae* switches to aerobic respiration, using ethanol as a carbon source. This process is known as diauxic shift. This phenomenon is similar to what happens in Sherry wines that use specialized "sherry" or "flor" strains of *S. cerevisiae* [296]. One unique characteristic of sherry strains of *S. cerevisiae*, compared to other fermentation strains, is their ability to form a biofilm or "flor" on the surface of alcoholic wine material. In this biofilm, ethanol is oxidized to acetaldehyde under the action of alcohol dehydrogenase [297], Figure 4. The ability of sherry yeast to work under high alcohol content conditions is their adaptive mechanism, which affects the oenological characteristics [298]. This reversion of metabolic pathways might be a promising alternative to reducing the ethanol contents of wine after fermentation. Ethanol degradation by yeasts involves a three-step pathway, beginning with its oxidation to acetaldehyde by alcohol dehydrogenase enzyme (ADH), followed by the conversion of acetaldehyde to acetate by the aldehyde dehydrogenase (ALDH), and, finally, acetyl-CoA synthetase (ACS) ligates acetate with coenzyme A to produce acetyl-CoA [299], Figure 4. However, ADH and ADLH have several isozymes in *S. cerevisiae*, and, at least for ADH, those isozymes can substitute functionally for one another, even though the ethanol production yield or oxidation rate is quite different among them [299]. The alcohol dehydrogenase ADH1 is regarded as primarily responsible for the regeneration of NAD^+ from NADH by reducing acetaldehyde to ethanol [300]. Growth conditions can repress the activity of this enzyme, while others are derepressed to reutilize the previously produced ethanol. One of the critical enzymes is alcohol dehydrogenase 2 (ADH2), which is thought to catalyze ethanol oxidation preferentially to acetaldehyde due to its relatively low Km for ethanol. The oxidation of ethanol forms acetaldehyde, which is converted to acetate by ALDH2 and activated into acetyl-CoA, entering the glyoxylate and TCA cycles [301]. Even in the first steps of this conversion of ethanol to acetyl-CoA, there is the need for a transcriptional activator, Cat8p, essential for the growth of yeast on nonfermentable carbon sources, with the expression of the *Cat8* gene and transcriptional activation by Cat8p regulated by glucose [302]. This transcriptional activator controls many genes essential to yeast use of ethanol, going from ethanol to acetyl-CoA and even four steps of the glyoxylate cycle, besides other proteins with functions not linked directly to the utilization of ethanol [303]. If glucose is present, *Cat8* expression is repressed by Mig1 (a Cys2His2 zinc finger protein), possibly by directly binding this regulator to the *Cat8* promoter [304]. This protein can be targeted by Snf1, a central serine–threonine kinase, leading to positive regulation of the expression of *Cat8* [304]. This complex set of regulations for ethanol oxidation in yeasts provides numerous targets for future metabolic engineering, aiming to reduce the ethanol in a post-fermentation phase.

As referred before, the use of non-*Saccharomyces* (NS) yeasts during fermentation can be an option to reduce alcohol content in wines. Moreover, some commercial *S. cerevisiae* strains also have this ability. Therefore, can these yeasts be used as a potential approach to reduce alcohol content in wines post-fermentation? Studies have highlighted the capability of specific yeast strains to consume acetic acid during refermentation, enhancing sensory qualities by reducing undesirable acidity levels in wines [305–309]. Interestingly, during the deacetification processes, ethanol content also decreased. In the work of Vilela-Moura et al. [305], during the deacetification process, it was observed that the amount of ethanol present was reduced by 37.5% under aerobic conditions and by 13.5% under limited aerobic conditions. Additionally, when using immobilized yeasts in double-layer alginate-chitosan beads, a decrease in the ethanol content between 6–11.2% was also observed. Therefore, by understanding and comprehending the pathways of ethanol degradation and exploring the metabolic versatility of yeasts, the possibility of modifying the composition of wines in a post-fermentation stage will increasingly become a reality, making way for new strategies that will help mitigate the adverse effects of climate change on viticulture.

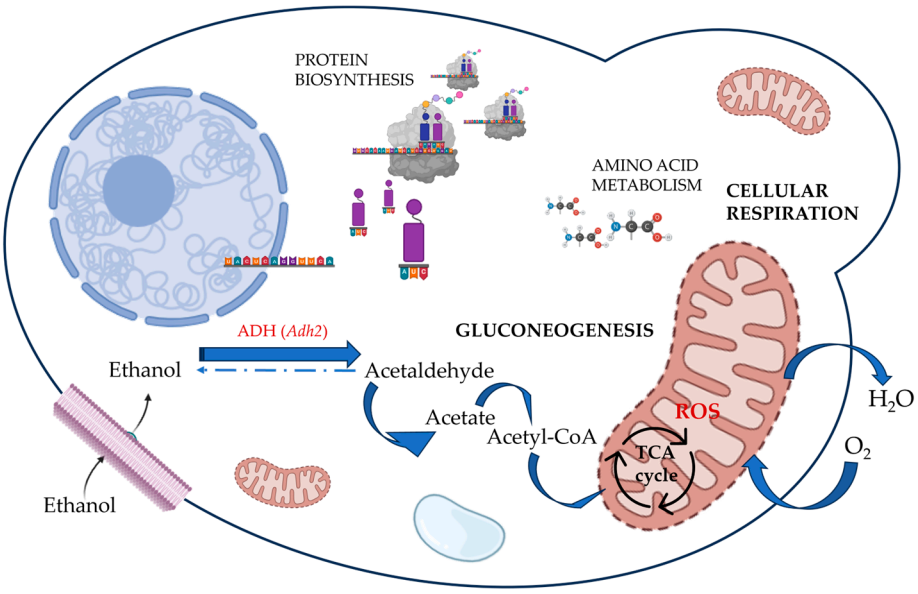

Figure 4. Schematic representation of yeast cells' cellular respiration and ethanol consumption. Yeast proliferation under the prevailing oxidative conditions is also facilitated by the antioxidant defense system protecting cells from reactive oxygen species (ROS) formed during the oxidative metabolism of non-fermentable carbon sources such as ethanol. ROS are deleterious on mitochondrial DNA (mtDNA), probably due to the former's proximity to the major sites of the endogenous production of ROS. Moreno-García et al. [310], in a work about differential proteome analysis of a "flor" yeast strain under biofilm formation in sherry wines, detected proteins preventing these adverse effects and various others repairing the resulting damage.

3. Consumers Perception and Behavior Related to Low-Alcohol Wine

As mentioned above, consumer preferences and behavior regarding wine have undergone significant shifts in recent years. One such change pertains to the growing demand for wines with low alcohol content (9% to 13% *v*/*v*). With increasing awareness of health and well-being, as well as social responsibility and safety considerations, consumers are becoming more attentive and open to alternatives that align with their values and lifestyles [23–26,311]. In this regard, wines with low alcohol content have emerged as a new wine category, progressively gaining popularity and capturing consumers' interest.

But what exactly constitutes wine with low alcohol content? The term 'low alcohol wine' may vary between countries and according to prevailing legislation. For instance, in Australia and New Zealand, a beverage with more than 1.15% alcohol by volume

cannot be considered low alcohol, while in the United Kingdom, the limit is 1.2% [23]. The taxation applied to wines also varies; some countries employ fixed rates, while in others, taxes are based on alcohol concentration [312]. The precise definition of wines with low alcohol content is not universal, as it may vary according to regional norms and regulations established by specific governmental bodies or wine authorities. Frequently, the term 'wines with reduced alcohol content' applies to wines that possess significantly lower alcohol content compared to traditional wines [313]. In Figure 5, wines with reduced alcohol content are generally classified as detailed.

Figure 5. A suggested classification of wines with reduced alcohol content.

The growing consumer concern regarding health issues leads them to choose healthier products. In the context of wine, this translates into the preference for wines with reduced alcohol content. According to Bucher et al. [312], beverages with low alcohol content can be considered healthier for consumers aiming to maintain a balanced and healthy lifestyle and a conscious diet. In addition to containing fewer calories than traditional alcoholic beverages, these drinks may have a lesser impact on the consumer's overall health [314].

Numerous studies emphasize the harmful effects of alcohol consumption on human health. Alcohol is classified by the World Health Organization (WHO) as a toxic and psychoactive substance that induces addiction [315]. Moreover, it is considered a risk factor for premature death, with approximately three million deaths per year attributed to alcohol consumption. It is also linked to the development of various diseases, including cancer, stroke, liver diseases, high blood pressure, and mental health disorders. Additionally, alcohol intake is associated with higher risks of accidents and injuries [311,312,316].

Currently, available information regarding the impact of alcohol and wine on health is contradictory and confusing. Despite the potential harms of alcohol consumption, several decades of studies have found beneficial effects of "moderate wine consumption" [317]. This is attributed to the presence of phenolic compounds derived from grapes in wine, which suggests that moderate wine consumption may offer health benefits, unlike other alcoholic beverages [318].

"Moderate consumption", according to many health guidelines for healthy adults, is defined as the intake of two standard drinks per day (or "unit of alcohol" in the UK), not exceeding four standard drinks [312] per day. The definition of a traditional drink pertains to the amount of alcohol an average adult can metabolize in an hour. However, it is essential to highlight that the alcohol content in a standard drink can vary across countries, not only in Europe but globally (Figure 6): countries like France and Spain define a traditional drink as one containing 10 g of pure alcohol, as in Australia, whereas in the UK and Iceland, it is 8 g. In the USA, a standard drink contains 14 g of pure alcohol, while Japan has 20 g of alcohol [319,320].

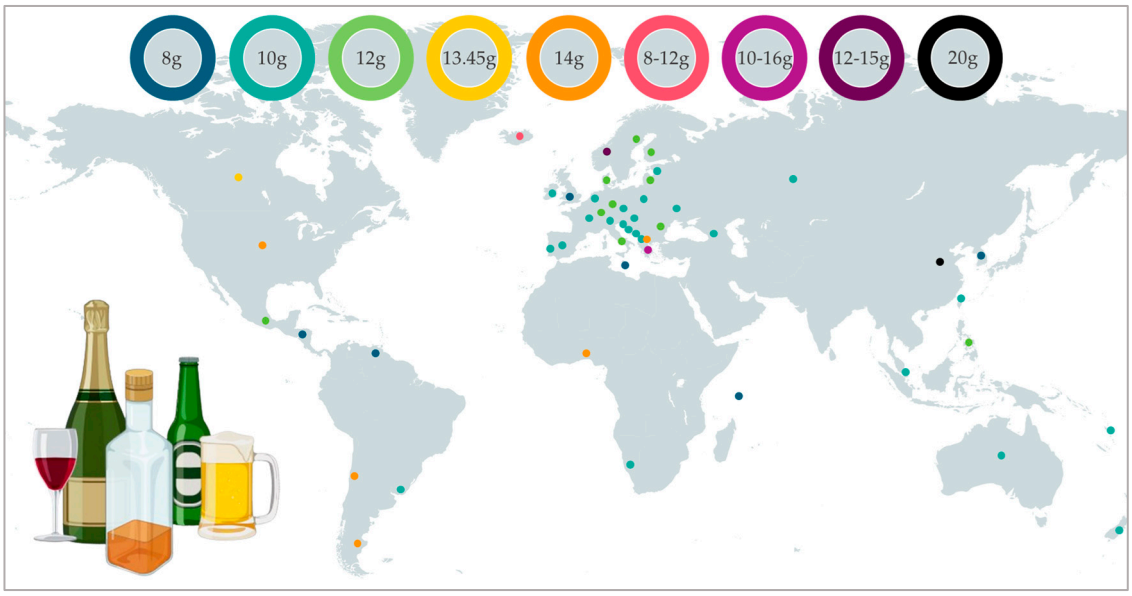

Figure 6. Grams of alcohol in a standard drink by country, according to [319,321].

According to the review conducted by Minzer et al. [322], when consumed moderately and regularly, wine can benefit heart health, reduce the risk of strokes and diabetes, and aid in preventing conditions such as hypertension, dyslipidemia, cancer, and dementia. Furthermore, the phenolic compounds in wine have been linked to improved lipoproteins and endothelial function, protecting against oxidative stress and vascular damage [318,323]. However, do consumers truly understand what "moderate drinking" entails and what constitutes a standard drink? According to Mongan and Long [319], consumers do not understand these concepts. They struggle to define moderate wine consumption and the number of standard drinks that can be considered healthy.

While the debate continues on whether the potential positive effects of wine outweigh the negative ones, consumers are encouraged to consider alternatives as a thoughtful approach to enjoying this versatile beverage [313]. This may involve selecting wines with reduced alcohol content or exploring the increasing availability of non-alcoholic wine options.

Therefore, low-alcohol wine emerges as a healthier and safer option that has piqued the interest of consumers conscious of the adverse effects of alcohol consumption on health, who aim to enjoy wine without compromising their well-being. However, according to Bucher et al. [324], public awareness regarding the advantages and quality of low-alcoholic wine remains somewhat limited, necessitating further studies and the need to educate consumers about the available options in the market.

4. Final Remarks

Considering the expected increase in temperature in the upcoming decades, it is essential for research and the wine industry to investigate the relationship between the final wine alcohol content, bioactive compounds, and various climatic conditions. This knowledge will help develop suitable strategies for viticultural and enological practices, ensuring the production of high-quality wines rich in health-benefiting compounds and low in alcohol concentration.

Producing low-alcohol wines involves various viticultural practices, starting from the vineyard management stage. It is important to note that the goal is not just to reduce alcohol but to balance alcohol, acidity, and other components to produce a harmonious and expressive wine that reflects its terroir. Sustainable and holistic vineyard management practices often play a significant role in achieving these goals.

Reducing alcohol production during fermentation is a complex task because alcohol is a natural byproduct of fermentation, where yeast converts sugars into alcohol and carbon dioxide. However, winemakers can use several strategies and techniques, such as the choice of yeast species, the time of inoculum, and temperature, among other factors, to influence or control wine alcohol levels.

Regarding physical methods for alcohol removal in wines, the choice of method depends on factors such as the wine's composition, the desired level of alcohol removal, and economic considerations. Each method has advantages and limitations, and the selection is often based on the specific application's requirements. Furthermore, it is essential to discover cost-effective techniques to reduce the wine's alcohol content when it exceeds the desired limit during fermentation.

The current post-fermentation procedures involve physical methods for alcohol removal, such as extraction, membrane separation, or heat treatment, which require expensive and specialized equipment. Therefore, bio-dealcoholization of wines could be an attractive alternative strategy. Yeasts can perform the process without specific equipment, making this a cost-effective procedure.

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