applied biosciences

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Review

Wine Grapes Ripening: A Review on Climate Effect and Analytical Approach to Increase Wine Quality

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Abstract: Red wine grapes have an important impact on the economy of many regions, both for wine quality and for their richness in phenolic compounds, which have many health benefits. Climate has been changing substantially in the last years, which affects greatly grape polyphenolic composition and wine quality. In this review, we will unveil the importance of climate in grape development, both physically and chemically, the different methodologies used to evaluate grape quality, the interesting new approaches using NIR spectroscopy, and the functional properties of grapes and red wine, due to their high phenolic content. Climate has an impact in the development of phenolic compounds in grapes, namely in the anthocyanins biosynthesis. The phenolic chemical composition changes during maturation, therefore, it is essential to keep on track the accumulation of these key compounds. This information is crucial to help producers choose the best harvest date since specific compounds like polyphenols are responsible for the color, taste, and mouthfeel of wines, which directly affects wine quality. The usage of different methodologies to assess quality parameters in grapes and wine, can be used to provide essential information to create the chemical profile of each variety to develop calibration methods. NIR spectroscopy seems to be a reliable method to be used in vineyards during grape maturation to provide real time information on quality parameters to producers since many reliable calibration models have been developed over time.

Keywords: red wine grapes; wine grapes; grape quality; climate change; quality assessment

Citation: Rouxinol, M.I.; Martins, M.R.; Barroso, J.M.; Rato, A.E. Wine Grapes Ripening: A Review on Climate Effect and Analytical Approach to Increase Wine Quality. *Appl. Biosci.* **2023**, 2, 347–372. https://doi.org/10.3390/applbiosci2030023

Academic Editors: Adriana Basile, Viviana Maresca and Piergiorgio Cianciullo

Received: 7 April 2023
Revised: 28 June 2023
Accepted: 30 June 2023
Published: 10 July 2023

1. Introduction

Portugal is known for its long-standing tradition in wine production. In Alentejo, south region of Portugal, there are a great diversity of grape cultivars and terroirs contributing to the variety and quality of the wines produced here. The terroir in Alentejo region has a particular impact on berry growth and development contributing to specific characteristics to the grapes that can result in unique wines. Although terroir has a great impact in grape quality, the genetic characteristics also play a significant role [1], and the interaction between both result in wines of higher quality and distinctiveness. In addition to the impact of grape varieties and terroir in wine quality, there is a continued and growing interest in the improvement of wine organoleptic characteristics [2]. The composition of grapes at harvest will impact wine quality, thus it is fundamental to evaluate the berry composition to determine the best harvest date to create higher quality wines [3,4]. It is widely recognized that phenolic compounds are determinant for wine quality [5,6], thus it is important to know how these compounds develop during maturation and how they are affected by external factors, including weather [1,7,8]. During maturation, the chemical composition of grapes changes; therefore, it is essential to keep on track the biosynthesis and accumulation of some compounds from veraison until harvest [9,10]. This information is crucial to help producers choose the best harvest date since specific compounds like polyphenols are responsible for the color, taste, and mouthfeel of wines, which directly affects wine quality.

Recently, there have been some interesting advances in analytical instrumentation to identify and quantify chemical compounds present in grapes that are essential for quality purposes [11–13]. Chromatographic techniques [14–16], spectroscopic methods [17–19], mass spectrometry [20,21], and multivariate analysis [12,22,23] offer a comprehensive approach to understanding the chemical profile of grapes. Simultaneously with routine chemical analysis to quantify some grape key compounds such as phenolic compounds, it is important to create a chemical profile of grapes with impact in specific characteristics of the resulting wine, especially flavor, color, body, and mouthfeel [18,24,25]. Although these methodologies provide the information needed for quality control, they don't provide in situ information for producers. NIR spectroscopy is a good alternative to provide producers real-time answers for their quality concerns [13], although it needs reference methods to develop accurate calibration models.

The synthesis of compounds essential for wine quality depends on many abiotic factors, namely climate. This review will target the challenges that producers face on grape production, the impact of climate changes on grape ripening and composition, the methods to assess grape quality, and the benefits of consuming phenolic rich foods like grapes and wine, including methodologies like NIR spectroscopy that develop models based on reference methods and can help producers to assess quality in situ. These are summarized in Figure 1.

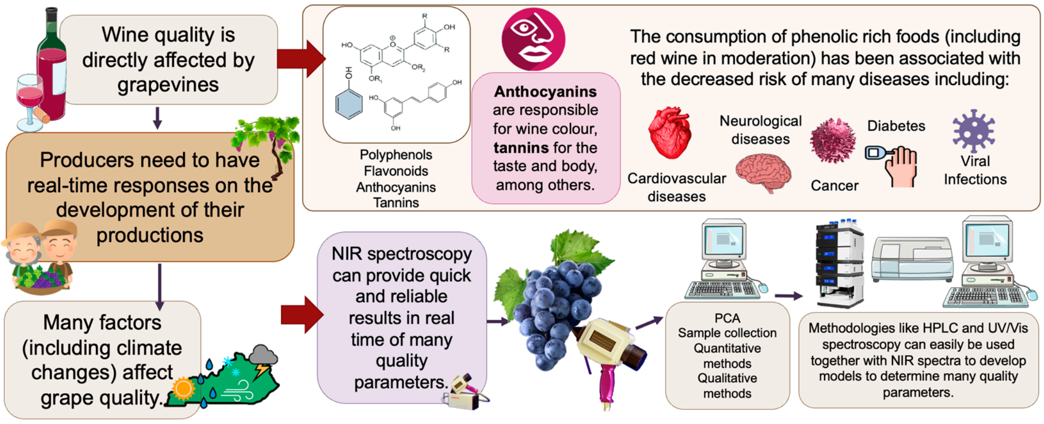

Figure 1. Grape quality is influenced by many factors. Producers need real time answers to assure the quality of their productions. Phenolic rich grapes can be beneficial for human health.

Understanding how climate variations affect grape growth, development, and composition is crucial for vineyard management and ensuring sustainable wine production. Furthermore, climate changes can influence the synthesis and accumulation of phenolic compounds in red wine grapes that contribute to the color, flavor, and health benefits of red wine.

The objective of this study was to perform a literature review on the impact of climate changes on grape cultivation, how it affects the quality of red wine, and methodologies to determine the presence and concentration of quality compounds in red wine grapes.

To carry out this review, an extensive exploration of the Scopus and ScienceDirect databases was performed from 2000 to 2023. The search included articles published in English and included only research papers that featured experimental design and appropriate data analysis methods, with a focus on various key concepts, including grape production, climate, grape and wine quality, bioactive compounds, methodologies for assessing quality compounds, and the health benefits associated with wine consumption.

Overall, a literature review on the importance of climate changes in red wine grapes, their impact on compound synthesis and accumulation, and the relevant analytical methodologies provide a comprehensive understanding of the complex relationship between climate, grape composition, and wine quality. This knowledge contributes to informed decision-making, adaptation strategies in the face of climate change, and the production of high-quality red wines.

2. Grape Production

The industry of wine has a huge impact in the economy of many countries, including Portugal. The production of red wine grapes has a significant impact in many regions [26]. Taxonomically, grapes are classified under the order of Ramnales, the family of Vitaceae, and the genera *Vitis* [27]. *Vitis* genera has more than 70 species grown widely around the world. [7,28]. Different cultivars have different genetic characteristics that will affect the final grape yield [29–31] and wine quality [32]. According to the International Organisation of Vine and Wine–OIV, the worldwide production of grapes in 2020 was 78 million tons, and of this amount, 57% corresponded to wine grapes [33]. The global vineyard area is estimated to be approximately 7.4 million hectares. Five countries are responsible for producing around 50% of the world's wine, and out of these five countries, four are located in the Mediterranean basin [34]. Despite fluctuations in production levels over the past few decades, Europe remains the largest global producer of grapes [35]. Grapes have a significant impact in the Mediterranean basin due to its cultural, economic, and ecological importance [36]. According to the International Organisation of Vine and Wine (OIV), the most produced wine grape varieties in the Mediterranean countries like Portugal, Spain, France, and Italy are "Cabernet Sauvignon", "Merlot", "Tempranillo", and "Syrah". "Touriga Nacional" and "Touriga Franca" are also prevalent in Portugal [37]. According to the Portuguese organisation responsible for the certification, control and protection of Alentejo wines (CVRA–Comissão Vitivinícola Regional Alentejana), the main red wine grape varieties produced in Alentejo are "Alfrocheiro", "Alicante Bouschet", "Aragonês", "Cabernet Sauvignon", "Castelão", "Syrah", "Touriga Franca", and "Trincadeira" [38]. According to FAO (Food and Agriculture Organization of the United Nations) [35] Portugal is one of the main worldwide producers of grapes, producing more than 743,000 tonnes from 2000 until 2018.

Portugal is located in the Mediterranean Basin, and its climate is characterized by mild winters and very hot and dry summers [39]. This region is expected to face severe climatic changes in the future [40] due to the increasing of temperatures [36] and water scarcity [41]. In Mediterranean region, there are several agronomic problems associated with viticulture, and one of the most concerning issues is water scarcity, mainly in the summer [42]. Vines are sensitive to climate changes [40] and this will influence grape final quality. Many grape compounds important to wine quality are affected by severe weather conditions. The synthesis and accumulation of phenolic compounds, such as anthocyanins concentration and profile, are affected by the weather changes [43,44]. Many contradictory information is found regarding the effect of irrigation in grape composition. In fact, in a study performed in "Touriga Franca" variety it was found a higher concentration of anthocyanins in stressed plants [45]. However, in a Mediterranean climate, irrigation is essential to achieve better productions, however it is not yet clear the impact of irrigation in grape quality. In two consequent years it was studied the importance of the irrigation efficiency in "Aragonês" grapes quality, and the results were inconsistent comparing both years [42].

3. Climate Influence on Grape Quality

3.1. The Impact of Temperature

The influence of climate on grapes is significant, and extreme high-temperature events may have implications for grape berry development and, consequently, wine quality [46,47]. Some areas have great conditions for wine grapes production due to specific microclimates that positively influence grape development. It is expected that the future warmer and dryer years can have a negative impact on viticulture in the Mediterranean-climate regions [29].

Mild climates are favorable to grape production and grapevines growth habits are well adapted to these conditions. However, the grape production areas are changing mostly due to climate change and the use of irrigation in the vineyards. The wine grape production has expanded into cool and cold areas that were, in the past, thought to be inaccessible to this crop. The choice of specific cultivars, training systems, soil cover, type of pruning, the usage of mulch, etc., are extremely important in vine production since these are fundamental tools to extend grape growth to several areas, potentially overcoming the environmental limitations. *V. vinifera* can stand temperatures around −15 °C without suffering damage [28]. It has also been known that the climate influences grape quality, and therefore, wine characteristics.

Warmer temperatures increase metabolic rates and affect some metabolite synthesis and accumulation (including secondary metabolites like polyphenols and flavonoids like anthocyanins) [48]. High temperatures accelerate grape maturation, leading to a higher total soluble solid (TSS) content [4]. Phenolic compounds are also sensitive to temperatures [49]. Climate changes significantly impact the phenylpropanoid pathway, which is responsible for the biosynthesis of polyphenols. These changes can disrupt the synthesis and accumulation of these metabolites and also influence the induction of enzymes and genes related to their production [50]. Enzymes involved in the biosynthesis of anthocyanins exhibit optimal activity within the temperature range of 17 °C to 26 °C. However, high temperatures exceeding 35 °C can induce anthocyanin degradation and inhibit the accumulation of anthocyanins [51,52]. A study found that moderate exposition to radiation and temperature increases the accumulation of anthocyanins [53]. Many studies have shown the impact of different climates in anthocyanins accumulation [1,47,54] and organic acids accumulation [55–57]. In a study performed in Alentejo, it was found that despite total anthocyanin content have increased during maturation in both years a much warmer and dryer year (with less pluviosity) had a positive impact on the synthesis and accumulation of anthocyanins [1]. In addition, the temperature plays a significant role in wine quality. In the case of northern European wines, the cooler climate leads to a higher content in grape organic acids and, consequently, to a higher wine acidity [58].

The effect of the rising temperatures in the grape quality and wine industry is well established, since different climates seem to modulate grape characteristics, including phenolic composition and berry size [59,60]. Plants including vines, are poikilothermic organisms since they are affected by the temperature, which affects vine's phenology, vegetative cycles, and grape quality. In winemaking regions, it has been observed that the dates for bud break, flowering, and fruit maturity are beginning earlier [4,61]. Also, the harvest dates have advanced 2–3 weeks during the last 1030 years [4].

3.2. The Impact of UV Radiation

The Earth's atmosphere attenuates UV radiation at its surface, which constitutes a portion of the natural radiance. The three main types of UV radiation are UVA (315–400 nm), UVB (280–315 nm), and UVC (100–280 nm). However, only UVA and UVB radiation reach the Earth's surface, as UVC radiation is effectively blocked by the ozone layer [62]. The plant's response to UV radiation is contingent upon the energy received and the specific range within the spectrum [63]. UVA and UVB radiation are crucial in plant growth, with UVB radiation having significant effects due to the involvement of the UVB photoreceptor, UVR8. The majority of UV radiation reaching the Earth's surface consists of UVA radiation. UVB radiation, on the other hand, is mostly absorbed by the ozone layer (approximately 95%) and can potentially stress plants by affecting proteins, lipids, and nucleic acids. Currently, there is no evidence of the existence of a specific photoreceptor for UVA radiation in plants [64]. Plants have evolved a wide range of acclimatization strategies to mitigate excessive absorption of UV radiation and minimize the adverse effects of overexposure. Rather than perceiving UV levels solely as stress factors, they should be viewed as regulatory and environmental stimuli capable of modulating plant physiology and morphology. UVA radiation, in particular, has distinct effects on plants as it stimulates the synthesis and accumulation of beneficial compounds, such as flavonoids, which contribute to overall plant health [65]. At the earth's surface, higher UV levels are associated with smaller leaves, shorter internodes, and greater growth of lateral shoots [66]. Plants also have mechanisms to repair the damage on the photosynthetic pathway, on the DNA, membranes, and fruits amino acids and aroma compounds [28].

It is known that 385 nm radiation has the potential to increase plant development, increasing the polyphenol content in leaves and antioxidant activity [65]. Although plants have mechanisms to deal with high UV radiation, which include the synthesis of flavanols, alkaloids, waxes, and free radical scavengers [67].

The impact of total UV radiation on the phenolic composition and antioxidant capacity of grape berries and wines was investigated in Tempranillo grapes, also known as 'Aragonês', in this study, 47 compounds, including flavonols and anthocyanins, were identified, and their levels increased in grape skins exposed to UV radiation. However, flavanols and hydroxybenzoic acids did not exhibit significant changes in response to variations in UV radiation. These characteristics were also observed in Tempranillo vines in Spain that underwent the same UV exposure [68].

In a previous study in Alentejo it was observed that in the presence of high levels of UV radiation, the accumulation of flavonoids and anthocyanins increased [1]. Excessive UV radiation seems to influenced the development of various compounds in in 'Syrah', 'Aragonês', 'Trincadeira', and 'Touriga Nacional' grapes.

3.3. The Influence of Water Availability

Wine-producing regions all around the world have already experienced seasonal drought [69]. According to the global climate models, there will be an increase in aridity compromising wine production and quality [70]. The impact of global warming on grapevine plants' development is evident, resulting in alterations in their phenology and leading to earlier harvests. Additionally, the frequency of extreme weather events such as heatwaves and heavy rains may increase adversely impacting grape yield and quality. The response of grapevines to soil and atmospheric water deficit, primarily regulated by stomatal control, varies depending on the genotype. Under mild to moderate water deficit conditions, plants activate defense mechanisms by closing their stomata to minimize water loss, subsequently affecting carbon assimilation [71].

Grapevines are generally considered "drought-avoiding" species due to their efficient stomatal control. However, some genotypes seem to have better stomata control than others in water deficit situations, therefore these genotypes can be classified as isohydric (drought avoiders). Other genotypes, with a lower control of stomatal aperture under water stress, are considered anisohydric, with a positive response [71].

It is expected that the future warmer and dryer years might have a negative impact on viticulture in the Mediterranean-climate regions [29]. In grapes, water deficiency strongly influences ripening, wine composition, and berry size. Smaller berries have a higher berry skin/flesh ratio due to an increase in the berry skin proportion and a decrease in the flesh pulp, however is important to consider that this ratio can be influenced by various factors including irrigation. Some authors claim that irrigation can promote larger berry size which may result in a lower skin to flesh ratio and potentially lead to a lower level of phenolic compounds in the wine [72,73]. Furthermore, the water accumulation effect that occurs during ripening, results in the dilution of grape compounds [10]. However, irrigation in the vineyard is an ongoing debate topic among researchers in this field, and there is not a consensus in this subject.

In "Touriga Franca", the effect of two different irrigation regimes was studied, to understand how it would impact the anthocyanin content in this variety. There were not significative differences found between regimes, but in both cases, the total anthocyanin content increased during maturation and had a small decrease at harvest [45].

There are many studies on the impact of water stress in "Tempranillo"; hence, this variety seems to be more impacted by water stress. The impact of cluster tinning and water deficit during ripening in "Tempranillo" grapes has been studied. Although water stress has been observed to affect the phenolic and flavonoid content in this particular variety, thinning practices appear to exert a more pronounced influence on the development and accumulation of these compounds [74]. Additionally, it was found that the main phenolic compounds affected by water availability were proanthocyanidins and flavonols, which increased with irrigation at all phenological stages. In this study, the total phenolic content evolutive pattern didn't seem to be affected by water availability [8]. In fact, irrigation plays a crucial role in ensuring an adequate water supply for wine production [42].

Furthermore, the water accumulation effect that occurs during ripening results in the dilution of compounds [10]. Many factors influence the harvest date, the quality parameters for red wine grapes such as sugar content, titratable acidity (TA), pH, color, tannins, and flavor [28]. Technological maturation is closely linked to the levels of sugars, titratable acidity, and pH. The concentration of sugars determines the potential alcohol content, while titratable acidity and pH are important factors in controlling the quality and color of wine. Phenolic maturation, on the other hand, is critical for achieving desired sensory characteristics in the wine such as color intensity and flavor complexity [75].

4. Grape Ripening

Grapes, as non-climacteric fruits, originate from the ovary and develop into berries comprising skin, flesh, seeds, and a fully formed vascular system. Within these components, various compounds accumulate, including sugars, organic acids, amino acids, minerals, aromatic compounds, and phenols [7]. In vineyards, berry growth is well documented [76–78] and is characterized by a double sigmoidal curve [8]. In the initial phase, the embryo starts formatting the seeds and there are frequent cell divisions, resulting in the berry enlargement, associated with the accumulation of some compounds, such as organic acids and tannins. At the first phase of grape growth, the phloem unloading is shifted to an apoplastic pathway [79]. During the lag phase, berries do not have changes in weight or volume. This phase ends with the start of ripening/veraison/*vérasion* (a French term that describes color changes, which means that other modifications are occurring). During veraison, red cultivars start producing and accumulating anthocyanins [79]. Although during phase II, the seeds maturate and start to lignify (developing a thick outer layer) [28]. After this period, the berry softens and becomes translucid, starts gaining color, and grows faster. During this phase, an increase in the size of the central mesocarp cells results in a cell expansion in the berries. Malic acid starts to metabolize, sugars (glucose and fructose) accumulate, and aroma and color compounds develop, including flavonoids (namely anthocyanins) [80]. The process of grape ripening is a highly complex phenomenon which involves a combination of environmental conditions, genetic characteristics, hormonal activity, pigment biosynthesis, and the metabolism of sugars, acids, and flavor-related compounds. Key indicators of fruit quality include total soluble solids, total acidity, and their ratio. As maturation progresses, there is an increase in the content of total soluble solids, attributed to the synthesis and accumulation of glucose and fructose, while the titratable acidity tends to decrease [81]. At the onset of ripening, the concentration of flavanols is high but tends to diminish as the berries expand and polymers undergo oxidative crosslinking. Following veraison, there is typically a decline in flavanols, which then levels off during the final weeks leading up to harvest. As for red grape varieties, the accumulation of anthocyanins in their skins begins during veraison and reaches its peak during the later stages of berry ripening, at a time when synthesis diminishes or ceases. Generally, the accumulation of skin anthocyanins shows a linear progression from veraison until the harvest period [82]. The ratio of sugars to organic acids is related to flavors quality and (in some fruits) determines the optimum time for harvest, since it is considered a quality index [83]. Polyphenols play a significant role in determining the quality of wine as they are closely associated with its color, flavors, and taste. They often form intermolecular interactions with volatile compounds, thereby influencing the overall aroma of the wine [5].

5. Plant Cell Wall Structure and Composition

Grape's mesocarp cell walls are composed of 90% polysaccharides and about 10% proteins, which is a typical type I cell wall model, whereas cellulose and polygalacturonans are about 30–40% [84]. Approximately half of the exocarp is composed of polysaccharides, with around 30% consisting of glycosyl residues that share a similar composition to the mesocarp walls. Another 20% is primarily comprised of pectin with methyl esterification. The remaining portion contains insoluble proanthocyanidins, structural proteins, and lignin [81,85]. The plant cell wall serves as a macromolecular structure that envelops and safeguards the cell. Additionally, it functions as a crucial reservoir of carbohydrates, facilitates cell-to-cell interactions, and acts as a significant source of bioactive signaling molecules [80]. The grape berry skin cell wall plays a crucial role in the winemaking process as it contains phenolic compounds, which contribute to color, astringency, and antioxidant properties. These phenolic compounds can be either solubilized within the vacuole or bound to the cell wall polysaccharides [10].

The plant cell wall serves as the primary physical barrier against biotic and abiotic stresses, providing mechanical support and aiding in osmotic regulation. It is essential for maintaining the shape and integrity of the cell [80]. The cell wall is also involved in the response of cells to growth factors in the regulation of diffusion process through the apoplast [10]. It offers mechanical support (essential for the maintenance of the cell's shape), resistance to turgor pressure of the cell, controlling growth, regulating the diffusion through the apoplast, and protecting the plant from dehydration and the environment [10]. It is mainly composed of polysaccharide polymers, including cellulose, hemicellulose, and pectin, with the presence of glycoproteins and lignin [80]. Cellulose is a long chain linear polymer composed of only one monomer, consisting of c-1,4-linked cellobiose chain. Hydrogen bonds are responsible for the formation of a crystallin microfiber phase (microfibrils) that provide most of the strength to the plant cell-matrix and forms the framework that supports the cell. Cellulose microfibrils are embedded in a phase consisting of hemicelluloses and pectic polysaccharides. Hemicelluloses are a major component of cell walls and consists of non-cellulosic polysaccharides with a backbone connected by β1,4-glycosidic linkages. These cross-linking glycans can interact in a non-covalent way using hydrogen bonds with cellulose microfibrils, giving them the ability to coat and chain them together to form an extensive framework. Xyloglucans are the main hemicelluloses in the primary cell wall, corresponding to 15 to 25% of the constitution [86]. Xyloglucans and xylans are found in cell junctions in ripening fruits, which suggests that they might have a role in cell adhesion from hemicelluloses, which have been attributed to pectic homogalacturonans [10,87].

Pectins are built-in in the cellulose/hemicellulose system [87]. These hydrophilic gels contribute to the mechanical properties of the cell wall, playing roles in regulating hydration, facilitating ion transport, determining porosity and stiffness (which affects water holding capacity), controlling the permeability of cell wall enzymes, and providing structural strength to the matrix [10,81]. The major pectin domains consist of homogalacturonan (HG), rhamnogalacturonan-I (RG-I), and rhamnogalacturonan-II (RG-II). These pectins are known to be covalently interconnected, forming the pectic matrix, which is regarded as a complex macromolecule. However, the precise nature of their covalent linkages remains uncertain [10]. Homogalacturonan (HGs) consists of a linear chain of α-(1,4)-linked GalA without substitutions. Alongside occasional acetylation at the *O*-2 and *O*-3 sites, the α-(1,4)-linked GalA can undergo methylesterification and demethylesterification at the *O*-6 sites, which impacts the formation of calcium bridges between HGs. The branches of RG-I, which include α-1,5-linked L-arabinan and β-1,4-linked D-galactan, are commonly attached to rhamnosyl residues at *O*-4, thereby increasing the size of RG-I and introducing structural flexibility across different cell types and developmental stages. RG-II stands out as the most intricate pectic polymer, with over 20 linkages on 12 different sugars forming the HG-like backbone and four oligosaccharide side chains. RG-I exhibits a repetitive disaccharide unit backbone [α-D-GalA-(1,2)-α-L-Rha-(1,4)-] that undergoes acetylation at the GalA residues. It is anticipated that HG, RG-I, and RG-II are covalently interconnected via their backbones [86,87]. In addition to polysaccharides, the primary cell wall also constituted about 10% of structural proteins and protein rods that support brackets to the long polysaccharide chains [10].

The cell wall plays a crucial role in the expansion and softening of grape berries. This process involves the synthesis, disassembly, and rearrangement of hydrogen bonds among the components of the cell wall. Consequently, the cell wall undergoes modifications during maturation/ripening, leading to changes in the degree of polymerization in pectins and hemicelluloses [10,88]. During ripening, fruits tend to become softer due to changes in cell wall composition. Although these changes happen, most of them are subtle structural modifications of structural polysaccharides (for example, molecular mass, solubility, and degree of substitution of individual polysaccharides) [89]. This provides the flexibility needed for cells to expand, leading to alterations in structure resulting in changes in structure, flavors, and aromas [81]. In the beginning of the berry development, the cell wall is responsible for the expansion and softening of grape berries, and these changes include synthesis, disassembly, and rearrangements of hydrogen bonds of cell walls components. Changes in cell wall biosynthesis provide the flexibility needed for cells to expand, leading to alterations in its structure and in flavors, and aromas [81,90]. During maturation, in some varieties, the cell wall material decrease followed by the thinning of skins, although in other varieties, there aren't any changes in cell wall polysaccharides but rearrangements at the pectic fraction level [81,90]. Then, the cell wall loses structural polysaccharides followed by the thinning of skins in Trincadeira and Touriga Nacional [81], although in other varieties, there weren't significant changes in cell wall polysaccharides, but there are rearrangements, and new rearrangements at the pectic fraction level were observed [81,90]. The plant cell wall fraction is obtained through an extraction process using alcohol as a solvent to remove the soluble components of the cells. Alcohol insoluble residue (AIR) is the remaining material obtained after the extraction of cytosolic content from cells through cell lysis and it consists of a complex structure of polysaccharides that constitutes the plant cell wall fraction. The effect of two different climate years in cell wall indicate that in a year with lower water availability, the alcohol insoluble residue was higher which indicate a higher value of cell wall fraction [1]. The findings indicate that in a year with lower water availability, the alcohol insoluble residue was higher. This suggests that water scarcity can lead to thicker grape skins or skins with reduced water content within the cell vacuole, resulting in a higher percentage of AIR. During berry development, a decrease in pectic and hemi cellulosic polysaccharides has been referred by [73], who noticed in the pectic fraction, a temporary increase in neutral and acid sugars until veraison, followed by a decrease until harvest. Despite grapevines being a "drought-avoiding" species, some authors report a high sensitivity of the berry mesocarp to water stress which results in a higher contribution of skin and seeds to final berry size [81]. The correlation between the degree of polymerization and grape ripening as also already been studied, and it was found that overripe grapes extensively hydrolysed and depolymerized cell wall polysaccharides, probably due to natural grape tissue ripening enzymes [91].

Phenolic compounds interact with cell wall polysaccharides so it has been proposed that cell wall composition has an important role in polyphenols accessibility [92–94]. Alcohol insoluble residue (AIR) is the result of the extraction of cytosolic content after cell lysis, and it consists of a complex structure.

6. Grape Phenolic Compounds

Red wine grapes are rich in phenolic compounds. Since the 1990s, research has shown that phenolic compounds have many protective properties for human health [95,96], and many oenologists have been defending the role of the phenolic compound in wine quality (Table 1) [97–99]. Phenolic compounds are chemical substances that have hydroxyl substituents connected to a benzene ring [7,53]. These compounds possess one or more hydroxyl groups (–OH) attached to aromatic rings, and they serve various functions in the plant kingdom. They are abundantly found in numerous vegetables and fruits [100]. They are found dissolved in pulp cell vacuoles, adsorbed, or bound to polysaccharides in fibrovascular vessels, and their free form in the cytoplasm of the skin cells. The polyphenols present in the skins are bound to polysaccharides and membrane proteins and in the seeds, the polyphenols are found essentially in the outer tissue [101]. It is well established that phenolic compounds interact with polysaccharides of plant cell walls, so it has been proposed that cell wall composition has an important role in polyphenols accessibility [92–94].

These polyphenols are secondary metabolites synthesized through the shikimate/phenylpropanoid or polyketide acetate/malonate pathways, or sometimes both. They exhibit diverse physiological functions within plants [7]. Grapes contain a variety of primary phenol compounds, including phenolic acids, stilbenes, flavonoids (such as flavonols, flavan-3-ols, and anthocyanins), as well as hydroxybenzoic acids and hydroxycinnamic acids [102]. These compounds have multiple aromatic rings with hydroxyl groups [103]. They are mainly located on grape skins and seeds and pass to wine through fermentation.

Table 1. Phenolics present in grapes and their benefits.

Compound	Location	Function	References
Hydroxybenzoic and hydroxycinnamic acids	Seed; Skin; Pulp	Synthesis of key compounds in berry growth and development	[7,104]
		Free radical scavengers; antimicrobial agents	[7]
Stilbenes	Seeds and skins	Berry growth and development	[7,105,106]
		Protect the berry from biotic and abiotic stress	[7,105,106]
Flavonoids	Skins and seeds	Strong antioxidant capacity	[74,107]
		Impact on wine organoleptic characteristics	[5,47]
Anthocyanins	Skins	Responsible for the colors red, blue, and purple in plant tissues	[108]
		Important contributor to the sensory qualities	[109]

Hydroxybenzoic and hydroxycinnamic acids are the phenolic acids present in grapes synthesized by the phenylalanine pathway [28]. These phenolic compounds play a crucial role in the synthesis of important compounds during grape berry growth and development, including gallic acid, protocatechuic acid, gentisic acid, syringic acid, p-hydroxybenzoic acid, and vanillic acid [7,104]. Based on their structure, hydroxycinnamic acids can act as free radical scavengers or anti-microbial agents [7].

Stilbenes, which are derivatives of 1,2-diphenylethylene, are a significant class of polyphenols involved in the growth and development of grapes. They possess a fundamental structure consisting of 1,2-diphenylethylene and serve as phytoalexins, safeguarding the berries against biotic and abiotic stresses. Among them, trans-resveratrol is the simplest stilbene and acts as a precursor for the synthesis of other compounds within this class. It is present in both the seeds and skins of grapes [7,105,106].

Flavonoids, in grapes, are almost exclusively found in grape skins, and higher radiation levels will result in a higher concentration [28] of these compounds. Flavonoids have a general structure composed of two phenyl rings and a heterocyclic ring. Grapes primarily contain three subgroups of flavonoids: anthocyanins, flavonols, and flavan-3-ols. These subgroups are classified based on the oxidation status of their heterocyclic ring [7]. Flavonoids in red grapes are predominantly found in the berry skin's epidermis and seeds. They represent the largest group of soluble phenolic compounds and contribute significantly to the overall activity in grape-derived products [110]. These compounds have gained considerable interest since they have strong antioxidant capacity [74,106,111] and have also an impact on wine organoleptic characteristics such as color and aroma [5,47]. Anthocyanins are the pigments responsible for the red, blue, and purple colors observed in plant tissues [108]. In red grapes, these pigments are predominantly located in the grape skins [112] and play a significant role in determining the sensory characteristics of the resulting wine [109]. Malvidin-3-O-glucoside is the predominant anthocyanin found in grapes and wine, comprising approximately 40% of their total content [113]. Grapes contain both acylated and non-acylated anthocyanins, with non-acylated anthocyanins being the most commonly found in *V. vinifera* varieties [108,114]. Anthocyanins in grapes also have sugar residues that are acylated with aromatic compounds, which contribute to their chemical stability [114]. The color of wine is a crucial quality parameter and is determined by the phenolic compound content in grapes, as well as the oenological and storage conditions [98,102,103]. Tannins are responsible for the gustatory sensation of astringency together with flavan-3-Ols and proanthocyanidins, they contribute to the wine's body and mouthfeel [115].

The accumulation of phenolic compounds in grapes is influenced by many factors, including grape genotype, environmental factors, nutritional status, wounds, pathogenies, and growth [7]. Some authors have been studying the impact of different irrigation regimens in grape phenolic synthesis and accumulation. The impact of the irrigation regimen in berry development (including phenolic composition) in Aragonês was studied and authors found that the main phenolic compounds affected by water availability were proanthocyanidins and flavonols, increasing with irrigation at all phenological stages [8].

The utilization of analytical methods, rather than relying on organoleptic methods, is crucial for quality control due to their superior performance and objective nature [2,116]. Recently, there are many advances regarding to analytical instrumentation for the identification and quantification of chemical compounds related to grapes or wine color [117,118]. Most producers are aware of the importance of phenols for the quality of the wine [6]. Implementing objective composite analyses as a standard practice in evaluating grape quality will lead to more reliable and consistent data. This approach ensures the quality of musts, providing a guarantee for producing wines of higher quality [119].

7. Grape Quality Assessment Methods

7.1. Methods Used to Determine Phenolic Compounds in Grapes

Nowadays, there is a wide range of methodologies that allow the identification and quantification of phenolic compounds [116], from colorimetric methods using UV/Vis to chromatographic methods (Table 2). The determination and quantification of phenolic compounds can pose challenges due to their intricate complexity and structural diversity. Numerous methods are recognized and employed to quantify phenolic compounds in plant extracts [120]. Colorimetric methods are widely used in UV/Vis spectrophotometry since they are easy to perform, rapid, can be easily applicable as a routine laboratory methodology, and are low cost [24,116]. Although colorimetric methods based on UV/Vis have many advantages, these methods need to use reference substances (e.g., gallic acid) to assure the quantification of the phenolic hydroxyl groups present in samples. Polyphenols found in plant extracts undergo a reaction with redox reagents such as the Folin-Ciocalteu reagent, resulting in the formation of a blue complex that can be measured through visible-light spectrophotometry. The Folin-Ciocalteu reaction relies on the creation of a blue chromophore composed of a complex formed by phosphotungstic–phosphomolybdenum [120] in which the maximum absorption of the chromophores is dependent on the alkaline solution and the phenolic compound concentration present on the plant extract [121]. Since the reaction has a rapid decomposition in alkaline solutions, the Folin-Ciocalteu reagent includes lithium salts to prevent turbidity and facilitate the analysis [120]. Despite being widely used, the usage of the Folin-Ciocalteu method to determine total phenolic content in complex matrixes, other compounds highly present in plant food extracts, including reducing sugars and ascorbic acid, are also able to reduce the Folin-Ciocalteu reagent and therefore influence the total phenolic content, leading to over-estimation [122–124].

Table 2. Methods to determine phenolic compounds.

Compound Determined	Methodology Used	References
Total polyphenols	UV/Vis spectrophotometry: Folin Ciocalteu method	[120,122]
	HPLC-DAD with a RP column	[125]
Total flavonoids	UV/Vis spectrophotometry	[126,127]
	HPLC	[128]
Total tannins	UV/Vis spectrophotometry	[129]
Anthocyanins	The pH differential method	[9,130]
	Paper chromatography, thin-layer chromatography, column chromatography, solid-phase extraction, counter-current chromatography, UV/Vis spectroscopy	[128]
	HPLC–DAD using a reverse phase column	[131,132]
	HPLC with spectrophotometer detector UV, C18 column	[133]
	HPLC-DAD-MS with ion trap detector, equipped with an atmospheric pressure ionization source, using an electrospray ionisation interface.	[134]
	High performance liquid chromatography/quadrupole time mass spctrometer with a reverse-phase C18 column	[15,16,111,135,136]
	FT-IR	[102]

Total flavonoid content [126,127] and total tannin content [129] can also be determined using UV/Vis spectrophotometry.

There are different techniques to determine anthocyanin composition [9,137], the most frequently found are the pH differential method and the usage of HPLC systems. The pH differential method is a simple, quick, and accurate method to measure total monomeric anthocyanins in a sample [9,130]. The spectrophotometric analysis of anthocyanins involves measuring their absorbance at wavelengths ranging from 510 to 540 nm, which varies based on their chemical structure. Anthocyanin molecules exhibit absorption bands in the UV region at 260–280 nm and two in the visible region at 415 nm and 490–540 nm. Although the pH differential spectrophotometric method enables the accurate determination of total monomeric anthocyanin levels, it does not provide differentiation among different anthocyanin compounds [9]. The pH differential method obtained its initial approval from the Association of Analytical Communities (AOAC) in 2005 and was officially endorsed in 2007 [130]. Monomeric anthocyanins are sensible to pH changes, changing their color according to the pH of the solution they are in. Anthocyanin oxonium form (oxygen cation with three bonds) exists at pH 1.0, and the colorless hemiketal (results from the addition of alcohol) at pH 4.5. The absorbance difference at 520 nm is proportional to the pigment concentration present in samples [20,102]. Various methods, including paper chromatography, thin-layer chromatography, column chromatography, solid-phase extraction, counter-current chromatography, UV/Vis spectroscopy, HPLC, and mass spectrometry, are employed for the identification and quantification of anthocyanins [15,16,135,136]. Although the anthocyanin content measured is dependent on the method used for conducting the analysis [138].

For matrixes like grape juices or extracts, the quantification and identification should be done using more specific methods like chromatographic techniques. Their sensibility allows the separation and identification of different anthocyanins in complex matrixes, giving more specific information [20]. Although these methods are more recommendable, the diversity of protocols found in the literature make the selection of the best method difficult [132]. Additionally, separative methods demand expensive equipment to perform the analysis, produce chemical residues, and require sample preparation [116,139]. Flavonoids can also be determined by HPLC, allowing the identification of the different compounds present in the samples [53,128]. Although this approach is interesting to understand the individual flavonoid profile of each grape variety [140,141], it is extremely hard to identify each compound due to the lack of commercially available of flavonoid standards [53,128], although the anthocyanin profiling in red wine grapes has been explored using this technique [43,44]. The different anthocyanin profile of every red wine grape variety makes HPLC a very desired method for quantification [142–144]. However, HPLC has the potential to underestimate the quantity of anthocyanins in samples due to the reliance on a single anthocyanin as the standard for quantification [145]. Extensive research has been conducted on the quantification and identification of anthocyanins, utilizing high-performance liquid chromatography (HPLC) in conjunction with a diode array detector (DAD). This method has high sensitivity and the capability to identify multiple compounds within a single analysis [112,146].

Grape berries' composition is complex due to their constitution in phenolic compounds. Each variety has specific phenolic profiles that allow distinguishing varieties through their phenolic fingerprinting [18,99,147]. The need for precise and discerning analytical methods to determine polyphenols is steadily increasing. Quantification methodologies for phenolic compounds rely on the extraction and isolation of these compounds. While extraction plays a vital role, standardized methods for extracting key compounds are currently lacking. The International Organization of Vine and Wine recommends distinct sample preparation approaches based on the chosen quantification method [34]. In commonly used methods, it is necessary to destroy the samples either by grinding, drying, or lyophilizing with subsequent solvent extraction, and therefore, non-phenolic compounds such as sugars, organic acids, and proteins are also extracted, which may require subsequent purification processes. The extraction method significantly impacts the quantity and composition of phenolic compounds at the analytical level [7].

7.2. Non-Destructive Methods for Grape Quality Assessment

The wine industry recognizes the importance of methods to evaluate wine and grape quality with enhanced effectiveness and efficiency. An ideal method should demand minimal sample preparation, deliver rapid and reliable results, and encompass multiple parameters within a single reading [148]. Near-infrared spectroscopy (NIR) is a technique known for its simplicity, quickness, and non-destructive features that provides the user a multi-constituent analysis of different matrixes comparable with reference methods [12]. Additionally, this technology requires no or minimal sample preparation belonging to green chemistry processes [12,149].

One of the first applications of NIR technologies in agriculture was reported in the mid-1960s by the United States Department of Agriculture to detect the internal qualities of apples affected by a condition known as "water core" [149]. NIR technology was first used to predict the flavin content and moisture in black tea [150]. In the wine industry, knowing the critical parameters and grape attributes quickly and efficiently is crucial.

The initial application of NIR spectroscopy in the wine industry dates back to 1976 when Kaffka and Norris conducted a study. They examined 26 samples prepared by adding specific components of interest (such as ethanol, fructose, and tartaric acid) using a standard addition approach. The samples were scanned using three different path lengths (0.3, 1, and 5 mm) and represented variations within two fundamental wine matrixes. This enabled the identification of crucial wavelengths that could be employed in multiple linear regression (MLR) analysis [151]. NIR has been used for quantifying phenolic compounds in grapes and wine. These include the quantification of anthocyanins in grape homogenates by NIR-Vis reflectance and quantitative analysis of anthocyanins, polymeric pigments, and tannins in red wine fermentation [12,151,152]. One of the main problems of using NIR spectroscopy methods is the susceptibility of the predictive model to the matrix sample changes. In grapes and wine, the variety, soil type, and weather contribute to the matrix effect being important sources of variation [152].

From the beginning of the 2000s, many researchers have been trying to develop methods based in NIR to predict quality parameters in wine. Many new approaches have been developed to use NIR as a new method [12,153,154] to help producers to better understand how quality parameters evolve in the new climate situation, with more unpredictable events [119,154,155]. NIR spectroscopy has also already been used to predict the levels of malvidin-3-glucoside, pigmented polymers, and tannins in red wine, highlighting the potential of NIR spectroscopy as a rapid and non-destructive technique for phenolic compound analysis [154]. More recently, has also been developing methods to determine volatile compounds in 'vinho-verde' wines [12]. Some authors have also tried to develop methodologies to determine, total soluble solids (TSS); titratable acidity (TA), TSS/TA, pH, and BrimA ($TSS - k \cdot TA$), finding interesting results for new quick approaches to determine quality parameters [119].

This methodology has already been used in viticulture and shown promising results. There were also already established robust models utilizing NIR spectroscopy as a dependable approach for determining crucial compounds in grapes and wines [154]. These models were designed specifically to predict the phenolic composition in red wine fermentations, yielding highly accurate predictions. Thus, this technology holds the potential to serve as a rapid alternative method for estimating the concentration of phenolic compounds during red wine fermentations. In 2011, was conducted a study to explore the utilization of NIR spectroscopy for determining phenolic compounds, including anthocyanins and total phenolic compounds, in grape skins during ripening [11]. The employed procedure demonstrated outstanding potential for rapid, dependable, and cost-effective analysis. The results revealed that models developed using NIR spectroscopy, in conjunction with chemometric tools, facilitated the quantification of essential compounds, particularly total phenolic content, in grape skins throughout the maturation process. PLS analysis was used to explore the potential of NIR technology to determine volatile compounds in "*Vinho verde*" samples [12]. The results were great, finding R^2 values between 0.94 and 0.97, meaning that NIR technology seems to be a reliable approach to use in the wine industry.

Although multivariate methods possess immense potential, the partial least squares regression has emerged as a widely utilized approach for constructing multivariate classification models. This technique involves creating mathematical models that establish correlations between the presence of the analyte and the instrumental responses obtained from determining samples with known concentrations of the analyte [22]. It is also possible to develop a calibration model using manufactured samples of the analyte to prepare a series of calibration samples, evenly distributed over a range of concentration values [22] and for determining more than one quality parameter [13].

These recent studies have been showing NIR spectroscopy associated with chemometric tools a good, reliable, and cheaper alternative to wet chemical procedures that could help producers to better control their production and help in choosing the better harvest date.

7.3. Enzymatic Methods to Access Oxidative Stress in Grapes

Within plants, numerous enzymatic antioxidant mechanisms are distributed across various cellular compartments. These mechanisms play a vital role in inhibiting oxidation processes initiated by reactive oxygen species (ROS). The response of antioxidant enzymes and the concentration of antioxidant compounds under stress conditions exhibit significant variability among different plant species and even among cultivars within the same species [156]. The capacity to scavenge ROS has been linked to stress tolerance in plants. Consequently, the upregulation of antioxidant systems offers plants protection against the detrimental effects of ROS, which can impact berry development and quality [157].

The enzymatic antioxidant defence system in plants includes a set of antioxidant enzymes, which catalyze formation/regeneration reactions for the scavenging of ROS, or are directly involved in their removal. The main groups of antioxidant enzymes include enzymes like catalase (CAT, EC 1.11.1.6), peroxidase (POD, EC 1.11.1.7), superoxide dismutase (SOD, EC 1.15.1.1), and polyphenol oxidase (PPO, EC 1.30.3.1). This defense mechanism enables the removal of ROS, thereby safeguarding plant cells against oxidative damage. Superoxide dismutase (EC 1.15.1.1) plays a crucial role in converting the highly reactive superoxide anion into O2 and less reactive forms of H_2O_2. The resulting hydrogen peroxide can be further converted into water through the action of catalase (EC 1.11.1.6) or glutathione peroxidase (EC 1.11.1.9). Additionally, polyphenol oxidase (EC 1.10.3.1), a copper-containing metalloenzyme, facilitates the oxidation of phenolic compounds into quinones. These quinones subsequently undergo polymerization (via a non-enzymatic reaction) to form melanin pigments [158]. Polymerized quinones will lead to the formation of brown pigments and, consequently, changes in color and flavors of the final product [159]. Changes in PPO activity during maturation have been studied in red and white varieties, although studies have not revealed systematic evolution of grape's PPO activity despite the changes in other parameters like pH and degrees Brix of polyphenols constitution of H_2O_2 [160]. Primarily localized within the thylakoid lumen, this enzyme not only contributes to the plant's defense mechanisms but is also intricately involved in phenol metabolism. Phenols possess non-enzymatic antioxidant properties, thereby linking this enzyme to the plant's antioxidant defense system [157].

The increasing of ROS production due to environmental stress can cause cell damage, resulting from the oxidative destruction of many cell components [161]. Although, the role of ROS in abiotic stress conditions has been an increasing interest, being related to mechanisms of adaptation to stress, it has been referred that ROS induces the activation of defence mechanisms and stress response [161]. ROS represents not only a cellular indicator of stress conditions but also contributes to the signal transduction in response mechanisms [161].

Facing water scarcity, plants maximize water absorption through investment in root formation and stomata closure [71]. The limitation of water loss at the level of the leaves may also be associated with a reduction in the interception of solar radiation, resulting from the winding, change in the angle, and/or increase in the reflectance of the leaf [157]. The decrease in intracellular CO_2 after stomata closure in situations of prolonged water stress leads to an increase in the formation of ROS at the chloroplast level. Plants have developed physiological changes that allow them to avoid the effects of the excess of ROS caused by water stress, and these mechanisms allow the balance between the amount of light absorbed and the availability of CO_2, and, consequently, they can avoid the over-reduction of the photosynthetic apparatus and avoid the transfer of electrons to O_2 at the expense of CO_2 [157]. Water scarcity associated with higher medium temperatures and UV radiation affect the survival of the plants. However, plants developed mechanisms to support unfavorable conditions thus avoiding excessive ROS production. Facing water stress, plants maximize water absorption through investment in root formation and stoma closure [71].

Many studies on grapes have been conducted to understand how stress can affect different enzymatic activities [161–163]. Hydric stress appears to significantly impact enzymatic activity, namely POD, particularly as the harvest approaches. Under conditions of hydric stress and nearing the harvest date, the activity of POD increases. This observation suggests that plants allocate more resources to the final stage of their reproductive cycle when water availability is limited, highlighting the importance of water management during this critical period [157].

Different irrigation systems apparently affect the grapes enzymatic activity during ripening. Different irrigation systems were used in five different stages of maturation in Trincadeira, and the results have shown that non-irrigated grapes had an increase in polyphenol activity during the first week of maturation followed by a decrease until harvest when compared with irrigated systems, [157]. In V. vinifera in two different varieties (Kalecik Karasý and Sultani Çekirdeksiz), the evolution of glutathione peroxidase activity was studied during berry set, veraison, and maturity. In this study any known stress factors were not applied, and it was found that GPx activity decreased between veraison and harvest, meaning that this enzyme can be an indicator of quality in grapes at harvest [164], increasing in situations of stress [162].

The activity of the GPx activity during maturation infected with the fanleaf virus also decreases in V. vinifera cv. Trebbiano. Three different harvest times were studied to understand the effect of the fanleaf virus, and results have shown that the infected leaves showed increased concentration of superoxide radical and hydrogen peroxide, resulting in enhanced activity of superoxide dismutase [163].

GPx levels seem to naturally decrease during maturation, since different authors [165] have also found the behavior both in grape berries and skins. In a investigation focused on examining the glutathione content of berries and wines, as well as the activity of six enzymes involved in glutathione metabolism, in "Koshu" and "Cabernet Sauvignon" grapes, the results revealed that ripening-associated changes were comparable in both grape varieties, as the glutathione content increased during the ripening process [165]. However, catalase (CAT) activity was not detected in the study. In a study performed on Tempranillo grapes with different water status (rainfed and irrigated) and crop load (no cluster thinning and cluster thinning), SOD activity remained constant but higher during maturation in thinned treatment when compared with unthinned treatments. The thinned treatments exhibited low levels of nonspecific peroxidase activity. PPO kept unaffected independently of the regimen studied [74].

Polygalacturonase, peroxidase, and polyphenoloxidase can be used to help determine the best harvest date. Polygalacturonase promotes the physiological maturation of cell walls and decreases late in maturation [166]. It is known that when polyphenoloxidase and peroxidase are in high quantities in grapes, the fruits are more susceptible to oxidative reactions, causing darkening [167]; thus, lower amounts of these enzymes could be good indicators of grape quality.

8. Health Benefits of Red Wine Grape Consumption

Red wine holds a significant role in meals across numerous regions and is widely cultivated in vineyards worldwide. The cultural importance of wine is particularly pronounced in Mediterranean countries, where it is not only consumed as part of meals but also has a social component [168]. In fact, the Mediterranean diet, which was recognized as an Intangible Cultural Heritage of Humanity by UNESCO in 2010 [169], promotes moderate wine consumption alongside main meals [168,170]. This beverage possesses unique properties, mainly attributed to its abundant content of polyphenols and antioxidants. Notably, compounds such as gallic and caffeic acid found in wine and grapes are renowned for their beneficial effects on human health, including antioxidant, antimutagenic, and neuroprotective properties [171]. Moderate red wine drinkers can consume polyphenols at levels significantly higher than the average population, as highly tannic red wines may contain up to 3 g of total polyphenols per liter [172]. Overall, the presence of compounds like gallic and caffeic acid in wine and grapes contributes to the potential health benefits associated with their antioxidant, antimutagenic, and neuroprotective effects [171].

Damaging stimuli (such as pathogens, cellular damage, and irritants) cause specific responses in our body's immune system, namely inflammation. When inflammation becomes chronic, there is an increase of reactive nitrogen and oxygen species, causing an imbalance between the ability of the biological system's elimination and their accumulation of free radicals. If there is an accumulation of reactive oxygen species (ROS) in the organism, several diseases might occur, namely cancer, neurodegenerative diseases, atherosclerosis, chronic fatigue syndrome, and rheumatoid arthritis [173–175]. Recently, doctors, researchers, and consumers have been seeking the usage of specific plants with the antioxidant potential to scavenge free radical-induced tissue injury due to their healing potential [172,176–179]. Fruits, vegetables, and grains contain antioxidants with significant potential due to the presence of phenolic compounds in their composition. These phenolic compounds contribute to their high antioxidant capacity [158,180–182]. Polyphenols exert protective effects by exhibiting various mechanisms, including electron transfer to free radicals, chelation of metal catalysts, activation of antioxidant enzymes, reduction of alpha-tocopherol radicals, and inhibition of oxidases. These multifaceted actions contribute to the overall antioxidant properties of polyphenols [183]. Red wine grapes are rich in compounds with important antioxidant activities that can minimize the harmful effect of ROS that cause oxidative stress [184]. The imbalance between antioxidants, reactive oxygen species, and free radicals leads to changes in the cell's macromolecules, causing oxidative stress [185,186]. Damage in DNA, RNA, proteins, and lipids can result in an increased risk of chronic diseases like cancer diabetes, and cardiovascular diseases [7,187]. The consumption of polyphenols-rich food and supplements might help keep the normal antioxidant status of the body [9,188]. Grapes are known for being rich in many types of antioxidants compounds, and over the past years, there have been many studies to assure this theory [189–191]. In vitro, phenolic compounds show the ability to reduce inflammation [192,193], stop or reduce the growth of tumors [194], modulate the immune system [192], increase blood vessels resistance [193,195], and others.

Since the 1990s, studies have shown that phenolic compounds have many protective properties in human health [95,96], and many oenologists have been defending the role of the phenolic compound in wine quality, namely the moderate consumption of wine could have a positive effect in protecting cardiovascular health [97–99]. In a study previous performed it was found that found that despite the French had a diet rich in saturated fat, the deaths from coronary heart disease were lower than in any other European country, including Portugal, Spain, Yugoslavia, Belgium, Switzerland, UK, Germany, Sweden, and Ireland [196]. This theory was called by "The French Paradox". French people have a higher life expectancy and lower mortality rates due to cardiovascular diseases, and wine is usually consumed with meals moderately (2–3 glasses a day), reducing the negative effects of high cholesterol commonly found in their diet [110,191,197,198].

Anthocyanins, with their potent antioxidant activity, play a crucial role in protecting against various ailments, including neuronal and cardiovascular diseases, cancer, and diabetes, among others [20]. There are shreds of evidence of its effect on cancer treatment, human nutrition, and biological activity [25,199,200]. There also seems to be interest in anthocyanins, since they have an inhibitory effect on enzymes collagenase and elastase, reducing the aging of epidermal tissues [201].

Grape berry skins are primarily composed of water, sugar, cellulose, hemicellulose, and pectin [202]. Grapes contain polysaccharides that hold significant biological significance and possess a remarkable metabolic potential in living organisms. These polysaccharides exhibit a wide range of beneficial activities, including immunological, antitumor, antiadhesive, antiviral, anti-infective, antioxidant, antimutagenic, and hematopoietic effects. Additionally, the presence of uronic acid, which corresponds to pectin, contributes to the physiological, biological, and pharmacological properties of polysaccharides and glycoconjugates, further enhancing their overall impact [203].

In studies performed both in 2010 [204] and 2012 [105], the properties of phenolic compounds and the antioxidant properties of grapes were tested. The authors found that polyphenols in smooth muscle can reduce LDL-lipoproteins and reduce ROS even in very low concentrations in vitro. The differences between the moderate consumption of red wine and gin were studied, and it was found that the moderate intake of wine reduced plasma SOD activity and reduced MDA levels, concluding that red wine intake has greater antioxidant effects, probably due to their high phenolic content [205]. Other studies have also concluded that the moderate consumption of red wine can reduce coronary diseases, being even more beneficial than complete alcohol abstinence [206]. The plasmatic concentration of (+)-catechin remains high in the bloodstream after a meal, which might extend to a higher plasmatic antioxidant activity [207]. It was also found that grapevine leaf extracts can prevent liver disorders in Wistar rats [186]. Studies in vitro have shown promising results in the beneficial effects of the consumption of red wine: fruits with high content of polyphenols have a high potential to inhibit lower density lipid proteins [124].; It was also tested the antithrombotic effect of grape extracts and found that they could inhibit the synthesis of tissue factors by monocytes/macrophages, the responsible for thrombotic diseases [200].

A summary of the health benefits of the moderate consumption of red wine and phenolic compounds can be found in Table 3.

Table 3. Health benefits of wine and phenolic compounds.

Compound	Health Benefit	References
Phenolic compounds (Including Gallic and caffeic acids)	Can reduce coronary diseases	[206]
	high potential to inhibit lower density lipid proteins	[124]
	Reduce LDL-lipoproteins and reduce ROS even in very low concentrations in vitro	[143,205]
	The moderate intake of wine reduced plasma SOD activity and reduced MDA levels	[205]
	Inhibit lower density lipid proteins	[124]
	Antitrombotic effect	[200]
	Prebiotic effects	[208]
(+)-Catechin	higher plasmatic antioxidant activity	[207]
Grapevine leaf extracts	prevent liver disorders in Wistar rats	[186]
Tannic acid	anti-SARS-CoV-2 activity	[209]

The polyphenols present in red wine are considered to have these benefits since they are transformed by intestinal microbiota, preventing various diseases [207,210]. It is known that polyphenols that reach the intestine exert prebiotic effects that stimulate the growth or the inhibition of some bacteria [208]. Recently, with the COVID-19 pandemic, a study found that tannic acid (a polyphenol naturally present in red wine and red wine grapes) acts as a natural compound with potent anti-SARS-CoV-2 activity [209].

The moderate consumption of red wine can have countless benefits for human health since many studies have shown that the phenolic compounds present have a positive impact in stress related diseases and bacterial and viral infections.

9. Final Remarks

Mediterranean vineyards are susceptible to climate changes and water scarcity that affect the synthesis and accumulation of important grape compounds, such as phenolic compounds and anthocyanins, impacting the quality of grapes and contribute to wine quality. The wine producers face additional complications due to the conflicting information surrounding the impact of irrigation on grape composition. While irrigation is deemed essential for achieving better grape production in Mediterranean climates, its influence on grape quality appears to vary, as observed in studies on different grape varieties.

The effect of rising temperatures on grape quality is well established as different climates modulate grape characteristics, including phenolic composition and berry size. The impact of climate change is evident in the advancement of key phenological stages, such as bud break, flowering, and fruit maturity, with harvest dates occurring earlier in recent decades. These observations highlight the direct influence of temperature on vine phenology, vegetative cycles, and grape quality. Understanding the relationship between climate and grape development is vital for the wine industry. Adapting viticultural practices and implementing strategies to mitigate the negative effects of climate change are crucial to ensure the sustainability and continued success of grape production and the overall wine industry.

Red wine grapes are rich in phenolic compounds that have been shown to possess protective properties in human health. Oenologists have recognized the crucial role of phenolic compounds in wine quality. The accumulation of phenolic compounds in grapes is influenced by various factors, including grape genotype, environmental conditions, nutritional status, wounds, pathogens, and irrigation regimens.

Analytical methods have been developed to identify and quantify phenolic compounds, providing objective data for quality control in grape evaluation. Implementing these methods as a standard practice ensures the production of wines of higher quality. Colorimetric methods using UV/Vis spectrophotometry, such as the Folin-Ciocalteu method, are commonly employed for the determination of total polyphenols, total flavonoids, and total tannins. These methods are advantageous due to their ease of use, rapidity, and low cost. However, they require the use of reference substances and can be influenced by other compounds present in the samples, leading to overestimation. Chromatographic techniques, such as HPLC, offer more specific and sensitive analysis of phenolic compounds, allowing for the identification and quantification of individual compounds and HPLC-DAD (is frequently used for anthocyanin profiling in red wine grapes. Grape quality assessment can also be performed using non-destructive methods, with near-infrared spectroscopy being a popular technique. This technique offers simplicity, quickness, and non-destructive features, providing multi-constituent analysis of grape samples. It has been successfully applied for the quantification of phenolic compounds in grapes and wine. However, the predictive models developed using NIR spectroscopy can be influenced by variations in the sample matrix, such as grape variety, soil type, and weather conditions. The selection of assessment method depends on the specific requirements of the analysis, including the desired level of detail, sensitivity, cost, and the nature of the samples. Each method has its advantages and limitations, and researchers and industry professionals should consider these factors when selecting an appropriate method for grape quality assessment.

The moderate consumption of red wine and the intake of phenolic compounds can have numerous health benefits, including protection against stress-related diseases and bacterial and viral infections. However, it is important to note that moderation is key, and excessive alcohol consumption can lead to negative health effects.

Understanding the complex ripening process and the factors that influence grape composition is essential for grape producers and winemakers. By managing the timing of harvest and optimizing the accumulation of desirable compounds, such as sugars, organic acids, and polyphenols, winemakers can produce grapes and wines of superior quality, flavor, and aroma.

Author Contributions: Conceptualization, A.E.R., M.I.R., M.R.M. and J.M.B.; methodology, M.I.R., M.R.M. and A.E.R.; writing—original draft preparation, M.I.R., M.R.M. and A.E.R.; writing—review and editing, M.R.M., A.E.R. and M.I.R. All authors have read and agreed to the published version of the manuscript.

Funding: The authors thanks to the Projects UIDB/05183/2020 from MED-Mediterranean Institute for Agriculture Environment and Development; to the Projects UIDB/04449/2020 and UIDP/04449/2020 from HERCULES.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

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