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Opinion

Wine and Health: From the Perspective of Alvise Cornaro to the Latest Scientific Opinions

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Abstract: In this opinion article we explore the link between regular wine consumption and human health, starting from the teachings that Alvise Cornaro, a Scholar at the University of Padova, left us, especially on his "La Vita Sobria", a treatise published in Padova in 1558. A key role in his suggested diet is reserved for wine, an alcoholic beverage that, he advocated, should be consumed regularly, a concept that fits well with the central role that wine played in the Middle age society. Indeed, at that time, wine was consumed in large quantities, and it was generally mixed with water to make the latter safer for consumption. Monks and doctors also used wine as a medicine, as this was regularly administered to sick people of all ages to cure their illnesses. Wine maintained a similar role until the middle of the 20th Century, shifting from a source of energy to a pleasure, even if moderate wine consumption has been reported by epidemiological studies as having health benefits, particularly in relation to cardiovascular diseases. Conversely, any level of alcohol intake has recently been recognized as harmful, an occurrence that the modern wine industry is tackling by increasing the production of wines with reduced alcohol content. Nevertheless, nowadays, wine continues to be consumed for the pleasure it can provide and for its role as a social catalyzer.

Keywords: Alvise Cornaro; *Discorsi della Vita Sobria*; wine and health; red wine; white wine

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1. Alvise Cornaro and the Treatise on La Vita Sobria

Alvise Cornaro, a key figure in the context of Venetian society and culture of the sixteenth century, left a great artistic and intellectual heritage. He was born in Venice, probably in 1484, and his ancestors were wealthy, but lacked the aristocracy necessary to be introduced to the circles that mattered in his time. He studied law at the University of Padua, without obtaining a degree. Due to his uncommon intellectual abilities, he was able to exploit the wealth inherited from his family to acquire large properties in the Piove di Sacco area during Venetian land reclamation. In 1524, Giovanni Maria Falconetto built the Loggia and the Odeo Cornaro for him, an inner courtyard where people such as Ruzzante, Piero Valeriano, and Cornelio Musso gathered. The ideas of Cornaro himself are likely to have contributed to the realization of this monumental edifice, given that his "Treatise on architecture" demonstrates his skills and talents in this topic. Alvise Cornaro died in 1566 and was buried in the Basilica of the Saint Anthony in Padua [1].

The treatise on "the sober life" is one of his dissertations that fits very well into the debate of his time. It is a kind of vademecum for living long in health and, not surprisingly, entitled "*Discorsi della Vita Sobria*" (Discourse over the sober life) (Figure 1). It suggests how to train and help the body with a sort of regimen, or diet, which Alvise Cornaro had developed, experimenting on his own, without the help of medical doctors, to whom he had long relied, but of whom he had learned to be wary. He no longer intended to hear about bloodletting, purgatives, herbs, and so on.

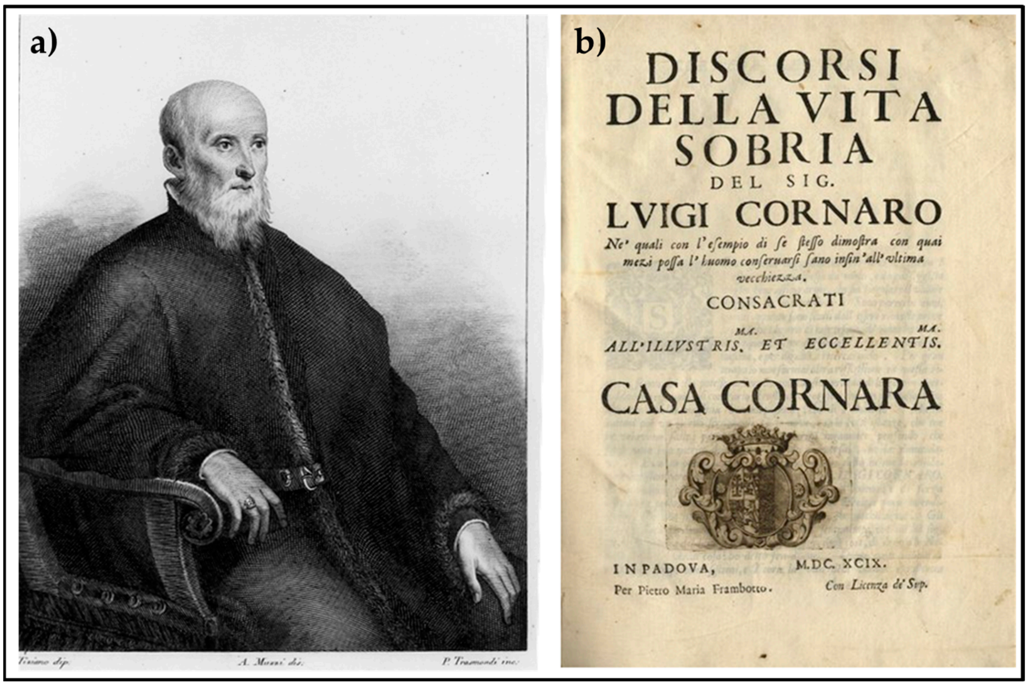

Figure 1. (**a**) Portrait of Alvise/Luigi Cornaro by Tintoretto, General Catalogue of Italian Cultural Heritage. (**b**) Front page of "*Discorsi Della Vita Sobria*".

During his youth, Cornaro did not forget food and other pleasures. However, over time, by attending the Academies, and by meeting with medical doctors and the most prominent people of the cultural elite, he had acquired his autonomy of thought, which he intended to keep firm, especially after the decision to become a citizen of Padova (Padua), perfectly and vividly inserted in the city context.

The wealth of Alvise Cornaro was superior to that of someone of the Venetian nobility [2], and he could rightly consider himself an established man, able to do but also suggest. The advice he intended to offer was a conquest of his thought, which remained brilliant and alive despite the years.

Therefore, "*Discorsi della Vita Sobria*" [3], published in Padua in 1558, can be considered his testament. The treatise explains the rules for reaching old age unscathed, and is based on three fundamental principles, a synthesis of which can be considered the Cornaro "trinity": «*la Signora Continenza, madre della virtuosa Signora Vita Regolata*, *della quale ne è figliuola la bella Signora Sanità*»: in brief, Mrs. Continence, mother of Mrs. Regular Life, whose daughter is Mrs. Health. However, these seemingly straightforward rules contained other thoughts. In fact, from sobriety is derived serenity and joy, precious allies to ward off the fear of death, but above all, that of the final judgment. Indeed, Alvise Cornaro admitted between the lines of his dissertation that he feared the final verdict on the previous life, the not-sober one.

Therefore, how should one proceed to find a compromise with the theories of the time regarding human health?

Leaving aside Hippocrates and Galen and their insistence on the four elements and the four humors, Alvise Cornaro stubbornly believed that every human "complex", strong, or weak, can be shaped and guided by the healthy rule of behavior which he designed for himself. This original thought sometimes did not consider the laws of nature and the divine, even if the death of two very young grandchildren struck him, showing that the end also affected those young and sober.

The dietary teaching of Cornaro can be summarized in a few brief tips: « . . . *E li miei cibi sono questi: prima il pane, la panatella o brodetto con ovo o altre simili bone menestrine; di carne* *mangio carne di vittello, capretto e di castrato; mangio polli di ogni sorte, mangio pernici e ucelli, come è il tordo; mangio anchora delli pesci, come è fra li salsi la orata e simili, e fra li dolci il lucio e simili: questi sono cibi tutti appropriati al vecchio, et debbe pur contentarsi di questi, e non volerne d'altri, sendo tanti* [. . .] *tra pane, un rosso d'uovo, carne et minestra mangiavo tanto che in tutto pesasse oncie dodeci alla sottile* [. . .] *et beveva oncie quatordici di vino*». These can briefly be translated as: " . . . and my foods are these: first bread, than soups with eggs; as meat I eat veal, goat and mutton, poultry of all sorts, partridges and birds; I also eat sea fish as sea bream, and freshwater fish as pike: these are all foods suitable to elderly people that should be satisfied by them [. . .], all together I eat 12 ounces of food and drink 14 ounces of wine". The indication of the weight (oncie) shows how meticulously he measured his food, even if Girolamo Cardano concluded that Cornaro seemed to speak more like a philosopher than a doctor. The fact that even a character such as Girolamo Cardano was involved in this discussion contributes to explaining the interest that fueled Alvise Cornaro's writing.

The old Cornaro wanted to teach the doctors of the time, and his satisfaction of having "rocked the boat" was evident. Therefore, the Venetian who became Paduan [4] demonstrated that he could build palaces and reclaim lands, buy houses on the Euganean Hills, discuss in the Academies, support penniless poets, but also taught how much and what one should eat and drink. His diet suited an eighty-year-old person with a quiet life [5]. Moreover, it was easily traceable back to the teachings of the ancients. In particular, to the Pythagoreans and Epicureans, and their moderate *refectio*, fueled by the doctrines of the legendary masters, with ethical, philosophical and religious contents. In brief, to control body and mind but wisely calibrate the diet to the strength of one's physique. This concept is also found in Cornaro's suggestions: "everyone can and must be his own doctor, dosing the quantity and quality of food and beverage in a way that they suit the body functions without causing any bad mood" («[. . .] *il cibo, che ho sempre mangiato, et il vino, che ho sempre bevuto, essendo tali quali si convengono alla mia complessione, et in quantità quanto si conviene, come hanno lasciata la loro virtù al corpo, se ne sono usciti senza difficultà, non havendo prima generato in me alcun cattivo humore*») [3]. These can briefly be translated as: " . . . the food, that I always ate, and the wine, that I always drank, being suitable for my body, and in adequate quantity, as they left their virtue on the body, they exited without difficulty, not having previously generated in me any disease".

However, the amount of wine indicated by Cornaro was surprising. It was higher than food, a suggestion that now is against every rule. Why these suggestions for wine? Only history can address this question, highlighting wine's safety in contrast to the bad quality of water and the wine's role as an antiseptic and pain reliever.

2. The Wine Mission

Ancient wine was quite different from the wine that we appreciate today, particularly due to the lack of microbiological knowledge. Wines were not well-protected from oxygen as preservatives and temperature control systems were not available, with the result that wines were unsuitable for ageing and could easily spoil [6], so it was common among monks to use spice and herbs to flavor the wines, thus covering their off-flavors [7]. As reported by Montanari [8], in the Middle Ages wine played an absolutely central role in the diet. Therefore, the quantity of wine that was normally drunk from the Middle Ages to the central part of the 20th century was very high.

For example, during the communal age, it is estimated that three to four liters of wine per day per capita were consumed in both urban and rural communities. Wine was more important than water itself, because water was generally of bad quality. Until the 19th century, and in some cases up to the 20th century, in the countryside as in the cities, the poor hygienic quality of the water was one of the most serious problems of the food supply. This is also why wine was essential: its moderate alcohol content and acidity made it a safe beverage. Indeed, for a very long time, it was not possible to drink water that was not "sanitized" by adding wine to it, so that it was common to drink water diluted with wine. This is why the Latin verb *miscere* simultaneously means "to pour" and "to mix", two activities that explain how the action of pouring was typically aimed to mix. Moreover, besides the connection with this sanitizing function, the premodern culture also assigned a therapeutic role to wine. Therefore, in the monastic infirmaries, in the Hospital practices, as well as in the daily habits of the city and rural population, drinking wine was considered sort of a "universal remedy" for all kinds of illnesses. This was a belief rooted in the medical culture from Hippocrates and Galen, but the Christian tradition also provided essential insights. Indeed, in Paul's first letter to Timothy, mixing wine with water was recommended to soothe physical pain. The link between wine consumption and health benefits was also very strong in public hospitals. Indeed, during the late Middle Ages wine was mainly used internally, meaning that the sick people had to drink wine in proportion to the severity of their illness [7]. For example, at the Hôtel-Dieu in Paris (15th–16th centuries), wine was abundantly present in the daily diet of sick people of all ages.

Many documents have reported the health benefits of wine, from improving the safety of drinking water to its role as an antiseptic and pain reliever [9]. However, nowadays, is the link between wine and health still clear and widely recognized? Indeed, today, wine is no longer essential to make water drinkable or as an antiseptic, and the debate on wine health claims also embraces the danger caused by its uncontrolled consumption. The main culprit is the alcohol content, even if numerous epidemiological studies confirm the role of moderate alcohol consumption in preventing some disorders, such as coronary heart disease.

3. Wine and Health

The potential health benefits of wine were highlighted by epidemiological studies in which regular and moderate wine consumption is associated to a lower cardiovascular mortality [10–12]. This was prompted by the phenomenon of the "French paradox" in which the mortality derived from coronary heart disease due to saturated fat and cholesterol dietary intake is reduced by moderate wine consumption [13]. Since these reports, many attempts have been made to identify the nutritional/epidemiologic basis for this seemingly incongruous association [14].

The effect of acute and long-term wine consumption on lipid metabolism is mainly attributed to the effect of the ethanol contained in wine [15]. The probable mechanism to explain the role of alcohol in preventing coronary heart disease is related to an increased rate of high-density lipoprotein (HDL), of their different fractions (HDL2 and HDL3) and components (Apo A-I and ApoA-II), all being negatively correlated with the risk of ischemic heart disease [16–18].

In addition to reducing the cardiovascular risk, ethanol increases myocardial blood flow. This induced vasodilation is a result of the increased content of nitric oxide resulting from the augmented activity of nitric oxide synthase [19,20]. Epidemiological, animal, and cellular studies have led to the idea that ethanol can also directly induce cell survival programs that render the cells resistant to ischemia/reperfusion (I/R)-induced tissue injury [20,21]. In particular, ethanol generates a mild oxidative stress that has a protective effect against I/R-induced damage. However, a Global Burden of Diseases (GBD) study on impact of alcohol consumption on different types of population indicates that these benefits apply only to middle-aged and older people [22].

Alcohol metabolism occurs in the liver where it is broken down through multiple enzymatic and non-enzymatic pathways. First, it is metabolized to acetaldehyde mainly through alcohol dehydrogenase, and then acetaldehyde is converted to acetic acid with the catalysis of aldehyde dehydrogenase [23]. Cytochrome P450 (CYP) enzymes also oxidize ethanol, particularly P450 2E1 (CYP2E1), which converts ethanol to acetaldehyde and then to acetic acid, reactions also performed by alcohol and aldehyde dehydrogenases [24]. However, CYP2E1 activity also results in the production of reactive oxygen species (ROS) that promote oxidative stress [25]. On the other hand, alcohol is a risk component in a considerable number of illnesses such as certain types of cancer, neuropsychiatric conditions, diabetes, stroke, ischemic heart diseases, cardiovascular and digestive disorders. Indeed, the consumption of alcohol has been clearly linked to the risk of developing cancers [22], a fact that in the past was certainly not known. Numerous attempts have been made to confirm the causal relation between alcohol consumption and cancer development. This task has been typically approached by means of observational studies that, however, often present limitations such as, for example, the lack of sufficient adjustment of confounding factors (e.g., smoking for oral cavity cancer), reverse causality, and the accuracy of recording alcohol exposure by participants [26].

In this context, alcohol intake remains a crucial factor because the average volume of alcohol consumed, drinking patterns, and the type of alcoholic beverages are likely to have a causal impact on mortality and morbidity related to chronic diseases [27]. To date, there is no international consensus on what a standard "drink unit" represents in terms of alcohol content [28]. Kalinowski and Humphreys [29] analyzed the policies of 75 governments and reported that only 37 of them had a definition of a "standard drink". On average, a "standard drink" contains 10 g of pure ethanol, but with a wide range from 8 g (UK, Iceland) to 20 g (Austria). Obviously, the drink volumes corresponding to a "standard drink" change depending on the type of alcoholic beverage [29]. According to the 2020–2025 Dietary Guidelines for Americans [30], one drink is defined as 12 fluid ounces of regular beer (5% alcohol), 5 fluid ounces of wine (12% alcohol), or 1.5 fluid ounces of 80 proof (40% alcohol) spirits. Therefore, one "standard drink" contains 17 g of alcohol.

In addition, the definitions of low-risk, light, or moderate alcohol consumption vary significantly between countries. According to Kalinowski and Humphreys [29], in the 37 countries considered, the definition of "low-risk" alcohol consumption ranges from 10 to 42 g of ethanol per day for women (98 to 140 g per week) and 10 to 56 g per day for men (150 to 280 g per week). Other definitions mention "light consumption" up to 0.4 servings/day (women) and up to 0.9 servings/day (men), where a serving corresponds to 15 g of ethanol [31], while "light to moderate consumption" is defined as 0.5 to 1 serving per day [32].

Many food guides and scientific sources mention and recommend moderate consumption of alcohol, which also has different meanings. For some authors, and the World Health Organization (WHO), a "moderate consumption" is represented by two 100 mL-glasses of wine (10 g of ethanol each) per day. In addition, it is recommended not to drink for at least 2 days per week [33,34]. The recommendation changes based on gender, as the 2020–2025 Dietary Guidelines for Americans [30] indicate that moderate consumption is represented by 1 "standard drink" for women and up to 2 "standard drinks" per day for men. Some more recent classifications introduced the type of drinker as factor guiding the recommendations [31]. McEvoy et al. [12] used the following classification: "very light drinkers" (1 to 4 drinks in 14 days), "light drinkers" (5 to 14 drinks in 14 days), "moderate drinkers" (15 to 28 drinks in 14 days), and "risky drinkers" (>28 drinks in 14 days). Finally, it is known that the aptitude towards alcohol consumption greatly differs between countries [12], as demonstrated by Davies et al., who compared responses to alcohol health information labels by people who drink alcohol from 29 countries [35]. However, Furtwængler and De Visser [28] suggested that all countries should be encouraged to define a "standard drink" as 10 g ethanol. They also recommended that women should drink no more than 2 "standard drinks" per day, and no more than 12 "standard drinks" per week, while men should drink no more than 3 standard drinks per day and no more than 18 standard drinks per week. In addition, women and men should have at least one alcohol-free day per week [27]. Other studies indicate that the consumption of 2 glasses of wine per day, along with other lifestyle changes such as moderate exercise, eating fruit, and not smoking, will increase life expectancy [36,37].

Recently, a more drastic approach to alcohol intake has been proposed, with the conclusion also adopted by the WHO that, despite the positive impacts on the above-reviewed cardiovascular system, no safe amount of alcohol consumption for cancer and health can be established [22].

Wines can be differentiated according to their composition, taste, and alcoholic content, but are basically classified as red, white, or rosé [38,39]; so, the question could be: what kind of wine is the healthiest?

3.1. Red or White Wines?

Wine is an alcoholic beverage obtained from fermented grape juice, and diverse main styles of wine are commercially available. Besides the diversity due to the intrinsic characteristics of the grape varieties used, wine styles have often developed in relationship with the traditions and the unique geographical and climatic conditions in which they originated [40].

Among the different chemicals present in wines, polyphenols are strongly involved in determining wine quality, as these compounds mainly affect color, taste, and mouthfeel. Bedsides, these substances constitute the most notable class of bioactive compounds present in wine, so much so that the so-called "French paradox" was attributed to their health benefits. Many internal and external factors have proved to significantly affect the concentration of phenolic compounds in wines. It is possible to distinguish three decisive levels affecting the quantity and quality of phenolic compounds, which are mainly present in the grape skins and seeds: the grape itself, as harvested in the vineyard (variety, climate conditions, organic and conventional cultivation, biostimulants . . .); the winemaking process (length and mode of skin contact, temperature, thermovinification, yeast strain and bacteria, additives, fining agents, filtration . . .); and finally, the mode of aging the wine (time, temperature, oxygen, container . . .) [41,42]. However, the vinification technique in general, and the length and modalities of skin maceration in particular, have the greatest impact on the final concentration of phenolics in wines. Indeed, wines undergoing the most extensive macerations (e.g., premium red wines) possess the highest content in phenolic compounds [43], while wines with limited (e.g., rosé wines) or without skin maceration (e.g., white wines) contain proportionally lower amounts of these substances. When looking at the quantities retrievable in commercial wines, the total phenolic content (TPC) of red and white wines, expressed as gallic acid equivalents (GAE), typically vary in the range of 900–1200 (for reds) and 190–290 mg GAE/L (for whites), depending on the ageing time [40]. Catechin is the one of the most important phenolics in wine, with concentrations ranging between 3 to 73 mg/L (Table 1).

Several studies have evaluated the possible mechanisms involved in the beneficial action of some specific wine polyphenolic compounds. For instance, the potential positive health effect of resveratrol and flavonoids of red wine has been related to changes in lipid profiles, improvement of endothelial function and glucose metabolism, reduction of insulin resistance, LDL-C cholesterol oxidative stress, and increase of the bioactivity of nitric oxide, thus generating a comprehensive suppressive effect towards oxidative and inflammatory stress [44–47]. In addition, Liu et al. found that flavonoids regulated alcohol and lipid metabolism and significantly reduced lipid accumulation, total cholesterol and triglyceride levels, and inflammatory factors [48]. Moreover, they downregulated the expression of genes related to alcohol and lipid metabolism, endoplasmic reticulum stress, and DNA damage. Indeed, the beneficial effects of wine are ascribed to the presence and number of natural antioxidants such as polyphenolic compounds [49]. Therefore, white wines, which naturally contain fewer phenolic compounds than reds (Table 1), should be less effective as carriers of bioactive polyphenols. This is why epidemiological studies are generally based on red wine consumption, and further research on the potential impact on health of white wines is still needed.

Table 1. Phenolic compounds of red and white wines, expressed as gallic acid equivalents (mg GAE/L).

Compounds	Red Wine (mg/L)	Reference	White Wine (mg/L)	Reference
Flavonoids				
Anthocyanins	21.3–736 73.27–337.21	[50] [51]	-	[50]
Flavonols	100 86.81–178.50	[42] [51]	-	[52]
Flavanols	800 81.70–169.33	[42] [51]	15–25	[50,53]
(+)-Catechin	13.8–390	[50]	38.0 ± 31.9	[40]
Catechin	3.02–72.89	[41]	4.25–9.92	[41]
Flavanones (Naringenin)	25	[50]	7.7	[50]
Hydrolyzable tannins (from oak)	0–250	[52]	0–100	[52]
Proanthocyanidins and condensed tannins	750–1000	[52]	20–25	[52]
Total (Flavonoids)	1365–1500	[52]	40–45	[52]
Non-flavonoids				
Benzoic acids	60	[52]	10.0–15	[52]
Hydroxycinnamates	60–165	[52]	130–154	[52]
Hydroxycinnamic acids	100	[50]	30	[50]
Gallic acid	up to 70	[42]	13.1 ± 7.0	[40]
Stilbenes	0.40–35.5	[54]	0.04–0.56	[54]
Resveratrol	0–9.84	[54]	0.018–0.073	[54]
Tyrosol	20–60	[55]	45	[55]
Hydroxytyrosol	3.89	[42]	2.69	[56]
Total (Non-flavonoids)	232–377	[52]	164.5–245.5	[52]
Total phenols	1732–1742 2567	[52] [57]	209.5–285.5 626 ± 160	[52] [40]

In any case, the health benefits of wine phenolics should be evaluated in relation to the quantity assumed. Considering the total phenolic average content of wines (shown in Table 1), and the definitions of "standard drinks", the calculation of the daily intake of phenolic compounds could be attempted. Assuming a daily intake of 1 glass of wine per day (125 mL), the phenolic compounds assumed could be in the order of ~200–300 mg for red wines, and of ~25–80 mg for whites. Therefore, the amount of bioactive polyphenols derived from wine consumption is limited. Moreover, their fate and bioavailability in the human body has to be considered [58], posing additional questions on the possible effects of wine phenolics on human health.

3.2. Wine with Reduced Alcohol Content

Following the current debate on the perceived negative role of wine caused by its alcohol content [22], an emerging category of beverages with reduced quantity of alcohol is being intensively studied, with the aim of proposing wines that still possess the bioactive compounds potentially responsible for the health benefits, while having fewer negative effects.

Wines with a reduced alcohol content can be classified as de-alcoholised, or no-alcohol, (<0.5% *v*/*v*), low-alcohol (0.5–1.2% *v*/*v*), or reduced-alcohol (1.2% to 5.5–6.5% *v*/*v*) as reported by Pickering [59]. In this respect, low alcohol wines can be obtained by reducing the accumulation of sugar in the berries or operating during winemaking.

The reduction of the sugar content of the grapes, a problem of increasing relevance at the time of global warming, can be obtained with different strategies, from selecting specific varieties or clones, applying antiperspirants, choosing appropriate irrigation techniques, increasing the crop load, and shading the bunches, as reported by Novello and de Palma [60]. However, agronomical practices can only limit sugar accumulation in grape berries. Therefore, currently, the main tools suitable to achieve a significant alcohol reduction in finished wines are based on interventions made in the winery, such as application of membrane technologies and modified distillation [61]. For example, it is possible to produce non-alcoholic wines (<0.5 vol.%) using one-step pervaporation membrane technology [61]. Another possibility is the reduction of the concentration of fermentable sugar in grapes or juices, which can be obtained in different ways such as the utilization of the juice of unripe berries, the dilution of the juice, the concentration and fractionation by freezing, and the application of sugar-degrading enzymes such as glucose oxidase. Alternatively, other methods that remove alcohol from wine have been proposed, including thermal processes (vacuum distillation or atmospheric pressure), the use of membranes (dialysis, reverse osmosis), adsorption (resins, silica gel), and extraction (organic solvents, supercritical carbon dioxide) [59]. A strategy is also the pre-fermentative addition to grape juice of either juice obtained from unripen grapes (green harvest wine) or water, where the addition of the latter offers many advantages to manage the alcohol content of wine since its quality attributes do not change significantly [62]. Recently, Bovo et al. evaluated the behavior of *Saccharomyces* yeasts in the production of low-alcohol wine from unripe grapes with low sugar and high malic acid concentration, concluding that this strategy needs yeast selection programs [63]. Other strategies to reduce the alcohol content are based on the use of non-*Saccharomyces* yeasts. A decrease of alcohol content between 0.6 and 1.2% (*v/v*) in white wines can be obtained by co-fermentations of *Metschnikowia pulcherrima* and *Saccharomyces cerevisiae* [64]. On the order hand, Contreras et al. evaluated non-*Saccharomyces* yeasts in fermentations with limited aeration to produce wines with reduced alcohol content, showing that *T. delbrueckii* AWRI1152 and *Z. bailii* AWRI1578 have the potential to reduce ethanol between 1.5% and 2.0% (v/v) [65]. Additionally, Canonico et al. found a reduction in ethanol concentration between 0.9% and 1.6% (v/v) with *M. pulcherrima*, *T. delbrueckii*, and *Z. bailianized* [66], while Varela et al. showed 1.7–1.8% reductions at the laboratory level using *M. pulcherrima* and *S. uvarum*, and between 1.0% v/v (*M. pulcherrima*) and 1.7% v/v (*S. uvarum*) at the pilot scale [67,68]. Finally, new strategies are based on the development of *Saccharomyces cerevisiae* wine strains with reduced ethanol production through metabolic engineering (direct limitation of the ethanol formation pathway, redirection of sugars to biomass, overproduction of glycerol), and evolutionary engineering (redirection to the pentose phosphate pathway, overproduction of glycerol) [69].

Nevertheless, despite the advantages that a larger consumption of low-alcohol wines could have on consumers' health, more studies are required to develop products of a quality comparable with that of common wines.

4. Conclusions

While the debate on the impact of wine consumption on health is still open, a large body of scientific literature agrees on the fact that a moderate wine intake during meals seems to have health benefits, especially for protection from cardiovascular diseases [70]. Indeed, this effect has been linked to the so-called French paradox, but it is also one of the pillars of the Mediterranean diet, which is universally recognized as the one that makes you live longer and healthier. However, the aspects related to wine consumption are controversial, due to the content, in wine, of ethanol, a compound harmful for human health, especially when consumed in large quantities. Indeed, the content in alcohol of wines is used as the main argument against the health benefits' claims of a moderate wine consumption. While in the past people considered wine a source of energy and an insurance for the safety of drinking water, nowadays consumers have shifted towards a hedonistic use of wine. This implies a continuous improvement of the "technical" quality of the product, but also aspects related to well-being, which includes not only the physical health as defined by physicians, but also the possibility to be happy in the relationships with themselves and with others. This means that wine is now consumed for the pleasure it can provide by stimulating the senses, particularly through the intensity of its aromas, fragrances, and tastes. In addition, nowadays wine plays a strong role as a social catalyzer, as it is typically consumed together with friends and family. Indeed, moderate wine consumption can positively affect the mood of consumers, thus favoring social interactions. The role of wine as a "bridge" between well-being and health [71] gives a perspective that remembers the vision and suggestions of Alvise Cornaro for enjoying life forever despite age. However, today, the quality of wine is entirely different from the past, and Alvise Cornaro would also appreciate our good quality wine and would be able to recognize its close link with the territory. As old Hellenes assessed, the first glass is health, and the second is satisfaction.

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