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Review Article

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Bridging the Gap: The challenge of Standardizing Antioxidant Assessment for Highly Active Grape Pomace Extracts

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ABSTRACT

Oxidative stress, a foundational imbalance linked to chronic inflammation, is implicated in numerous debilitating diseases, spurring interest in functional foods rich in natural antioxidants. Grape pomace (GP), an abundant agricultural by-product, is exceptionally rich in polyphenols and exhibits antioxidant properties superior to other berry wastes, making it a powerful long-term nutritional solution. This review provides a critical analysis of methodologies used to quantify GP's antioxidant activity (AO): spectrophotometric, electrochemical, chromatographic, nanosensors, and biosensors. While newer sensor technologies offer high sensitivity and a theoretically better correlation with in vivo systems, most traditional chemical assays suffer from poor reproducibility and a lack of correlation between in vitro results and biological outcomes. The core challenge lies in the chemical diversity of antioxidants, where no single test can fully assess the capacity to neutralize all relevant radicals. Consequently, accurately measuring the antioxidant potential of GP currently requires a multi-system approach, such as calculating the Relative Antioxidant Capacity Index (RACI), integrating comprehensive chromatographic profiling with detection methods or using Caenorhabditis elegans and rats as in vivo models. However, the absence of a universal, standardized working protocol—both for extraction and analytical measurement—significantly hinders reproducibility across laboratories and makes definitive statements about the antioxidant power of grape pomace polyphenols difficult. Addressing this lack of standardization is the crucial next step for validating GP as a bioactive ingredient. The novelty of this article consist of the critical synthesis of why diverse methods (from spectrophotometry to nanosensors and in vivo AO assays) fail individually and why RACI or similar multi-metric approaches are necessary, connecting this failure back to the chemical complexity of GP.

Keywords: Antioxidant Assays, Grape Pomace, Oxidative Stress, Biosensors, Raci - Relative Antioxidant Capacity Index

Oxidative Stress Leads to Chronic Inflammation, Causing Multiple Diseases

There is a trend for developing functional foods with plant-based extracts rich in antioxidants to fight against the key element responsible for multiple diseases, namely oxidative stress. Oxidative stress is defined as an imbalance between antioxidants and reactive species or free radicals, which induces inflammatory reactions throughout the body, including DNA damage [1].

Oxidative stress is created by internal factors such as natural reactions, metabolic or physiological states, or disease, as well as external factors like environmental pollution (air, soil, water,

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and pesticides) [2]. An external factor, for example, is cigarette smoking. Notably, just one cigarette can generate up to 1015 free radicals [3].

Free radicals can be classified into three categories according to the nature of the reactive atoms: reactive oxygen species (ROS), reactive nitrogen species (RNS), and reactive sulfur species (RSS) [4]. Furthermore, they can also be classified as free-radical species (hydroxyl, superoxide, hydroperoxyl, lipid peroxyl, nitrogen dioxide, protein radical) and non-free-radical species (hydrogen, singlet oxygen, ozone, lipid hydroperoxide, hypochlorous acid, peroxynitrile, nitrosyl cation) [5].

This redox balance must be theoretically understood as an equilibrium, because an excess of antioxidant species can also lead to health problems by undergoing transformations, that result in prooxidant species [6,7]. However, prooxidant activity of phenolic compounds are responsible for their antifungal effect [8]. Nevertheless, radical species should not be always presented in the darkest position, because in low concentration they are involved in cellular response and participate in various signaling pathways [9].

Chen et. al, mentions four most common used methods for the determination of oxidative stress [10]:

- fluorescent dyes like H2DCFDA to detect hydrogen peroxide (H_2O_2)
- quantifying lipid peroxidation products like malondialdehyde (MDA) or F2-isoprostanes
- alterations in antioxidant enzyme activities such as superoxide dismutase (SOD) and catalase (CAT)
- measuring plasma total antioxidant capacity (TAC)

Grape Pomace

Grape pomace (GP) represents an inexpensive waste product with very high antioxidant activity (AO) an enormous environmental impact, accounting for 20–25% of the entire wine-making industry's waste [11]. Total polyphenol content is the major contributor to the AO of the grape pomace and its superiority has been proven compared to pomace from other fruits (e.g., apricot, black currant), because GP has a higher concentration of polyphenols that directly correlates with its antioxidant power [12,13]. Therefore, a diet rich in antioxidants, such as one utilizing GP, can be beneficial when integrated into a self-aware lifestyle.

Dry Grape Pomace Nutritional Composition

The nutritional composition of GP includes about 38% carbohydrates (reported to dry weight, DW), which represents the highest component, followed by dietary fiber at 36% of DW [14]. Proteins and lipids are present in only tiny amounts. Lipid content ranges from 3.4 % to 8.9 % of DW, and the oil extracted from grape seeds contains high amounts of polyunsaturated fatty acids (PUFAs), primarily linoleic acid about 70–75% [15]. According to Zhou et al., a comparison of in vitro antioxidant assays like Ferric reducing antioxidant power (FRAP) and 2,2-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) indicates that the highest antioxidant activity (76%) comes from the grape seed, followed by grape skin (23%, or 3.3 times less), and around 1% from the grape pulp. With other words, grape seeds remain at the top for their antioxidant donating activity [16].

Polyphenols Mainly Responsible for the Antioxidant Activity of Grape Pomace

Phenolic compounds are the most relevant compounds of GP, generated as secondary metabolites with a defense mechanism role to fight unfavorable conditions such as drought, heavy metal interaction, salinity, temperature variations, fungal disease, and UV radiation [17]. The more stressful the environmental factors are, the more polyphenols are produced in the grape, as a protective response. GP is very rich in polyphenols; up to 70% of the phenols remain in GP after the wine-making process, mainly found in the seed skin. The total polyphenolic content (TPC) represents 0.28% to 8.70% of GP [18]. Cotoras et al., states that, phenolic compounds have pointed them out as powerful in vitro antioxidants, even more potent than Vitamins C and E and the carotenoids [8].

According to figure 1, the two main groups defining polyphenols are divided into flavonoid compounds (like anthocyanins and flavanols) and non-flavonoid compounds (like phenolic acids and stilbenes). Resveratrol, which belongs to the stilbene's family, is a highly studied molecule responsible for the cardioprotective effect of red wines, known as the 'French Paradox' [19]. Seif et.al confirms through in vivo-study on rats the nephroprotective effects of resveratrol in lead acetate (PbAc)-induced kidney damage [20].

Flavanols and procyanidin dimers, which are the main polyphenols in grape seeds, show strong correlations with both TPC and antioxidant assays. Notably, GP skins exhibited a more diverse phenolic profile compared to seeds. Not all grape species exhibit similar antioxidant activity; some Vitis vinifera species, such as Grenache, Syrah, and Alicante, distinguished themselves through higher phenolic content and antioxidant capacity [21]. The phenolic profile composition (Table 1) is strongly linked to the species, geographical position, harvest time, climate, and finally, the extraction methods used [9]. TPC from red GP varieties is overall 1.5 times higher than TPC from white GP varieties [23].

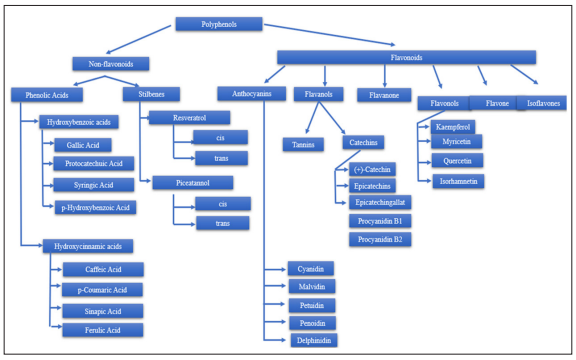

Figure 1: Structural classification of grape pomace polyphenols. Flavonoid compounds (flavanols, anthocyanins, and flavonols) and non-flavonoid compounds (phenolic acids and stilbenes) are divided according to their core chemical skeletons and representative antioxidant activity

Table 1: Principal phenolic compounds identified in grape pomace and their associated antioxidant activities. Data include major subclasses (flavonoids, phenolic acids, stilbenes) and representative compounds responsible for radical scavenging and metal-chelating effects

Principal phenolic compounds	Antioxidant activities
Flavonoids	This is the largest group of polyphenols and include flavan-3-ols as biggest subgroup. Flavan-3-ols include catechins, epicatechins, and their polymers called proanthocyanidins (or condensed tannins) [21]. The seeds are characterized by huge amount of proanthocyanidins 3532 mg/100 g responsible for the antioxidant activity [16]. According to Bocsan et. al (2022), the highest antioxidant property of grape pomace components is assigned to (+)-catechin gallate, followed by (-)-epicatechingallate, (+)-gallocatechin, (+)-catechin, and (-)-epigallocatechin. Proanthocyanidin have 20 % more antioxidant capacity compared to vitamin E and 50% compared to vitamin C, figure 2 [24].
Anthocyanins	Anthocyanins are natural pigments responsible for the red, blue, and purple colors. In grapes, these pigments are located exclusively in the skins. Important anthocyanins include malvidin-3-O-glucoside, petunidin-rutinoside, and cyanidin-3-O-glucoside [21]. These three anthocyanins are especially responsible for the abbility to regulate oxidative stress through the transcription factor Nrf2 [25]. For example, Alicante GP skins exhibited the highest anthocyanin content, reaching up to 5000 µg/g DW, with 3-O-glucosides as the dominant forms, particularly malvidin-3-O-glucoside, which contributes to its intense pigmentation and strong antioxidant properties. Also, Cabernet Sauvignon and Merlot, are very rich in anthocyanins [22].
Flavonols	Flavonols include quercetin, kaempferol, and myricetin. Kaempferol and quercetin are present in both white and red grape varieties, while myricetin and isorhamnetin are specific to red grapes [22].
Phenolic acids	Phenolic acids are non-flavonoids compounds, which include hydroxybenzoic acids and hydroxycinnamic acids. Hydroxycinnamic acids are the predominant phenolic compounds in grapes and include caffeic, ferulic, and p-coumaric acids. These compounds often conjugate with tartaric acid, forming caftaric, fertaric, and coutaric acids. Significant amounts of these compounds are also present in GP skin. Hydroxybenzoic acids are represented by vanillic, syringic, gallic, protocatechuic, and ellagic acids. Species like Chardonnay and Sauvignon Blanc present lower anthocyanin and tannin content, but are rich in phenolic acids, what gives them high antioxidant capacity [21].
Stilbenes	Stilbenes represented by resveratrol, one of most studied molecules, is mostly found in grape skin. Concord species is very rich in resveratrol [21]. According to Nimal et. al, resveratrol has the highest antioxidant activity regarding the peroxyl radical assay followed by catechin, epicathechin the same as gallocahtechin and then the gallic acid similar to ellagic acid [26].

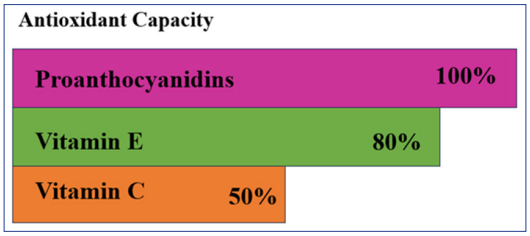

Figure 2: Comparative antioxidant capacity of grape seed proanthocyanidins relative to vitamins E and C. Data adapted from Bocsan et al. illustrating superior radical-scavenging efficiency of condensed tannins [24]

Increasing the Phenolic Content and the Antioxidant Activity Through Various Methods

Through fermentation, the phenolic content is increased, as is the antioxidant activity, by the liberation of flavan-3-ol monomers and procyanidins from the protective seed walls. Aspergillus niger and Aspergillus oryzae were analysed by Meini et al and can increase the antioxidant content through solid-state fermentation [27]. Fungal solid-state fermentation with species like Aspergillus niger, Eurotium cristatum and especially Monascus anka increase the phenolic content by around 6 times and the antioxidant capacity by around 2-3 times [28].

Antioxidant Mechanism of Polyphenols

The antioxidant activity of polyphenols stems from their ability to act as hydrogen-donating radical scavengers, participate in electron transfer, and function as singlet oxygen quenchers and metal chelators [29]. There are many methods for testing antioxidant activity (Figure 3), ranging from in vitro chemical-based methods including spectrophotometric methods and chromatographic methods, to electrochemical exemplified by recent technologies like bio- and nanosensors, cell-based methods and in vivo antioxidant assays using Caenorhabditis elegans and rats as models [9,30].

Chemical-Based Antioxidant Assays

The primary spectroscopic methods utilized in antioxidant analysis comprise Mass Spectrometry (MS), Nuclear Magnetic Resonance (NMR) Spectroscopy, UV–visible Spectroscopy, and Fluorescence Spectroscopy [31]. The most simple, inexpensive, and highly sensitive methods for measuring antioxidant capacity are the in vitro UV-visible spectroscopy methods (Table 2), which measure the absorbance at a specific wavelength and offer reproducible results within a calibration scale [5].

Note: DPPH—2,2-diphenyl-1-picrylhydrazyl; ABTS—2,2-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid); FRAP—

Ferric reducing antioxidant power, CUPRAC—Cupric reducing antioxidant capacity; ORAC—Oxygen radical absorbance capacity; FC—Folin-Ciocalteu, TRAP- total radical-trapping antioxidant parameter, catalase-like assay (H2O2 neutralization assay), cellular antioxidant activity (CAA assay), the antioxidant power 1 assay (AOP1 assay), nuclear factor erythroid 2 / antioxidant response element (Nrf2/ARE assay).

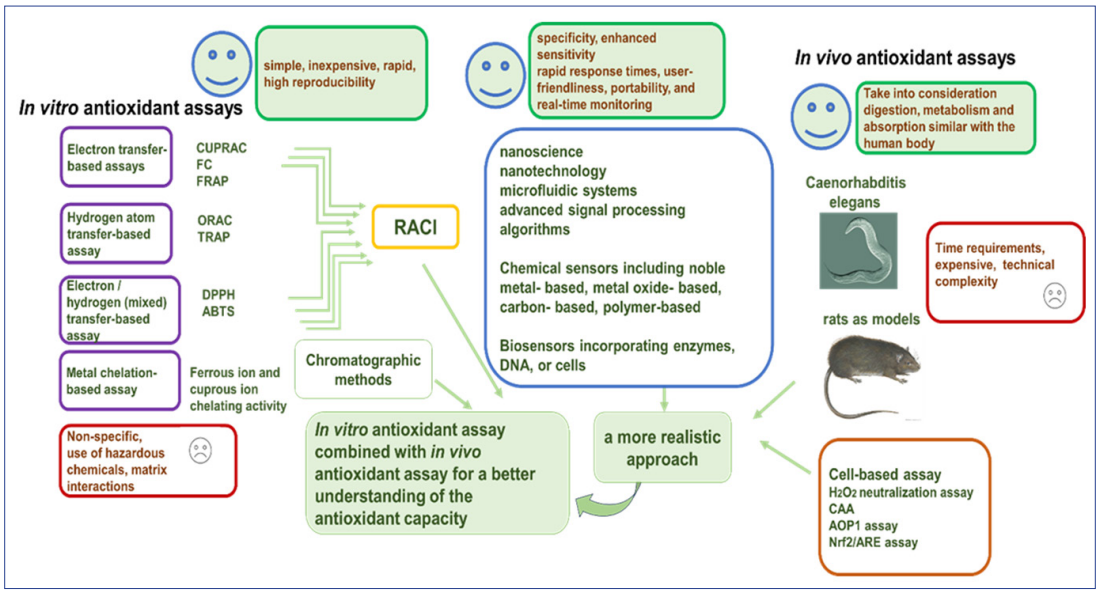

Figure 3: Overview of antioxidant assays applied to grape pomace analysis. The figure summarizes major in vitro AO assays such as spectrophotometric (DPPH, ABTS, FRAP, CUPRAC, ORAC, FC), chromatographic, electrochemical methods, which are mostly used for total antioxidant evaluation. In vivo AO assays that use C. elegans and rats as models can very well explain the digestion, absorption and metabolization of polyphenols in human systems.

Table 2: Comparative characteristics of UV–Vis spectrophotometric assays applied for grape pomace antioxidant assessment. The table summarizes assay principles, major advantages and limitations, and key findings from representative studies correlating phenolic content with antioxidant response

Chemical-based AO assays	Principle	Strength	Limitations	Summary of the assay's performance characteristics
DPPH	antioxidant reaction with an organic radical (517 nm)	simple, inexpensive, rapid	DPPH radical chromogens dissolve only organic solvents (lipophilic) [32]	Higher TPC concentration correlated with higher DPPH [33]. Strong Pearson correlation of TPC-DPPH, DPPH-TAC (total anthocyanin content) [2]. Ponticelli et. al showed that for the Torresco Viticus variety the DPPH results were the highest applying microwave method with 988.88 +/- 53.81 mg TE/g, TE means Trolox equivalent [34].
ABTS	antioxidant reaction with an organic radical (734 nm)	reproductible, determinate hydrophilic and lipophilic antioxidants	It does not exist in biological system, takes long time (12-16h) together with DPPH, it is not suitable for some highly reactive radicals [32]	Kiss et. al (2025) underlines that the strongest inter-assay correlation was between FRAP and ABTS. Using Sperman test, results showed a strong correlation of TPC with the spectrophotometric measurements: ABTS, DPPH, ORAC, FRAP [22].
FRAP	antioxidant reaction with a Fe (III) complex (593 nm)	simple, inexpensive, can screen biological samples including saliva	non-specific to phenolics [32]	Higher TPC concentration corelated with higher FRAP [33]. Torresco Viticus variety showed FRAP with 915.69 +/- 47.22 mg TE/g the highest when the extration was subjected to accelerate solvent extraction ASE method [30].

FC	colorimetry method based on SET reactions, determinate the total phenolic content TPC (760 nm)	simple, rapid and reproducible, direct correlation between phenolic compounds and antioxidant activity, can screen many samples in a timely fashion	non-specific to phenolics determine just hydrophilic antioxidants [32]	Isabella grape (La Plata, Argentina) pomace exhibited a higher TPC than Cabernet (Veneto, Italy) [33]. A strong correlation TPC - TAC was measured at the following Vitis vinifera L. varieties (Tinta Negra, Complexa, Malvasia Roxa, Malvasia, Sercial, Verdelho, Boal, Terrantez) [23].
ORAC	measures the ability of an antioxidant to protect a fluorescent probe from damage by peroxyl radicals.	can determine lipophilic and hydrophilic antioxidants in modified procedures (Priori et. al, 2003) Controversially, correlates better with in vivo antioxidant mechanism [35].	Withdrawn in 2012 by the U.S. Department of Agriculture (USDA) due to a lack of physiological proof for its relevance to human health in vivo. FC and ABTS have partially replace it [36].	The antioxidant capacity measured through Oxygen radical absorbance capacity assay ORAC for the seed extracts of Grenache Vitis vinifera species is with 432 mM Trolox / g, one of the highest, because of its association of greater monomer content, mainly cis isomers, and shorter proanthocyanidins Karastergiou et. al, [22].

Relative Antioxidant Capacity Index (RACI) as an Advance Tool for Comparing Different Grape Pomace Varieties

Sun and Tanumihardjo reflect the benefit for the determination of the relative antioxidant capacity index (RACI), because of building a simplistic scale for easily comparing different products by their antioxidant activity [37]. RACI represents an average of a standard score calculated based on raw data obtained from several in vitro assays such as ABTS, FRAP, ORAC Cu2+, ORAC OH*, ORAC ROO*, phenol antioxidant index (PAOXI) derived from FC, total radical-trapping antioxidant parameter (TRAP), which correlates with each of the aforementioned assays. RACI is thus a unitless numerical scale that makes it possible to compare products based on their antioxidant power. Ideally, RACI would also be composed of in vivo assays that show the bioavailability of antioxidants in human systems. In other words, calculating RACI based on in vitro assays gives us a superior view of antioxidant capacity, thus being able to put on an even clearer scale the antioxidant capacity for different products, but only the union with in vivo methods brings us closer to a complete understanding of the antioxidant capacity.

Chromatographic Methods

Chromatographic methods provide a complex view of the sample compounds with precise separation and quantification, making them indispensable for obtaining the complete profile of the tested sample. HPLC coupled with mass spectrometry (MS) provides detailed information about the molecular weight and fragmentation patterns [31]. The most used solvent for separating phenolic compounds is acetonitrile, and the most common detector is the reverse phase C18 octadecylsilane stationary phase detector, which typically implies multiwavelength detection [38].

Furthermore, HPLC coupled with UV-visible spectroscopic methods (like DPPH) shows significant advantages compared to UV-spectroscopic methods alone. However, traditional detection methods such as ELISA, HPLC, and spectrophotometric assays typically provide only snapshot measurements, without showing real-time measurement [10,31].

New Methods for Real-Time Antioxidant Assay: Electrochemical Sensors

Real time measurements can be determinate by using electrochemical methods. Electrochemical sensors convert chemical information from oxidized and reduced species into measurable electrical signals. They can be divided into chemical sensors with noble metals, metal oxide, carbone, and different polymers and biosensors that are DNA-based, live cell-based and enzyme-based. Nanosensors, employing nanomaterials, offer enhanced sensitivity to detect subtle changes in antioxidant behavior at the nanoscale. This technique shows a very low limit of detection, up to 10-9 M [10,31].

Metallic electrodes have excellent conductivity and stability, such as gold (Au), platinum (Pt), silver (Ag), as well as graphene electrodes. The concept of biosensors, enriched with different living cells, has been developed from the underlying electrochemical principles such as voltammetry, which encompasses several methods like as cyclic voltammetry (CV), differential pulse voltammetry (DPV), and square wave voltammetry (SWV). Amperometry is characterized by maintaining a constant potential and measuring the current generated from the oxidation or reduction of specific electroactive compounds. This technique is highly sensitive and capable of detecting low concentrations of analytes, which is particularly advantageous in trace analysis. Biamperometry is more efficient than amperometry because it offers better sensitivity and a higher signal-to-noise ratio compared to single-channel amperometry [31].

An obstacle to using enzyme-based biosensors is the immobilization of the enzyme on the electrode, which can sometimes be difficult. However, this is often achieved by absorption on a substrate, immobilization in a carbon paste or PVC matrix, entrapment in a polymeric matrix, covalent binding, cross-linking, or encapsulation on liposomes, among many other methods [39].

One of the main challenges faced by electrochemical sensors is the simultaneous detection of phenolic compounds with similar structures that have overlapping redox potentials [26].

Furthermore, an electrochemical sensor is only capable of determining one or few compounds simultaneously, usually less than 5 compounds [40]. However, this issue can be resolved by coupling chromatographic separation and microfluidic chip strategies with sensing detection [26].

A very important aspect when using electrochemical sensors is that they must be optimally calibrated; otherwise, false-positive signals can lead to a misinterpretation of the redox status [10]. Despite their potential, electrochemical sensors face challenges such as stability, reproducibility, and interference, which need to be addressed for their widespread application in food analysis [31,40].

There is no Single in Vitro Antioxidant Assay Sufficient to Determine the Antioxidant Activity Accurately Due to its Low Correlation With In Vivo Antioxidant Assay

The intestinal absorption of polyphenols responsible for the antioxidant effects is very poor, only 5-10 % of the hydrolyzed polyphenols are absorbed by the portal vein, that lead to liver for further metabolization [41]. Herrera-Bravo et al gives the example of anthocyanins, which are very unstable, easily oxidized, and sensitive to many factors, such as pH and temperature [25]. Untea et al also states that the total polyphenols of grape pomace that are extractable represent just 2%. Moreover, Cotoras et al didn't find any correlation between the in vitro cyclic voltammetry analyze on GP and its antifungal effects derived from its prooxidant character utilizing in vivo tests with the fungus species Botrytis cinerea [38,12].

This means that antioxidant properties determined in vitro cannot really correlate with antioxidant properties in vivo due to extremely low bioavailability resulted from the poor absorption of polyphenols by the human body.

In vivo antioxidants act in a different manner and can, for example, reach the mitochondria of mammalian cells and make electron transport and oxidative phosphorylation more efficient [42].

In addition, in vitro assays face the problem of reproducibility [32]. Some authors suggest that the absence of a direct correlation between TPC and antioxidant activity (AA) may be due to a saturation effect, for example, in the DPPH method [43]. Moreover, Kotha et. al underline that antioxidant assays cannot be compared or inter-converted, because each method employs different mechanisms, pH, temperature, and sample matrix [9]. Adrar et al propose a combination of electrochemical sensors with different cell-based antioxidant assay for the determination of antioxidants in food industry (Table 3) [41].

Cell-based antioxidant and in vivo antioxidant assays

Cell-based antioxidant assays explore the inhibition effect of free radical oxidation at cell level [30].

Catalase-like assay (H2O2 neutralization assay), cellular antioxidant activity (CAA assay), the antioxidant power 1 assay (AOP1 assay) and nuclear factor erythroid 2 / antioxidant response element (Nrf2/ARE assay) are very studied at the moment, because they offer a more realistic approach of the antioxidant's activity at cell level, which are exposed to oxidative stress (Adrar et. al, 2025). For example, Nrf2 as a transcription factor, which accumulates in cell cytoplasm through exposure to oxidative stress, represents a key molecule for the developing of inflammatory process (Herrera-Bravo et.al, 2022). ARE is an important protective element and a transcriptional regulator upstream activated by to increasing concentration of Nrf2 [30].

Dufour et.al, used three cell-based antioxidant assay CAA, AOP1 and nuclear factor erythroid 2 / antioxidant response element (Nrf2/ARE assay), which was assessed using an ARE-luciferase assay, to exemplify the indirect antioxidant response of grape pomace extract supplements with increased selenium content. Grape pomace extract was particularly effective in inhibiting free radicals highlighted by AOP1 and activating the ARE pathway,whereas sodium selenite exerted its effects through potent ARE activation at sub-microgram levels [7]. Lang et al, in her review about the methods for detecting antioxidants in phenolic compounds, stated that the use of living organisms such as Caenorhabditis elegans or rats as models for in vivo antioxidant assays is superior to cell assays and ultimately to chemical assays [30]. The use of in vivo models like C. elegans and rats can optimally explain digestion, metabolism, and absorption of the polyphenols contained in grape pomace, while cell assays can very well analyze the activity of antioxidants at cell level exposed to oxidative stress [44].

Table 3: A summary of main advantages and disadvantages regarding the in vitro and in vivo antioxidant assays

Antioxidant assays	Advantages	Disadvantages	Reference
Chemical based antioxidant assay	rapid, inexpensive, most commonly used	poor in vivo correlation, non-specific, matrix interference, some methods require time (ABTS)	[22,32]
Electrochemical sensors	portable device, doesn't require a laboratory conditions, easy to use improved sensitivity and specificity, real-time monitoring, better in vitro – in vivo correlation	can determine just one or few compounds simultaneously, matrix interference, the immobilization of the enzyme on the electrode is difficult to realize, inadequate calibration leads to false-positive results	[10,31]

Cell based assay	very good projection of the antioxidant activity in living cells exposed to oxidative stress	expensive, don't show digestion, absorption and metabolism in order to be compared with human systems	[7,30]
In vivo assays	show digestion, absorption and metabolism and are optimal to be compared with human systems	Expensive, require time	[30]

Conclusions

Grape pomace, as a valuable by-product from the wine industry, has high antioxidant activity and can be used as an important solution to daily exposure to oxidative stress. Analysis of the various antioxidant methods currently available clearly shows that the antioxidant activity cannot be calculated comprehensively through a single test. This is because antioxidants represent a diverse group of molecules, each capable of neutralizing specific radicals or oxidants, depending on their distinct chemical structures. Furthermore, chemical-based antioxidant assays may not directly reflect outcomes in biological systems, given the complexity of the latter and the diversity of chemical compounds in natural products. Without a consensus among scientists on a standardized and validated working protocol, it is difficult to make a clear statement about the antioxidant capacity of grape pomace polyphenols. RACI index is an important toll for the comparation of different grape pomace varieties. The development of RACI index and the utilization of high sensitivity electrochemical sensors made a step forward regarding the performance of the in vivo based AO assays, however, due to the extensive digestion of the polyphenols in our body (just 5-10% of the polyphenols from the grape pomace are finally absorbed through portal vein and then metabolized by the liver), these methods don't show a very good correlation with in vivo AO assays. Cell based AO assays offer a more realistic approach and in vivo AO assays reproduce optimal the intestinal tract digestion, absorption and metabolization of the polyphenols, offering more details about their bioavailability in human body. The only current solution for providing an accurate vitro-in vivo AO assay correlation is at the moment a multisystem approach.

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Conflicts of Interest

The authors declare that they do not have any conflict of interest.

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