PLANT SCIENCE TODAY
Vol 12(sp1): 1-11
https://doi.org/10.14719/pst.9690

eISSN 2348-1900

REVIEW ARTICLE

Precision enology: CRISPR, AI and non-thermal innovations for optimizing wine's bioactive legacy

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Received: 29 May 2025; Accepted: 21 August 2025; Available online: Version 1.0: 08 October 2025

Cite this article: Priyadharshini D, Muthuvel I, Saraswathy S, Balakrishnan M, Raveendran M, Jegadeeswari V, Ramalakshmi A. Precision enology: CRISPR, AI and non-thermal innovations for optimizing wine's bioactive legacy. Plant Science Today. 2025; 12(sp1): 1-11. https://doi.org/10.14719/pst.9690

Abstract

This review critically examines the mechanisms by which winemaking processes and preservation techniques modulate the retention of bioactive compounds, shaping wine's nutraceutical potential. Traditional practices (fermentation dynamics, barrel aging) and modern innovations (non-*Saccharomyces* yeasts, CRISPR engineering, enzyme-assisted extraction) are scrutinized for their impact on bioactive composition, emphasizing heat, oxygen and sulphite sensitivity. Preservation strategies from SO_2 to pulsed electric fields and nanotechnology are evaluated for balancing microbial stability, oxidation control and consumer demands. Wine's polyphenols (resveratrol, quercetin), flavonoids and anthocyanins demonstrate cardioprotective, antioxidant and microbiota-modulating effects, yet controversies persist, alcohol's health risks counterpose bioactive benefits, while epidemiological ambiguities in dosage-response relationships and confounding lifestyle factors challenge causal inferences. Case studies contrasting organic/conventional production and aging methods reveal trade-offs between sensory quality and bioactive retention. This review hypothesizes that synergistic integration of precision technologies (e.g., CRISPR yeast engineering, AI-driven fermentation) with non-thermal preservation can maximize bioactive retention while mitigating health risks. Urgency stems from consumer demand for health-functional wines and regulatory pressures to reduce sulphites and alcohol. Critical gaps remain in elucidating bioavailability mechanisms; sustainable processing aligned with circular economy principles and harmonizing health claims with regulatory frameworks. The review advocates for precision enology and transdisciplinary collaboration to advance wine as a functional food, urging rigorous, evidence-based innovation to reconcile tradition with health science, ensuring safety and efficacy in redefining wine's cultural and nutraceutical legacy.

Keywords: bioactive compounds; CRISPR engineering; non-*Saccharomyces* yeasts; nutraceutical potential; polyphenols; precision enology

Introduction

Winemaking, one of humanity's oldest biotechnological endeavours, has evolved from rudimentary fermentation practices to a sophisticated global industry intertwined with cultural identity and scientific innovation. According to archaeological evidence wine production began as early as 6000 BCE in the South Caucasus, where Neolithic communities fermented *Vitis vinifera* grapes in clay vessels (1). Ancient civilizations, including the Egyptians, Greeks and Romans, refined these techniques, using wine for rituals, trade and medicinal purposes. Historical records note that Hippocrates, for instance, prescribed wine for digestive ailments (2). By the middle ages, monastic orders had systematised viticulture, while Louis Pasteur's 19th-century breakthroughs in microbial control revolutionized fermentation processes, enabling industrialisation (3). Today, the industry merges tradition with innovation employing auto-mated temperature-controlled tanks and AI-driven analytics to sustain a $400 billion global market rooted in 8000 years of craftsmanship (4). Parallel to this technological evolution is a paradigm shift in how wine is perceived: no longer merely a cultural staple, it is increasingly framed as a functional food with nutraceutical potential. Research in the 1990s on the "French Paradox", which linked moderate red wine consumption to lower cardiovascular mortality despite high saturated fat diets sparked this re-evaluation (5). Subsequent research identified polyphenols notably resveratrol, quercetin and anthocyanins as key bioactive compounds exerting antioxidant, anti-inflammatory and cardioprotective effects (6). Epidemiological data suggests that moderate intake (1-2 glasses daily) correlates with a 20-30 % reduced risk of coronary heart disease (7). However, the health narrative remains contentious. Critics emphasize methodological flaws in such studies, including inconsistent lifestyle variables and ethanol's inherent toxicity (8). Reinforcing this skepticism, the World Health Organization (WHO) categorizes ethanol as a group 1 carcinogen, asserting no safe threshold for alcohol consumption (9). This duality places wine at a crossroads: celebrated as a cultural legacy with emerging therapeutic potential, yet entangled in debates over public health risks.

This review evaluates how winemaking techniques and preservation strategies shape wine's bioactive compounds and their health impacts. First, we examine how methods like maceration time, yeast selection and sulphite use influence polyphenol levels. For example, studies confirm that red wines retain significantly higher resveratrol concentrations (5-14 mg/L) due to extended skin contact during fermentation, compared to white wines, which average ≤0.6 mg/L (10). However, as highlighted by recent research, modern filtration systems designed to clarify wine can inadvertently remove up to 30 % of these beneficial compounds, raising questions about balancing aesthetics with nutritional value (11). Second, we weigh wine's potential benefits against its risks, such as ethanol's contribution to oxidative stress. Non-alcoholic alternatives, developed using advanced methods like vacuum distillation, aim to preserve polyphenols while eliminating alcohol. Yet, as noted in industry analyses, these alternatives often struggle with flavour stability and texture, limiting their appeal despite their health-focused design (12). Longitudinal studies are needed to isolate ethanol's harms from polyphenols' protective effects, while sustainable practices such as repurposing grape pomace into functional food additives could reduce waste and enhance nutritional value, as proposed in recent circular economy models (13). We hypothesize that synthesizing insights from enology, nutrition and environmental science will uncover synergistic pathways for innovation. These pathways will enable the simultaneous achievement of preserving wine's cultural heritage, enhancing its health benefits and improving ecological resilience. This review employs a systematic, interdisciplinary methodology: comprehensive literature synthesis across the three core fields; Development of an integrative framework mapping interactions between cultural, health and environmental factors across the wine value chain; visual process mapping to identify critical innovation points; analysis to derive actionable strategies for sustainable innovation. Fig. 1 illustrates the sequential stages of grape harvesting and processing and Fig. 2 maps the core oenological procedures, including primary fermentation, malolactic conversion and filtration.

Winemaking processes: traditional to modern techniques

Fermentation dynamics

Traditional winemaking depends on spontaneous fermentation driven by wild yeast strains native to grape skins, including *Saccharomyces cerevisiae* and non-*Saccharomyces* species such as *Candida* and *Hanseniaspora* (2). These indigenous microbes are critical to a wine's regional identity. For example, studies of Georgian *qvevri* wines demonstrate that *S. cerevisiae* becomes dominant after 7-10 days of fermentation, generating phenolic profiles unique to the region (14). Historical European methods, such as foot-treading grapes in open vats, intentionally exposed fermenting musts to oxygen, a practice shown in 18th-century records to enhance fruity aromas through ester production (15). However, research into preindustrial methods highlights a key drawback unpredictable fermentation caused by microbial competition frequently led to spoilage and shortened shelf life (16). Table 1 provides the list of microbes involved in fermentation.

Table 1. Microbes involved in fermentation

Microbe Type	Examples	Function	Reference
Yeast (fungi)	*Saccharomyces cerevisiae, Saccharomyces uvarum, Torulaspora delbrueckii*	Primary fermentation, converting sugars (glucose and fructose) to ethanol and CO_2	(20)
Native yeast	*Kloeckera apiculata, Metschnikowia pulcherrima, Candida zemplinica*	Contribute to aroma and flavour profile, can initiate fermentation before *S. cerevisiae*	(21)
Bacteria	*Oenococcus oeni, Lactobacillus plantarum, Pediococcus pentosaceus*	Malolactic fermentation, converting harsh malic acid to softer lactic acid	(22)
Native bacteria	*Weissella confusa, Lactobacillus hilgardii, Leuconostoc mesenteroides*	Can contribute to desirable sensory characteristics and influence malolactic fermentation. Dosage at 10^5-10^6 CFU/mL if used in co-inoculation with *Saccharomyces.*	(23)

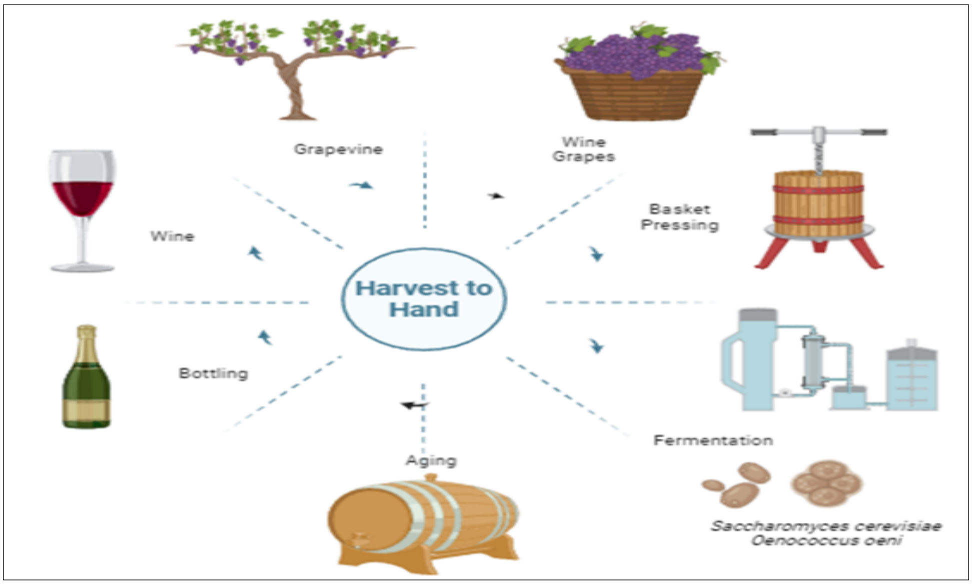

Fig. 1. Grapes- harvest to hand.

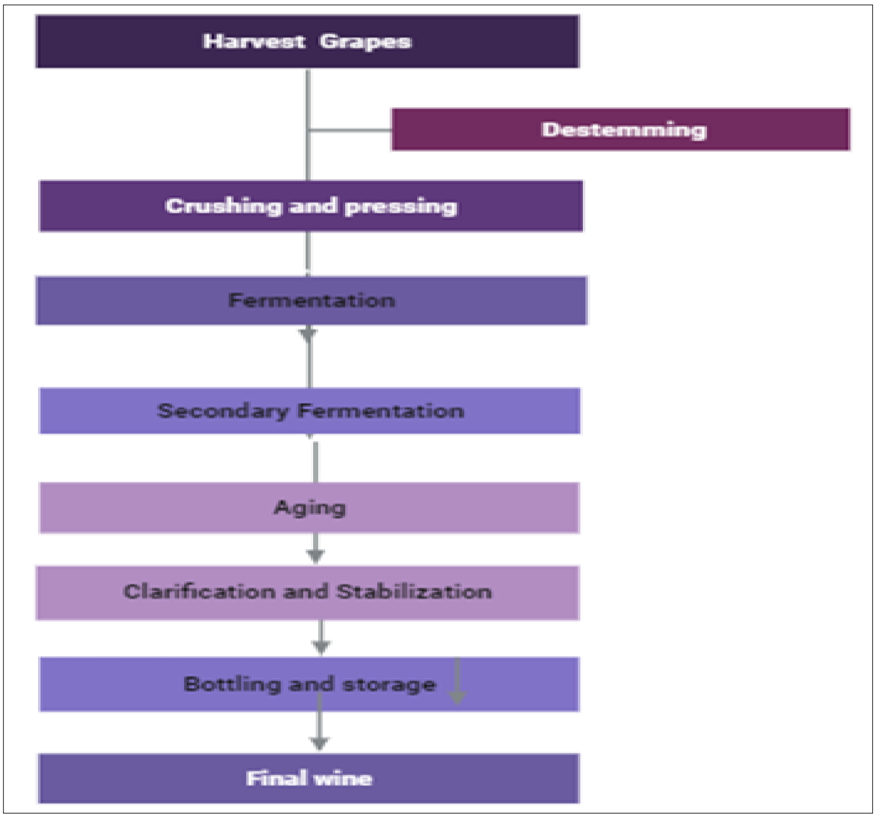

Fig. 2. Oenological procedure.

Terroir the synergy of soil, climate and topography directly shapes grape biochemistry and wine composition. For example, analyses of Burgundy's limestone-rich soils demonstrate how they enhance tartaric acid retention in Chardonnay grapes, improving acidity and aging potential (17). Similarly, studies of high-altitude vineyards in Mendoza, Argentina, reveal that intense UV exposure increases flavonoid synthesis in Malbec grapes by up to 40 %, elevating antioxidant levels (18). Comparative research across wine regions underscores how these geoclimatic factors ensure that identical grape cultivars develop unique bioactive profiles depending on their growing environment (19).

CRISPR engineering

CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) technology has revolutionized microbial engineering, offering precise genetic tools to optimize yeast strains used in winemaking. By targeting genes in *Saccharomyces cerevisiae* and non-*Saccharomyces* species, CRISPR enables enhancements in stress resilience (e.g., heat, oxidation) and bioactive compound retention, though challenges remain. Research demonstrates that CRISPR-Cas9-driven overexpression of heat shock proteins *HSP26* and *HSP104* in *S. cerevisiae* improves yeast survival at 42 °C, stabilizing phenolic compound production during fermentation (24). Similarly, studies show that disabling the oxidative stress-related *TIR1* gene in *S. cerevisiae* boosts glutathione synthesis by 30 %, enhancing oxidative stability in wines (25). CRISPR has also been used to delete the *SSU1* sulphite efflux pump gene in commercial strains, a modification shown to increase intracellular sulphite retention, reducing reliance on added preservatives like SO_2 (26). Despite its potential, CRISPR applications face hurdles. For example, unintended off-target edits may disrupt metabolic pathways critical to flavour or bioactive profiles, necessitating rigorous screening protocols (27). Regulatory barriers further complicate adoption, as CRISPR-engineered strains require extensive approval processes in many regions, slowing commercial use (28). While CRISPR shows promise for optimizing yeast resilience and bioactive preservation, studies emphasize the need for large -scale trials to assess long-term impacts on wine composition. Balancing genetic precision with compositional integrity remains a key priority for advancing sustainable winemaking practices.

Modern innovations

Modern winemaking relies on precision technologies to balance tradition with innovation. Research shows that temperature-controlled stainless-steel tanks (maintained at 12-30 °C) optimize yeast activity and preserve delicate aromas during fermentation (29). Enzymatic treatments further enhance efficiency: studies demonstrate that pectinases increase juice yields by 15-20 %, while β-glucosidases improve anthocyanin extraction in red wines, intensifying colour and antioxidant content (30). Automation tools like IoT sensors and AI-driven fermentation monitors now play a critical role, with recent trials reporting 95 % accuracy in predicting microbial shifts to minimize batch inconsistencies (31). For example, optical sensors deployed in Bordeaux vineyards track tannin polymerization in real time, enabling data-driven adjustments to maceration periods (32).

Beyond fermentation, the industry is addressing its environmental footprint. Winemaking generates 20-30 % by-product waste (e.g., pomace, stems), but analyses show that grape pomace rich in proanthocyanidins (up to 55 mg/g dry weight) can be processed into antioxidant-rich flour for functional foods (33). Innovative startups like WTRMLN WTR® use reverse osmosis to recover polyphenols from wastewater, achieving 85 % resveratrol retention while reducing waste (34). These efforts align with the EU's Circular Economy Action Plan, which aims to cut agro-industrial waste by 50 % by 2030 through sustainable repurposing strategies (35).

Processing parameters

Research demonstrates that maceration temperatures of 25-30 °C boost anthocyanin extraction in red wines by 30 %, but this thermal efficiency comes at a cost: accelerated resveratrol degradation (36). Conversely, studies highlight that low pH environments (<3.5) stabilize polyphenols while suppressing *Saccharomyces cerevisiae* activity, requiring specialized pH-tolerant yeast strains to maintain fermentation efficiency. Controlled micro-oxygenation (5-10 mg/L/month), as shown in trials with Cabernet Sauvignon (37), softens tannins but poses risks overexposure oxidizes 60 % of quercetin within six months. Similarly, analyses of aged wines reveal that dissolved oxygen levels exceeding 15 mg/L reduce cardioprotective procyanidins by 25 % during aging (38). To counter oxidation, nitrogen-sparging (oxygen-free bottling) preserves 90 % of catechins in white wines, though recent findings caution that this method can trigger reductive off-aromas like hydrogen sulphide's "rotten egg" scent (39). Table 2 represents the various chemical components present in wine.

Chemical composition shifts

Bioactive variability across wine types

Studies indicate that prolonged skin contact (1-4 weeks) in red wines like Pinot Noir elevates resveratrol concentrations of 5-14 mg/L and complex tannins at 2-4 g/L compounds linked to anti-inflammatory benefits (47). In contrast, research notes that minimal skin contact in white wines limits polyphenol content to <1 g/L but preserves hydroxycinnamic acids like caftaric acid, which provide moderate antioxidant activity (48). Short maceration (6-24 hr) creates rosés with intermediate phenolic levels (1-2 g/L). For example, analyses of Syrah rosés reveal higher quercetin concentrations (8 mg/L), a trait attributed to thicker grape skins (49). Research on Rioja reds demonstrates that oak barrel aging introduces vanillin and ellagitannins, boosting antioxidant capacity by 20 % (50). However, analyses of stainless-steel-fermented Sauvignon Blancs show these wines retain 50 % more thiols like 3-mercaptohexanol enhancing tropical fruit aromas but sacrificing phenolic complexity (51).

Preservation techniques and their implications

Traditional methods

Research shows that sulphur dioxide (SO_2) has been central to wine preservation since the early 20th century, inhibiting microbial growth and oxidative spoilage by disrupting microbial enzymes and cell membranes (52). Studies indicate that sulphite concentrations of 50-150 mg/L reduce *Brettanomyces* contamination by 99 % and prevent browning through quinone inhibition (53). However, analyses reveal that residual sulphites (≥10 mg/L) degrade heat-sensitive polyphenols like anthocyanins by 15-20 % over 12 months and trigger allergic reactions in 1-3 % of asthmatics (54). Regulatory frameworks like the EU's labelling mandate for wines exceeding 10 mg/L SO_2, alongside organic certifications (e.g., USDA) capping sulphites at 100 mg/L, drive demand for alternative preservatives (55). Historical and modern studies demonstrate that oak barrel ageing enhances wine stability through slow micro-oxygenation (1-5 mg O_2/L/year), which softens tannins and stabilizes colour by promoting acetaldehyde-mediated polymerisation of anthocyanins and tannins (56). Research on charred barrels highlights their release of lignin-derived antioxidants like vanillin (up to 4 mg/L), contributing to flavour complexity (57). However, barrels contaminated with *Brettanomyces* introduce ethylphenols (4-EP/4-EG), which impart "barnyard" aromas and reduce resveratrol content by 30 % (58). While modern cooperages employ steam treatments to minimize microbial risks, studies note that chemical leaching of compounds like oak lactones remains a challenge for producers prioritizing purity (59).

Emerging technologies

Studies demonstrate that cross flow microfiltration using membranes with 0.1-0.45 µm pores effectively removes spoilage microbes like *Acetobacter* while retaining 95 % of polyphenols, a significant improvement over traditional diatomaceous earth filtration, which strips 20 % of catechins. Premium wineries now employ tangential flow systems, which achieve sterile stabilization without heat, preserving resveratrol (up to 12 mg/L) and flavonols in delicate varieties like Pinot Noir (60). Recent innovations, such as graphene oxide membranes, selectively target spoilage yeasts, reducing reliance on sulphites while maintaining bioactive integrity (61). A previous study highlights the growing use of inert gases like argon or nitrogen to blanket wine surfaces, displacing oxygen and minimizing oxidation (62). Trials on red wines show argon blanketing preserves sensory qualities (e.g., aroma, colour) in opened bottles for extended periods, offering a chemical-free alternative to traditional preservatives (63). Fig. 3 visualizes the inert gas infusion technique for preserving wine.

Pulsed Electric Fields (PEF): enhancing bioactive retention

Research shows that PEF technology applies short, high-voltage pulses (10-50 kV/cm) to disrupt microbial membranes without heat, extending wine shelf-life by 6-8 months while preserving heat-sensitive compounds (64). Studies on Cabernet Sauvignon demonstrate that PEF pretreatment boosts anthocyanin extraction by 35 % and retains 90 % of quercetin compared to conventional thermovinification, which relies on heat to break down grape skins (65). Despite these benefits, industry adoption

Table 2. Chemical composition of wine

Component	Content (%)	Function in wine	Reference
Water	86	Primary solvent forming wine's liquid matrix; governs viscosity, density and structural mouthfeel.	(40)
Ethanol	12	Provides alcoholic warmth, body and perceived sweetness; acts as preservative and influences aroma volatility.	(41)
Glycerol	4-10	Contributes subtle sweetness, smoothness and oily mouthfeel; enhances palate weight (notably in botrytized wines).	(42)
Organic Acids	5-8	Tartaric, malic and lactic acids drive tartness/freshness; critical for pH balance (3.0-3.8), microbial stability and aging.	(43)
Polyphenols	1-3	Anthocyanins (red colour), tannins (bitterness/astringency) and resveratrol (antioxidant); define structure, aging potential and health benefits.	(44)
Higher Alcohols	Traces	Fusel alcohols (e.g., isoamyl alcohol) add aromatic complexity; low levels enhance fruitiness/ floral notes, excess causes harshness.	(45)
Minerals	Traces	Potassium, calcium, magnesium from soil/grape; influence taste (salinity), clarity (tartrate stability) and act as fermentation cofactors.	(46)

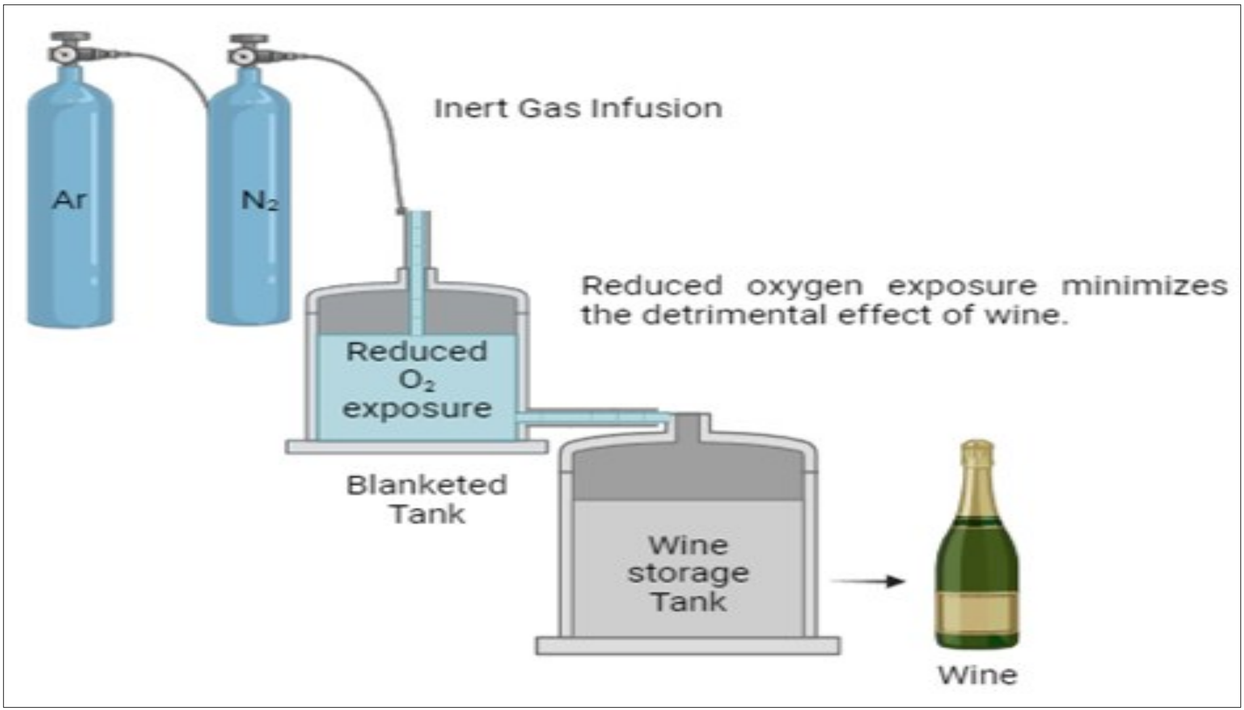

Fig. 3. Inert gas blanketing.

remains limited by high equipment costs. However, pilot projects in Spain highlight PEF's potential to reduce sulphite use by 40 %, offering a cost-effective pathway for sustainable winemaking (66).

Microwave Assisted Extraction (MAE)

MAE uses targeted microwave radiation to rapidly heat solvents and raw materials, accelerating the extraction of bioactive compounds while preserving their integrity. A previous study demonstrates that MAE effectively extracts antioxidants from grape by products, suggesting their potential use as natural preservatives in wine packaging (67). For pectin recovery, previous studies highlight MAE's efficiency in extracting high-quality pectin from grape pomace (68). Their work shows that combining high microwave power with acidic extraction conditions (pH ~1.8) optimizes both pectin yield and functional properties. Similarly, investigations into phenolic compounds reveal MAE's precision in isolating specific bioactive groups including tannins, flavonols and hydroxycinnamic acids from grape pomace (69). These findings underscore MAE's versatility in targeting compounds critical for nutraceutical and industrial applications. The diagram in Fig. 4 details the microwave assisted extraction for polyphenols.

Impact on nutraceuticals

Research demonstrates that while sulphites extend wine shelf-life to 3-5 years, they accelerate hydroxycinnamate oxidation (e.g., caftaric acid) by 25 % within 18 months (70). In contrast, membrane-filtered wines retain 80 % of initial polyphenols after 24 months but depend on refrigerated storage to avoid non-microbial haze. Emerging studies highlight PEF treated wines as a promising alternative, maintaining stable resveratrol levels (8-10 mg/L) for two years comparable to sulphite-preserved wines (71).

Regulatory disparities further complicate preservation strategies. The EU permits up to 200 mg/L SO_2 for sweet wines, while the U.S. FDA caps all wines at 350 mg/L, creating inconsistencies in bioactive retention. Organic wines, limited to ≤100 mg/L sulphites, show 15 % lower quercetin levels but greater microbial diversity, a feature studies link to enhanced

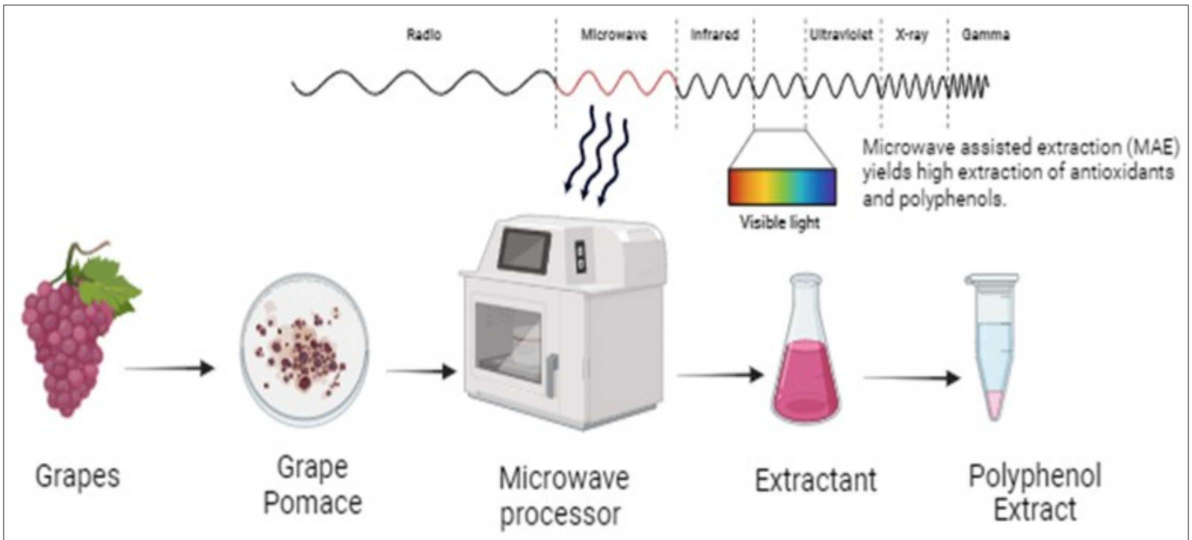

Fig. 4. Microwave assisted extraction.

terroir expression (72). Meanwhile, Japan's stringent "additive-free" certification (<10 mg/L SO_2) has driven innovations like lysozyme-based preservation, which preserves 95 % of anthocyanins but poses allergenicity risks, as noted in clinical trials (73).

Nutraceutical property

Polyphenols, the most studied bioactive compounds in grape wine, include resveratrol, quercetin and proanthocyanidins. Resveratrol, a stilbene predominantly found in grape skins, is concentrated in red wine due to prolonged skin contact during fermentation (3-5 mg/L in red wine vs <0.5 mg/L in white wine) (74). It exhibits antioxidant, anti-inflammatory and epigenetic modulation properties by activating sirtuins (e.g., SIRT1) and nuclear factor erythroid 2-related factor 2 (Nrf2) pathways (75). Quercetin, a flavonoid abundant in wine (2-15 mg/L), scavenges free radicals and inhibits pro-inflammatory enzymes like cyclooxygenase-2 (COX-2) (76). Flavonoids, including anthocyanins and catechins, contribute to wine's colour and bitterness while offering cardiovascular benefits via endothelial nitric oxide synthase (eNOS) activation (77). Tannins, polymeric phenols derived from grape seeds and stems, enhance wine's astringency and demonstrate anti-carcinogenic effects by binding to cellular proteins and inhibiting tumour proliferation. Fig. 5 traces the wine nutraceutical properties.

Health benefits of grape wine

Cardiovascular effects

Studies first identified the "French Paradox" the association between moderate wine intake (1-2 glasses/day) and reduced Cardiovascular Disease (CVD) risk highlighting wine's bioactive compounds as potential mediators (78). Research demonstrates that moderate wine drinkers exhibit 20-30 % lower CVD mortality than abstainers, a benefit linked to polyphenol activity (79). For example, resveratrol enhances endothelial function by boosting nitric oxide bioavailability, improving arterial flexibility, while flavonoids inhibit oxidation of LDL cholesterol, a key driver of atherosclerosis. Mechanistic studies reveal that wine polyphenols neutralize harmful free radicals (ROS) and stimulate the body's natural antioxidants like glutathione (80). Resveratrol further suppresses inflammation by blocking NF-κB, a master regulator of inflammatory cytokines such as TNF-α and IL-6 (81). Emerging evidence also connects resveratrol to reduced amyloid -beta plaque formation in Alzheimer's models, suggesting neuroprotective potential (82). Additionally, moderate wine consumption correlates with improved insulin sensitivity, likely through activation of AMPK, an enzyme central to metabolic regulation.

Controversies and risks

Research confirms that ethanol, a group 1 carcinogen per the WHO, elevates risks for liver, breast and oesophageal cancers, complicating wine's perceived health benefits (83). While some studies suggest a J-shaped curve linking moderate alcohol use to reduced CVD risk, this association remains controversial due to confounding factors like lifestyle differences among wine drinkers (84). Heavy consumption (>3 drinks/day) is unequivocally harmful, exacerbating hypertension, cirrhosis and addiction (85). Dealcoholized wines offer a compromise by retaining polyphenols without ethanol's toxicity. A randomized trial demonstrated that non-alcoholic red wine improves blood pressure and endothelial function as effectively as conventional wine (86). However, ethanol enhances polyphenol absorption and studies note that dealcoholized versions may suffer reduced bioavailability. Consumer acceptance also hinges on overcoming sensory challenges, such as altered tannin perception and flavour imbalances. Wine's polyphenols provide cardiovascular, antioxidant and anti-inflammatory benefits, but ethanol's risks demand cautious interpretation of "moderate" consumption guidelines. Non-alcoholic wines, while safer, require innovations to optimize bioactive retention and absorption efficiency. Future research should prioritize long-term trials comparing alcoholic and non-alcoholic variants, alongside mechanistic studies exploring polyphenol synergies to reconcile wine's cultural legacy with evidence-based health strategies.

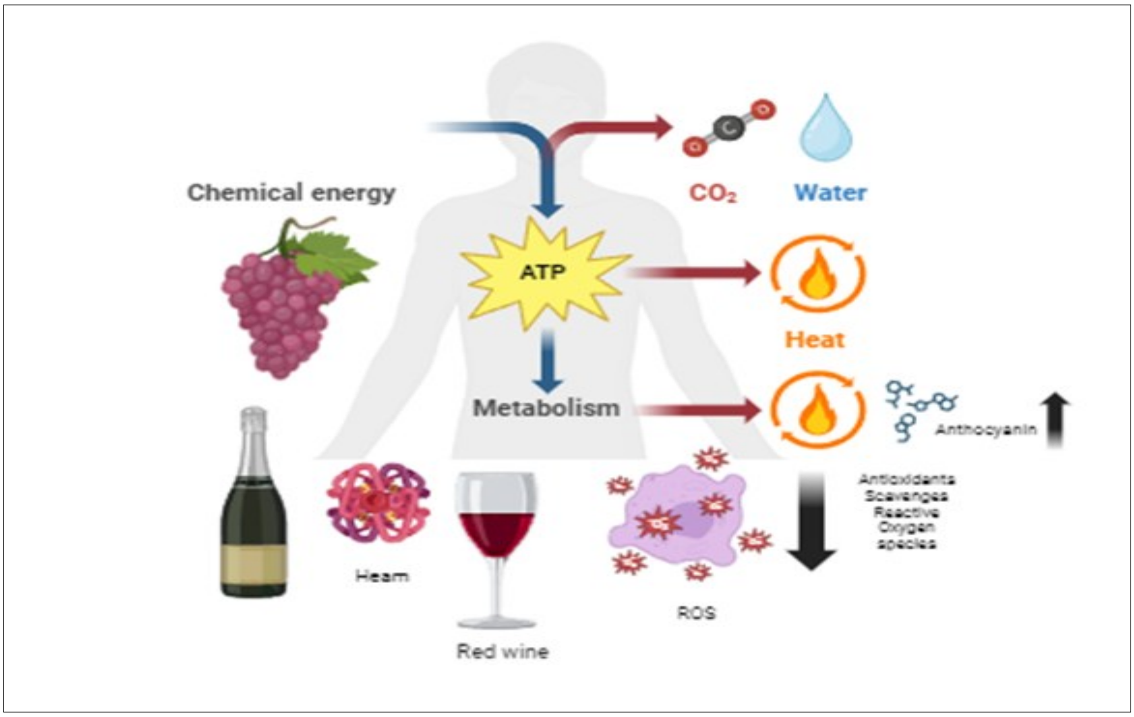

Fig. 5. The generation of Reactive Oxygen Species (ROS) and neutralization by wine antioxidants.

Research gaps

Longitudinal health studies

Research underscores that despite decades of studies linking moderate wine consumption to health benefits, longitudinal evidence remains limited (87). Most findings derive from short-term trials or observational studies prone to biases, such as socioeconomic confounders in the "healthy drinker" effect. For example, while the PREDIMED trial highlighted cardiovascular benefits of Mediterranean diets including wine, its 5-year follow-up was too brief to assess long-term risks like alcohol-related cancers (88). To resolve these ambiguities, experts argue that future studies must employ decade-spanning cohorts to clarify ethanol's dual role: balancing its cardioprotective polyphenols against carcinogenic metabolites like acetaldehyde (89). Research highlights that winemaking generates 20-30 % organic waste (e.g., grape pomace, seeds), yet less than 10 % is repurposed (90). Despite their underutilization, these by-products are rich in fibre, phenolic acids and oligosaccharides with prebiotic potential. However, scalability remains a barrier. For instance, studies note that extracting resveratrol from pomace requires costly enzymatic hydrolysis, limiting industrial adoption. Addressing these challenges demands collaboration between food scientists and engineers to develop cost-effective, eco-friendly methods for transforming waste into functional ingredients.

Personalized nutrition

The "one-size-fits-all" approach to wine's health effects fails to account for genetic and microbiome diversity. Research shows that genetic variations in the *ALDH2* enzyme, which breaks down acetaldehyde (a toxic ethanol metabolite), elevate cancer risks in East Asian populations with specific polymorphisms (91). Similarly, studies highlight that gut microbiota composition particularly the abundance of *Faecalibacterium prausnitzii*, a beneficial gut bacteria affects how well polyphenols like quercetin are absorbed, with significant variation between individuals (92). To address these disparities, experts advocate for precision nutrition models that integrate genomic and metabolomic data to personalize wine consumption guidelines.

Interdisciplinary challenges

Balancing innovation with tradition

Modern technologies like AI-driven fermentation clash with terroir-centric traditions. For example, machine learning algorithms can predict optimal yeast strains for flavour profiles, yet purists argue this undermines regional authenticity. Similarly, nano-preservation techniques extend shelf life but may alter sensory attributes prized by sommeliers. Stakeholder dialogues bridging enologists, technologists and cultural historians are critical to harmonizing progress with heritage.

Regulatory hurdles

Studies highlight that global disparities in wine regulations hinder technological advancement (93). For example, the EU prohibits health claims on alcohol labels, while the US permits qualified statements like "heart health" under TTB guidelines-a policy divide that stifles standardized messaging. Similarly, nano-enhanced wines face stricter scrutiny in the EU, where the EFSA mandates rigorous nanoparticle toxicity assessments, delaying market entry. To address these challenges, experts advocate for harmonized international standards through bodies like the OIV, which could accelerate the safe, transparent adoption of innovations without compromising safety. Regulatory disparities (e.g., EU vs. US sulphite limits) challenge scalable adoption of bioactive-preserving technologies. Harmonization via bodies like OIV is critical to validate our hypothesis that precision enology requires global standards.

Emerging trends

AI in fermentation

Artificial intelligence revolutionizes winemaking through predictive modelling. Neural networks analyse real-time fermentation data (pH, temperature) to adjust yeast activity, reducing spoilage risks (94). Startups like Tastry employ AI to design wines matching consumer flavour preferences, though critics warn of homogenizing regional diversity (95). Future applications may include blockchain-integrated AI for traceability, ensuring ethical sourcing.

Nano-preservation

Research demonstrates that nanotechnology enhances wine stability and bioactivity, particularly through silica nanoparticles that protect resveratrol from oxidation while boosting bioavailability by 40 % (96). However, studies reveal significant public skepticism, with 60 % of EU consumers rejecting nano-labelled wines due to safety concerns (97). To address this "nano -divide" the gap between technological innovation and public trust experts emphasize that transparent communication and rigorous toxicology studies are critical for fostering acceptance and ensuring safe adoption.

Terroir genomics

Advances in genomics are unravelling how terroir the interplay of soil and climate shapes grape biochemistry. For instance, CRISPR-Cas9 editing of *Vitis vinifera* genes, such as *UFGT* (critical for anthocyanin biosynthesis), enables the cultivation of drought-resistant, polyphenol-rich grape variants, as demonstrated in recent agronomic trials (98). Concurrently, metagenomic studies link microbial diversity in vineyard ecosystems to wine complexity, revealing how soil microbiomes influence flavour and bioactive compound profiles (99). Together, these tools empower winemakers to combat climate change while preserving wine's nutritional value. Transitioning from traditional winemaking to a wellbeing-focused industry requires addressing critical gaps: the lack of longitudinal health studies, underdeveloped waste valorisation methods and personalized nutrition frameworks. Emerging technologies like AI and terroir genomics offer transformative potential but demand stakeholder collaboration to balance innovation with cultural heritage. Future research must prioritize interdisciplinary approaches integrating ecology, nutrition and ethics to ensure wine's evolution aligns with global sustainability and public health goals.

Future prospective

The future of wine lies in merging tradition with cutting-edge science. Precision fermentation, AI-guided processing and microbiome engineering will sculpt bioactive profiles for enhanced sensory and health outcomes, while advanced preservation reduces sulphite dependence. Climate-adaptive techniques and targeted viticulture will safeguard bioactive potential in evolving conditions. Sustainable valorisation of byproducts and nutrigenomics will enable personalized functional applications beyond wine itself. Ultimately, rigorous clinical validation must transform wine's ancient health allure into evidence-based science.

Conclusion

This review underscores the critical interdependence of winemaking practices, preservation methods and health outcomes. While innovations like low-alcohol and natural wines address consumer trends, they often compromise bioactive retention or safety, highlighting a gap between marketability and validated health benefits. Techniques enhancing nutraceuticals exist, but trade-offs require rigorous assessment. Moving forward, transdisciplinary collaboration-integrating enology, nutrition, health sciences and policy is essential. Only through such partnerships can the industry harmonize tradition, sensory quality and nutraceutical integrity, evolving wine into a credible contributor to holistic wellbeing.

Acknowledgements

The first author extend her heartfelt gratitude to Dr. I Subbiah for suggesting this review topic and providing the outline.

Authors' contributions

All authors contributed to study conception and design. The first draft of the manuscript was written by DP. IM supervised the study. SS, MB, MR, VJand AR reviewedthe manuscript with valuable inputs. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest: The authors declare no conflict of interest.

Ethical issues: None

AI Declaration: Grammarly was employed while preparing the manuscript for grammar verification. All suggested changes were reviewed and approved by the author(s) and the scientific content, analysis and conclusions were developed independently.

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Peer review: Publisher thanks Sectional Editor and the other anonymous reviewers for their contribution to the peer review of this work.

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