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Contaminants in *Vitis vinifera* L. products: levels and potential risks for human health

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Abstract. Vitis vinifera L. derivatives are susceptible to contamination by biological agents (e.g., bacteria, viruses, fungi), and chemical agents (e.g., heavy metals, persistent organic pollutants). Given the widespread consumption of fresh grape and wine, environmental monitoring is crucial to ensure public health and consumer safety. This study aimed to systematically review the scientific literature on contaminants present in Vitis vinifera L. products, particularly wine, with a specific focus on emerging risks. Of the approximately 4000 articles retrieved from the literature, 152 were found to be relevant. Results showed a balanced focus on both chemical and biological contaminants. Among chemical contaminants, metals were the most extensively studied. Although many of the reported concentrations complied with existing regulatory limits, uncertainties remain for emerging contaminants like nickel, palladium, and platinum for which legal limits have not been established. Additionally, for emerging metals like palladium, rhodium, and platinum, there is a lack of toxicological data and regulatory frameworks. Regarding biological contamination, mycotoxins emerged as the most significant issue. Additional emerging contaminants were identified, including fumonisin, a mycotoxin of increasing relevance in Vitis vinifera L. products. The results show the importance of continuous monitoring and risk assessment of contaminants in wine and grape-based products to protect public health.

1. Introduction

Vitis vinifera L. cultivation is widespread globally [1]. However, according to the OIV's latest statistical report on the state of viticulture (2024), the global area, estimated at 7.1 million hectares in 2024, showed a 0.6 percent decline in 2023 [2]. In recent years, the viticulture sector has faced significant challenges, such as climate extremes and increased disease pressure. Adverse weather conditions, such as heat waves, heavy rains, or prolonged droughts, not only compromise the quality and yield of grape production but also lead to an increased dependence on agrochemicals to control plant diseases [2]. Beyond climatic and economic challenges, growing health and safety concerns have emerged regarding alcoholic beverages. Indeed, during winemaking certain chemical reactions can lead to the formation of potentially harmful compounds. For example, ethyl carbamate, a byproduct of Saccharomyces cerevisiae metabolism, and biogenic amines, produced by specific lactic acid bacteria, are of increasing concern because of their potential toxic effects [3]. Despite efforts to control contaminant formation in the Vitis vinifera L. products, especially through careful

monitoring during the production process, understanding of the toxicological impact, dose-response relationships and actual levels of some contaminants is still limited. This highlights the urgent need for an in-depth review to support more effective risk mitigation strategies. In the context of viticulture, grape-derived products (e.g., grapes, juice, wine) are also vulnerable to contamination from both biological and chemical sources. These contaminants originate primarily from two main pathways. The first is natural, linked to mineral content of the soil and the microbial environment [4]. For instance, metals are absorbed by grapevines through their root systems and contribute to the ionic profile of wine. The second is anthropogenic, stemming from human activities during both viticulture and winemaking [4]. This includes the use of fertilizers, pesticides, equipment, piping, fining agents, and additives. In addition, environmental pollution from industrial activities and traffic emissions also plays a role. These substances can be transferred into the final product, wine, juice, or grapes, potentially posing health risks to consumers [5]. To address these risks, wine producers and regulatory authorities implement rigorous quality control measures and analytical monitoring protocols. For

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example, the International Organisation of Vine and Wine (OIV) has established maximum allowable limits for some contaminants to protect the consumers [6]. However, in recent years, there has been increasing attention on emerging contaminants, a wide category including metals, pesticides, pharmaceutical residues, and environmental pollutants. These contaminants, even if not extensively studied in the context of winemaking, represent potential risks to both the health of consumers and the integrity of the wine production process. Given their global cultural and economic significance [2], grape derivatives must be carefully controlled. Understanding the source, origin, and health impacts of both metallic and non-metallic contaminants is critical. Investigating their toxicity and potential health implications provides the basis for better risk management and production practices. The primary objective of this paper is to provide a preliminary overview of contaminants potentially found in grape-derived products, particularly wine, that may raise food safety concerns. Specific attention is given to emerging contaminants, such as nickel, platinum, palladium, rhodium, and fumonisin B2, which are not yet subject to regulation but are increasingly detected in the food chain.

2. Materials and methods

The two most important scientific databases of references and abstracts on life sciences (PubMed, Embase) were systematically searched (from database inception to September 2024) using the terms "wine" or "grape" or "grape juice" and "grape-based alcoholic beverages" in combination with "contaminant" or "contamination" or "contaminants" or "environmental contaminant" or "biological contaminants" or "heavy metals" and "mycotoxins" Subsequently, the focus shifted towards scientific data relevant to the assessment of metal residues (e.g., zinc, aluminum, vanadium, tin, mercury, copper, arsenic, lead, palladium, platinum, rhodium, nickel, fumonisin B2, patulin) in wine and grape derivatives. Finally, attention was focused on collecting toxicological data specifically related to nickel, palladium, platinum, rhodium, and fumonisin B₂ in wine and grapes, considering the potential mechanisms affecting human health. The research has been systematically conducted using terms like "contaminants in wine" or "contaminants in grapes" or "heavy metals in wine" or "heavy metals in grapes", along with specific metal names, and terms referring to their biological or toxicological mechanisms and effects. During the article selection process, specific inclusion and exclusion criteria were applied. Articles comparing vineyards subjected to different treatments were excluded. Similarly, studies addressing products unrelated to grapes (e.g., other fruits or general alcoholic beverages) or their derivatives were omitted. Studies focused only on contaminants in biological fluids or those discussing decontamination methods were also excluded. Furthermore, papers that did not provide a specific analysis of grape or grape-derived product contamination were excluded, as detailed analytical data were considered essential to ensure the accuracy of the review. Studies that

did not clearly distinguish between grapes, grape juice, and wine were also not included in the final selection.

3. Results and Discussion

3.1. Contaminants in Vitis vinifera L. products

The literature search on contaminants in *Vitis vinifera* L. products initially resulted in a total of 3414 articles, which were reduced to 2538 after removing duplicates. Following a preliminary screening based on titles and abstracts, 419 articles were identified as potentially relevant for the analysis of chemical and biological contaminants in grape and derivatives. After a thorough full-text review, 152 articles were found to fully meet the eligibility criteria established in the systematic review protocol, as illustrated in **Figure 1**.

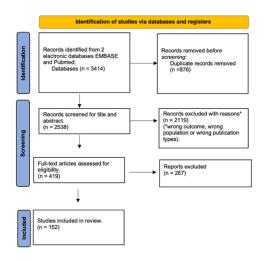


Figure 1. Systematic review selection process

In the comprehensive analysis of the 152 articles included in this systematic review, both chemical and biological contaminants were investigated with equal frequency. Specifically, 76 studies focused on chemical contamination, while the remaining 76 addressed biological contaminants, indicating a balanced interest across the two items by scientific research. With regard to chemical contamination, 20% of the total articles (31 out of 152) focused on the detection and quantification of heavy metals, with particular attention to lead, arsenic, and copper, elements often associated with environmental pollution and potential health risks. Other metals identified, with less frequency, included cadmium, manganese, vanadium, and aluminium. Additionally, 18% of the publications (27 articles out of 152) examined the presence of pesticide residues, mainly resulting from agricultural practices. Notably, 44% of these pesticiderelated studies specifically investigated fungicides, reflecting their widespread use in viticulture to control fungal diseases that affect grapevine health and productivity. The remaining 12% (18 articles out of 152) addressed a variety of other chemical contaminants. These included ethyl carbamates, a fermentation by-product with

phthalates potential toxicity [7]; and polydimethylsiloxanes, which are used in food packaging and processing [8]; as well as fluoride, organophosphate esters (OPEs), perchlorate, and butyltin compounds. These compounds, although different in chemical nature and origin, all raise concerns for their potential toxicity [9,10,11,12]. As for biological contaminants, 46% of the total studies (70 out of 152) focused on mycotoxins, a group of secondary metabolites produced by toxigenic fungi [13], which can contaminate grapes both in the field and during storage. Among these, ochratoxin A (OTA) emerged as the predominant contaminant, being the subject of 83% (58 out of 70) of the mycotoxin-related studies selected. OTA is of particular concern due to its nephrotoxic, immunotoxic, and potentially carcinogenic effects; its frequent detection in wine has made it a priority target for food safety authorities worldwide [14]. Additionally, a smaller number of studies, 4% of the total (6 out of 152), investigated the presence of biogenic amines, such as histamine and tyramine. These compounds are formed through microbial decarboxylation processes during fermentation and can cause adverse reactions in sensitive individuals, including nausea and tremors [15]. Overall, the findings from these 152 papers offer a vision of the types and frequency of contaminants found in Vitis vinifera L. products.

3.2. Chemical contaminants

From the systematic review of 152 studies, 76 articles specifically addressed the presence of chemical contaminants in grape-derived products, primarily wine. **Figure 2A** shows the frequency of bibliographic citations related to the different chemical contaminants with respect to the total, i.e. the 76 selected articles.

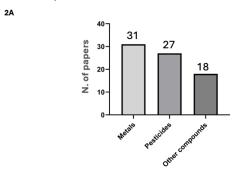


Figure 2A. Distribution of papers reporting data on chemical contaminants in *Vitis vinifera* L. derivatives. Total papers = 76

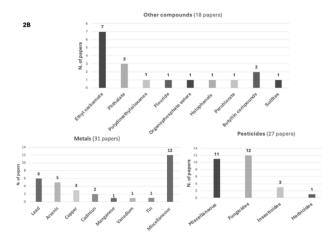


Figure 2B. Distribution of papers among the three main groups of chemical contaminants

Figure 2B shows the distribution of papers among the three main groups of contaminants. The most frequently cited metals were lead (19%), arsenic (16%), and copper (10%). Other metals (cadmium, manganese, vanadium, and tin) were considered in a smaller percentage of studies (from 3% to 6%). Notably, 38% of the studies considered several elements simultaneously. Among pesticides (27 articles out of 76), fungicides were the most frequently cited, appearing in 44% (12 out of 27) of the papers, followed by general pesticide residues in 41% (11 out of 27), insecticides in 11%, and herbicides in only 4%. Lastly, various chemical compounds, accounted for 24% (18 out of 76) of the chemical contaminants. Ethyl carbamate was the most reported within this group, being considered in 39% (7 out of 18) of the related studies. Phthalates were also relevant, appearing in 17% (3 out of 18) of the papers, while other substances such as polydimethylsiloxanes, fluoride, organophosphate esters, halophenols and haloanisoles, perchlorate, butyltin compounds, and sulphites were reported in 6% to 11% of the studies

3.2.1 Metals

Given the safety relevance of metals in food quality, **Figure 3** summarizes the concentration ranges reported in the studies included in this review.

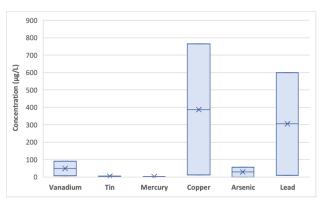


Figure 3. Box plot of metals concentrations reported in the selected literature. Since individual values are not available, the mean is shown instead of the median.

A significant number of the reviewed studies reported the presence of metals, with particular attention given to lead, arsenic, copper, tin, mercury, zinc, and vanadium. For example, lead was detected in most Hungarian wine samples. Specifically, 94.12% of the wines contained lead concentrations below 400 µg/L, 2.67% fell within the 400-600 μg/L range, and 3.21% (corresponding to 18 samples) exceeded 600 µg/L [16]. Lower concentrations (9.2-170 µg/L) were described by other authors [17, 18, 19]. These variations may reflect differences in regional soil composition, vineyard practices, and winemaking techniques. Vanadium concentrations ranged from 7.0 to 90.0 µg/L in red wines and 6.6 to 43.9 µg/L in white wines [20]. The metal source is probably linked to environmental contamination, as vanadium is an important component of various industrial activities. Due to its widespread use in metallurgy, fossil fuel combustion, and chemical manufacturing, significant amounts of vanadium are released into the environment, particularly into the soil, from where it can be taken up by grapevines and accumulate in grape and wine products [21]. Average concentrations of tin and mercury were also quantified in 122 red wines from different countries around the world, $(4.4 \pm 7.2 \mu g/L)$ and $0.22 \pm 0.12 \mu g/L$, respectively) [22]. It should be noted, however, that, based on current levels, moderate wine consumption should not pose a significant health risk to humans [22]. Copper levels were reported to range from 11 to 695 µg/L in red wines and from 121 to 765 μ g/L in white wines [23]. While these concentrations generally fall within legal limits, their variation may be influenced by factors such as fungicide use, soil characteristics, and winemaking processes. Similarly, arsenic levels in wine showed considerable variability depending on the geographical origin and the chemical composition of the soil. Reported concentrations range from 0.1 to 56 µg/L in red wines [24], 0.46 to 21 μg/L in both red and white wines [25]; other authors report values between 2.1 to 14.6 µg/L in other studies [26]. Although these values are typically below the established international safety thresholds, the presence of arsenic, even at low levels, raises concerns about long-term exposure for potential health risks [24,25,26]. Zinc concentrations in wine shows considerable variability depending on geographical origin, viticultural practices, and enological processes. Reported levels range from as low as 24-130 µg/L in Argentine samples to a maximum of 5500 µg/L in Greek wines, with the majority of values remaining below the widely accepted regulatory threshold of 5000 µg/L [27-51]. Elevated zinc concentrations are frequently associated with zinc-containing containers and agrochemicals, used during grape cultivation and wine processing [27,39]. It is important to emphasize that the transfer of heavy metals from grapes to wine depends on factors, including initial concentrations, agricultural practices, and winemaking processes. For instance, the study by Dumitriu et al., (2019) monitored the levels of metals such as cadmium and zinc in samples collected at key stages of the winemaking process [52]. The results showed a significant decrease in zinc concentration during crushing and fermentation, due to precipitation as insoluble tartrates and the removal of metal complexes through filtration. Cadmium, on the other

hand, was detected only during the destemming phase at very low concentrations and fell below the limit of quantification in the subsequent stages [52].

One of the more pressing issues identified in this review is the detection of emerging metals, such as platinum, palladium, and rhodium, which were identified as potential contaminants due to their presence in other foods and increasing environmental pollution [53, 54]. The increased environmental pollution associated with to the widespread use of these metals in catalytic converters and medical applications raised concerns regarding their potential risks. While the risk for human health and the environment remains a matter of debate, existing literature strongly suggests that the diet is a significant source of these metals [54]. This underlines the importance of focusing on these emerging chemical contaminants, which, although less frequently studied, may be of increasing toxicological interest.

Nickel

Nickel, an element of group VIIIb with atomic number 28, is commonly found in environmental sources like water, soil, air, and biological organisms, with its +2oxidation state (Ni²⁺) being most prevalent [55,56]. Although not essential for humans, nickel is required by certain organisms, but it could cause adverse health effects in humans, including dermatitis, cardiovascular issues, and respiratory tract cancer [57]. Exposure occurs mainly through inhalation in the workplace or oral ingestion from food and water, with nickel-induced neurotoxicity linked to oxidative stress [58,59]. Nickel allergy shows clinical patterns such as allergic contact dermatitis or systemic nickel allergy syndrome (SNAS), with symptoms ranging from gastrointestinal disturbances to headaches and fatigue [60]. Nickel presence measured in various studies shows different levels of contamination across regions. For instance, several studies reported nickel concentrations in wines from Romania, Ukraine, Turkey, Jordan and Argentina, ranging from 0.001 mg/L to 0.3 mg/L [61-63, 29, 39]. Higher concentrations in grapes and apples were observed in Alexandria and Giza (Egypt), raising concerns over pollution from industrial activities [64,65]. In addition to grapes, nickel contamination was observed in other fruits like apples, oranges and bananas [64,66,67]. It was interesting to note that some studies in the selected literature, have highlighted the potential protective effects of red grape polyphenols against nickel-induced clinical adverse effects, particularly allergic contact dermatitis [68,69]. These findings underline the variability in nickel contamination levels across different regions and fruits according to the proximity to polluted areas and storage conditions. The increase in post-implantation loss observed in a study performed in rat was identified as the most severe effect on which to base the risk characterization of Ni chronic oral exposure. Based on a BMDL10 (Benchmark Dose Lower Limit 10%) of 1.3 mg Ni/kg bw per day, EFSA established a tolerable daily intake (TDI) of 13 µg/kg bw [70].

• Platinum, Palladium and rhodium

Platinum, palladium, and rhodium, three rare metals increasingly used in industrial applications, have emerged as potential contaminants of concern in Vitis vinifera L. products due to growing environmental pollution. Platinum, widely used in the glass industry, catalytic converters, and medical devices [71], has been detected at low concentrations (<10 µg/L) in wines from France [72]. Its environmental presence varies with traffic density and industrial activity. Although current evidence suggests low health risks, some studies have linked platinum exposure to asthma, allergies, and other immunological effects Palladium and rhodium share environmental origins, particularly from motor vehicle emissions, industrial activities, and even jewellery production [71]. These metals can enter the grapevine ecosystem primarily through atmospheric deposition, potentially accumulating in grapes and wine. While, to date, few studies have quantified palladium and rhodium concentrations in Vitis vinifera L. products, their known associations with eye, nose, and throat irritations and respiratory issues underscore the importance of evaluating their occurrence and toxicological impact [75]. Therefore, considering the increasing air pollution and the lack of standardized monitoring for these elements, future research should give priority to their detection and risk assessment due to their presence in wine, especially in regions with high environmental contamination [76].

3.2.2 Pesticides

Pesticide residues in wine are relatively welldocumented and extensively controlled due to the established maximum residue limits (MRLs) for many pesticides. As a consequence, consumer health is suitable safeguarded. Data on level of some pesticides in wines were reported for pyrimethanil, chlorpyrifos and imidaclopril [77, 78, 79]. Additionally, sulfonylurea herbicides were detected in grapes, with levels below EU limits, prompting further questions about their origin and potential implications for consumer health [80]. In general, the transfer of pesticide residues from grapes to wine is influenced by the initial concentration present in the grapes, as well as the winemaking techniques applied. Pesticide transfer from grapes into wine during winemaking are linked to the logarithmic octanol-water coefficients of the substances under specific processing conditions [81]. According to the literature, the proportion of pesticide that migrate from grapes to wine can vary widely, ranging from 8.8% to 66% [82]. However, several processing techniques have been documented to significantly reduce these residue levels [81]. To support effective monitoring and ensure consumer safety, the OIV has established guidelines and official analytical methods for the detection and control of pesticide residues [6].

3.2.3 Other contaminants

Several other contaminants have been detected in wine, underlining the need for continuous monitoring. Data have been published for dibutyltin (DBT) and

monobutyltin (MBT) [12], and perchlorate [11]. Phthalates, which are widespread contaminants, were frequently detected in wines, with dibutyl phthalate (DBP), diethylhexyl phthalate (DEHP), and butyl benzyl phthalate (BBP) being the most common compounds. Specifically, in a study by Chatonnet and colleagues (2014), 40% of the wine samples considered contained BBP, with an average concentration of 0.026 mg/kg. Furthermore, 59% of the wines showed notable levels of DBP, with a median concentration of 0.0587 mg/kg [83]. Another type of contaminants, Organophosphate esters (OPEs), were found in wine at concentrations ranging from 0.29 to 3.05 µg/L [10]. Fluoride have been suggested as possible health concerns, when samples exceeding 1 ppm (the international limit) were identified [9]. Additionally, the presence of ethyl carbamate in various wines, grape juices and alcoholic beverages highlights the need for ongoing research to assess potential health risks associated with this contaminant [7, 84-87]. To support regulatory compliance, the OIV has established limits for some of these substances, providing reliable tools for monitoring and quantify these contaminants in wine [6].

3.3. Biological contaminants

From the systematic review of 152 studies, 76 papers specifically focused on the occurrence of biological contaminants in grape-derived products (mainly wine). **Figure 4** shows the frequency of citation of the most important biological contaminants.

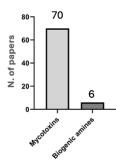


Figure 4. Distribution of papers reporting data on biological contaminants in *Vitis vinifera* L. derivatives. Total papers = 76

Among the 76 papers selected, a significant majority, accounting for 92%, were related to mycotoxins. Within this category, OTA was the most frequently reported contaminant, with 58 papers out of 70 (83%). Other types of mycotoxins (aflatoxins, patulin and fumonisin B) were considered in much smaller proportions. Biogenic amines have been less described, with only six papers selected (8%).

3.3.1 Mycotoxins

Due to their impact on food, mycotoxins have been widely investigated. **Figure 5** provides an overview of the concentration ranges reported in the literature included in this review.

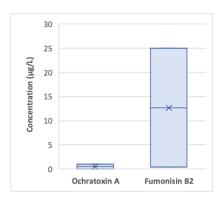


Figure 5. Box plot of mycotoxin concentration reported in the selected literature. Since individual values are not available, the mean is shown instead of the median.

Among biological contaminants, 46% of the studies focused on mycotoxins, with particular attention to ochratoxin A (OTA), a well-known compound produced mainly by Aspergillus species. OTA is the most extensively studied mycotoxins in wine and grape derivatives; only selected examples will be described here to illustrate its widespread occurrence across different regions and production systems. OTA was detected in most wine samples from Greece in two papers [88, 89]. Analyses of Italian wines showed the presence of OTA in most samples, although often below the legal limit [90, 91]. Wines from Argentina, analyzed with the QuEChERS-SPE method, showed OTA levels between 0.02 and 0.98 µg/L, all below the maximum legal limit of 2.0 µg/L [92]. Although concentrations are generally low, the widespread presence of OTA suggests the need for continuous monitoring in order to verify which production techniques could modulate contamination Accordingly, OIV has established both limits and official analytical methods to control OTA in grape derivatives [6]. Based on the findings from the general analysis of selected papers, some emerging mycotoxins have been identified (Figure 3); in particular, fumonisins, have received recent scientific attention due to their potential toxicological relevance and the increasing frequency of occurrence in grape and wine.

o Fumonisin B2

Aspergillus niger, known for its ability to produce ochratoxin A, is also responsible for the presence of fumonisin B₂ (FB₂) in grapes, as well as in other products like coffee and raisins [93-95]. A study of 51 wines from the Italian market detected the presence of FB₂ at low concentrations (0.4–2.4 µg/L) [93]. Similarly, the analysis of 77 wine samples from 13 countries detected FB₂ in 23% of the samples, with concentrations ranging from 1 to 25 μg/L [96]. These results underline the necessity for continuous monitoring of FB2 contamination in wines to ensure food safety and consumer protection. Safety assessments and exposure limits for the fumonisin group have been considered by EFSA Panel Members, who established a tolerable daily intake (TDI) for fumonisin B₁ (FB₁) of 1.0 μg/kg bw per day based on the increased incidence of megalocytic hepatocytes found in a chronic study performed in mice. Considered the limited data available on toxicity and mode of action together with the

structural similarities of different FBs, toxicological values defined for FB₁ were applied also to FB₂, FB₃ and FB₄ [97].

3.3.2 Biogenic amines

To better understand the occurring concentrations of biogenic amines in *Vitis vinifera* L. products, **Figure 6** illustrates the ranges of main biological amines, as reported by the authors of selected papers.

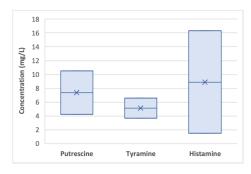


Figure 6. Box plot related to the concentration of biogenic amines reported in the selected literature. Since individual values are not available, the mean is shown instead of the median.

Biogenic amines (BAs) are a common class of naturally occurring wine contaminants, produced by microbial decarboxylase activity during fermentation. A study on red and white wines identified nine different BAs. Differences in concentration of putrescine, histamine, and tyramine were observed in wine, with higher values in red ones [15]. The analysis of commercial Primitivo wines indicated as the most common BAs: histamine (1.49 to 16.34 mg/L), 2-phenylethylamine (at less than 2.12 mg/L), tyramine, cadaverine, putrescine (5.41 to 9.51 mg/L), spermine, and spermidine [98]. In 110 Croatian red wines, histamine and tyramine were present in 88.2% and 82.7% of the samples, respectively [99]. Also, cadaverine and putrescine were identified. According to the literature, lactic acid bacteria are primarily responsible for BA release during winemaking [100]. However, the use of selected yeast strains and non-aminogenic starter cultures showed efficacy in limiting BA accumulation, improving both safety and overall wine quality [100].

4. Conclusions

Papers collected and evaluated in this review show a complex and evolving landscape of contamination in *Vitis vinifera* L. products, particularly in wine. The presence of both chemical and biological contaminants (some well-characterized, others emerging and poorly investigated), underlines the multifactorial origins of foodborne hazards, which include environmental conditions, agricultural inputs, industrial pollution, and oenological practices [52]. In particular, this review indicates the presence of several emerging metals, such as platinum, palladium, and rhodium, for which standardized monitoring protocols and regulatory limits must be defined. Although little studied, these substances may present toxicological risks as they

increasingly enter the food chain. The challenge is further amplified by climate change and environmental pollution, which can not only intensify contamination levels but also unpredictably influence the nature and distribution of these contaminants in grape-derived products [2]. Although the OIV has established analytical standards and thresholds for several common wine contaminants [6], a significant gap persists for newly recognized compounds, raising pressing questions about consumer exposure and longterm health effects. This highlights the urgent need to develop and validate new analytical approaches. Future research should therefore aim to fill these gaps by improving detection techniques and establishing appropriate regulatory frameworks for currently unregulated compounds. Such efforts are essential to ensure the continued improvement of food safety protocols and the protection of public health.

5. Acknowledgement

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