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REVIEW

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Scientific and technological research on the use of wine lees

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Abstract

Background Wine lees are defined as the residue formed at the bottom of the container during the wine fermentation stage. It consists of a solid phase composed of yeasts and bacteria responsible for vinification. In general, wine lees, despite being a material rich in polyphenols, are underused or discarded. In this context, the aim of this review is to present an overview of the use of wine lees in the food industry and other sectors, by means of scientific and technological surveys.

Methodology Bibliographical searches of the main works published on wine lees or grapes were carried out in articles selected in the Scopus and SciELO databases, while the search for the technology protected or described in patent documents involving wine lees and their main applications was carried out through the Espacenet online database combined with the private platform from Questel company: Orbit®.

Main text Wine lees represent an important fraction of winemaking by-products and contain several high-value components with potential to be exploited in industrial sectors, such as phenolic compounds. Through the Technological Prospection, it was demonstrated that wine lees are still poorly studied, with few patents filed on the technological/nutritional properties of wine lees. In 2016, there was a peak of patent filing growth and China was the country with the highest number of patents, totaling 31 deposits. Regarding the area of application, agriculture was the most common, followed by beverage production. Most of the inventors are of Asian origin, corroborating the results previously discussed regarding the distribution of patents per country, and this might probably be related to the high investment of these countries in various stages of education and technological research.

Conclusion The study suggests that different applications should aim at developing an integrated approach aimed at extracting from wine lees the highest number and quantities of compounds with possible applications in different sectors.

Keywords Grape, Lees, Winery by-product, Sustainability, Phenolics, Bioactive compounds

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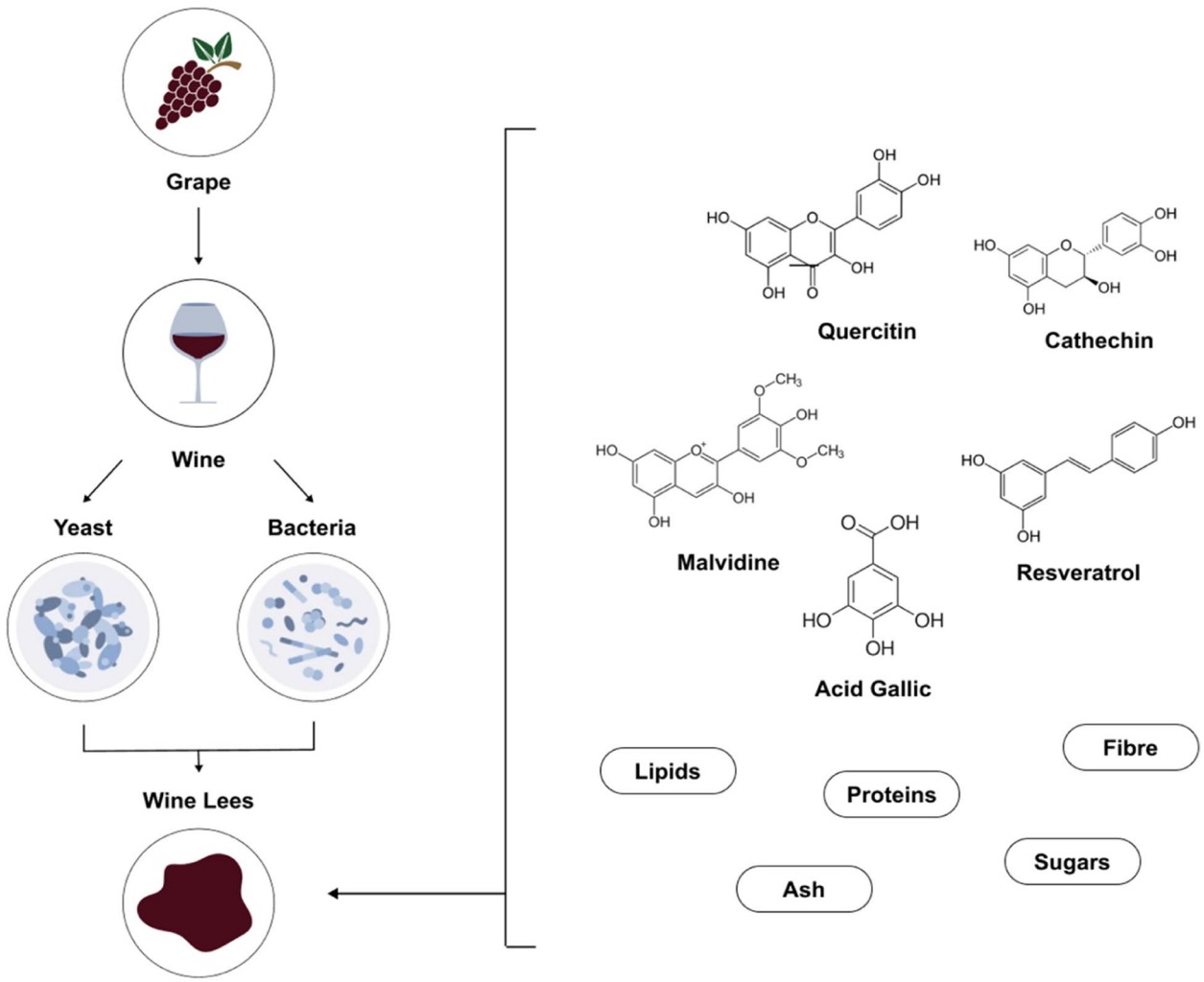
Graphical Abstract



Background

The agro-industrial food sector produces about 95-98 million tons of waste and by-products every year, becoming a target of environmental concern worldwide (Lafka et al. 2007). Among the activities that stand out in this scenario is the viniculture that, during the processing of 1 ton of grapes for wine production, generates around 0.13 tons of grape marc, 0.06 tons of wine lees and 1.65 m^3 of wastewater (Lucarini et al. 2018).

According to the International Organization of Vine and Wine (OIV), during 2021, 260,979 million hl of wine were produced, this figure corresponds to a decrease of 0.6% compared to the previous year. Among the countries that produced wine during this period, the first places in the ranking, respectively, were: Italy, France, Spain and the United States.

Between the by-products formed during winemaking, wine lees are detected in large volume, correspond to 25% (De Iseppi et al. 2020) and, despite being a material rich in dietary fiber and antioxidant compounds, they are little exploited and mostly destined for disposal or activities of low economic value (Teixeira et al. 2014).

By definition, wine lees are the residue generated at the bottom of containers after wine fermentation during storage, authorized treatments, as well as residue obtained by filtration or centrifugation. They consist of a solid phase, which has as main components yeasts and bacteria, responsible for the wine formation process (Palangkaraya et al. 2017).

Organic compounds with high oxygen demand, with values above 30,000 mg/L, are found in the composition of wine lees, which make them a potential environmental pollutant (Jara-Palacios 2019; Lafka et al. 2007). On the other hand, the presence of compounds such as anthocyanins and polyphenols in this residue raise the interest in research and reuse technologies (Delgado De La Torre et al. 2015; Pérez-Serradilla & de Castro 2008). Potential areas of applications, such as: food, cosmetics, chemicals, and pharmaceuticals have been studied in order to promote a sustainable end for wine lees (Teixeira et al. 2014).

In order to encourage innovation, besides being an excellent tool for planning and organizing of resources aimed at research, optimization of time and financial expenses, technological prospection about wine lees can be of great relevance to map the current situation in relation to the development of technologies, in addition to identifying the potential of this market, once detected the lack of publications for this purpose (Palangkaraya et al. 2017).

Finally, the aims of this review were twofold: an overview about wine lees regarding its composition, applications and sustainability; a prospection study using the patents with application of the grape lees.

Methodolgy

Bibliographical searches of the main works published on wine lees or grapes were carried out. The prospection of articles was carried out in the Scopus and SciELO (Scientific Electronic Library Online) databases, the terms applied were: grape AND lees OR wine AND lees. The selected scientific articles that met the criterial of originality, free access in English language, published between the years 2005 and 2021, with the themes of wine lees or wine lees and applications in the areas of production of wine, sparkling wine or other beverages, food, obtaining bioactive compounds, fertilizers, extraction methods, medicinal use, animal feed, were used for writing this review.

The search for the technology protected or described in patent documents involving wine lees and their main applications was carried out through the Espacenet online database where it has a repository of patent applications from more than 90 countries, combined with the private platform from Questel company: Orbit®, due to its comprehensive analysis tools, especially to search the predominant technological domains and clusters of keywords. As an advanced search strategy, the following terms were used: grapes, wine and lees, in addition to the international classification codes A23, A61 and C12. In this way, the documents were selected, composed by the terms in the title and/or in the abstract. For the qualitative analysis it was performed, when available, the reading of the description of the documents of each invention. The data, therefore, were extracted from the Espacenet database and, to illustrate, were organized in the form of tables and charts with the Microsoft Excel 2020 software. The data survey was carried out in the period from May to July 2022. Therefore, the patents discussed in this paper were published 18 months before the database search period. Furthermore, the term "patent document" refers to published and granted patent applications.

Main text

Wine lees: definition and physicochemical characteristics

According to the European Regulation (EEC) no 337/79, wine lees are defined as the residue formed at the bottom of containers containing wine after fermentation, during storage or after treatments, as well as the residue obtained after filtration or centrifugation. Wine lees have the appearance of sludge and are composed of microorganisms, tartaric acid, inorganic matter, and phenolic compounds (Pérez-Bibbins et al. 2015, b).

There are some ways of classifying wine lees, these being: first and second fermentation lees, formed during alcoholic and malolactic fermentations, respectively and aged wine lees, formed during aging in wooden barrels (Gómez et al. 2004). Another way to classify wine lees is by particle size, called heavy lees (between 100 µm and 2 µm, settling within 24 h) and light lees (< 100 µm, between 1 and 24 µm, and in suspension at least 24 h after agitation) (Jara-Palacios 2019).

The lees directly influence the coloring and organoleptic characteristics of the wine since they have direct contact with the phenolic compounds responsible for these parameters (Thangaraj 2015). They are also used for wine aging, specially sparkling and white wines. This traditional technique consists of placing wine on the lees to improve the quality of the wine by reducing astringency and bitterness, improving the structure and stability of the wine's color, in addition to enriching the wine with aromatic compounds (Jara-Palacios 2019).

Wine lees from alcoholic fermentation

Alcoholic fermentation, an essential stage for wine production, is a biochemical process that occurs through yeast that transforms the sugar present in the must (glucose and fructose) into carbon dioxide and ethanol (Schorn-García et al. 2021). As a by-product of this process, from dead or residual yeast cells, alcoholic fermentation wine lees are formed and deposited at the bottom of wine-making vessels (Barcia et al. 2014).

In general, the composition of grape lees is complex, as it depends directly on the species, terroir of grape

cultivation, as well as other biotic and abiotic factors (Pérez-Bibbins et al. 2015, b). Also the variation in the composition of wine lees is also explained by the presence of microorganisms and their autolysis products, as well as organic and inorganic residues (Antón-Díaz et al. 2016).

The analysis of the centesimal composition of lees of wine from alcoholic fermentation aims to identify quantitatively the macromolecules present, using different techniques to evaluate the parameters of protein, lipids, carbohydrates, sugar, fibers, ash and moisture content (Lima et al. 2014). The evaluation of these components is fundamental to obtain a nutritional balance during product development and can also be used for quality control or regulatory purposes (Thangaraj 2015).

Table 1 shows the centesimal composition of wine lees from alcoholic fermentation, described in different studies. In the research, it was evidenced that wine lees from the manufacture of wine from grapes of the *Vitis vinifera* (Tempranillo), have few differences in the quantification of ash and protein, when compared with scientific studies with the same variety. Wine fiber, possibly due to the various factors linked to the cultivation and variety of grape, as mentioned above (Rizzon et al. 1997).

During the pressing of grapes for wine production, in the fermentation stage, lipids from the skins and seeds are transferred to the must and, consequently, promote the exchange of lipids between the wine and the lees (Gómez et al. 2004).

Wine lees from malolactic fermentation

In order to adapt to the conditions of the medium (such as low pH, high alcohol content), during vinification, lactic bacteria become responsible for the transformation of malic acid into dicarboxylic acid, lactic acid and monocarboxylic acid, promoting the then known malolactic fermentation (Balmaseda et al. 2021).

During this process, volatile compounds are formed, which can enrich the aromatic quality of the wine, as well as modify parameters such as color and phenolic profile (Izquierdo-Cañas et al. 2016). The malolactic fermentation is common during the production of red wines, because besides offering biological stability to the wines, it regulates the quality of the vintages of the wineries, reducing the excess acidity in poor quality vintages (Rizzon et al., 1997).

Similarly, to alcoholic fermentation, after malolactic fermentation, lees of great oenological interest are formed at the bottom of the barrels due to their complex composition and ability to improve the organoleptic properties of wines with high acidity and astringency (Moreno-Arribas et al. 2008). Currently, malolactic lees have been used in the wine ageing stage as they promote yeast autolysis, which modifies the wine composition regarding active and volatile compounds, mannoproteins, lipids and enzymes, thus interfering in the improvement of wine quality (Ubeda et al. 2019).

Aging wine lees

The aging wine lees process is a technique that consists in the contact of yeast cells from the lees formed at the bottom of the barrels during the fermentation with the wine (Loira et al. 2013). The cellular autolysis that occurs during this process releases polysaccharides, proteins and peptides, amino acids and lipids from the yeasts to the wine. The release causes positive modification to the wine quality and organoleptic properties (Pérez-Serradilla & de Castro 2008).

Among the benefits of aging wine lees, mannoproteins released by yeast cells present on lees have demonstrated the ability to promote tartaric and protein stabilization. Besides, the lees have also been shown to protect the color of the wine against oxidation, in addition to altering the final balance of the aroma by binding volatile compounds (Liberatore et al. 2010).

Some volatile compounds capable of causing organoleptic defects in wine when present in higher concentration, such as 4-ethylphenol and 4-ethyl-guaiacol, are removed by the presence of lees during aging wine lees (Chassagne et al. 2005).

A study about the volatile composition of white wine stored in stainless steel tanks showed that the samples that had contact with the lees during the aging process had a higher phenolic compounds content than those no-lees aged wine (Bautista et al. 2007).

Table 1 Centesimal composition of alcoholic fermentation lees from scientific studies (g/100 g)

Type of grape	Ash	Proteins	Lipids	Sugars	Total dietary fibre	Reference
T	14.00 ± 0.10	21.20 ± 0.20	9.20 ± 0.40	–	–	(Cappello et al. 2017)
T	13.18 ± 0.92	20.32 ± 0.75	4.85 ± 1.15	< 0.50	82.32 ± 1.69	(Chassagne et al. 2005)
C	6.10 ± 0.10	9.50 ± 0.10	9.20 ± 0.40	–	–	(Cueva et al. 2016)
*	10.55 ± 0.05	15.11 ± 0.57	5.40 ± 0.46	4.13 ± 0.63	21.50 ± 0.35	(Bustos et al. 2004)

Samples represented by the letter T correspond to *Tempranillo grapes*; sample represented by the letter C corresponds to *Vitis coignetiae Pulliat ex Planch Crimson* variety grapes; sample represented by the icon * means that the grape variety was not informed

Microorganisms

The microbiota of grapes depends on factors such as environmental characteristics, geographical location, cultivation mode and water distribution, among others (Pinto et al. 2015). However, it is known that there are three fundamental microorganisms in the wine-making process, these being: *Saccharomyces cerevisiae* yeasts, non-*Saccharomyces* yeasts and lactic bacteria (Petri et al. 2013). In fermentation, microorganisms metabolize the sugar present in the grapes and produce several metabolites responsible for the quality of the wine, including aroma, flavor, hue, among others (Raspor et al. 2006). In relation to wine production, it is known that during industrial fermentation it is possible to inoculate microorganisms in order to improve the characteristics of the wine, on the other hand, the artisanal production fermentation occurs naturally and the microorganisms present are from the microbiota of the grape (Sannino et al. 2013).

Saccharomyces cerevisiae yeast

Saccharomyces cerevisiae is the most used yeast for wine production due to its higher resistance to the alcohol formed during fermentation, as well as to SO_2, the main preservative used in wine manufacturing (Morata et al. 2005). This yeast is known for its easy isolation and maintenance, low nutritional requirement and good growth in media constituted of industrial by-products (Verstrepen et al. 2003).

According to Table 2, in the *Saccharomyces cerevisiae* centesimal composition, the most important parameters of a yeast coming from alcohol distilleries are the proteins, fibers, ashes and the ribonucleic acid. The samples of this study obtained values of: protein - 62,4%, ashes - 13,0%, ribonucleic acid - 9,8% and total lipids - 8,5%, present in this yeast species.

Table 2 Centesimal composition of *Saccharomyces cerevisiae* yeast cells

Component (%)	Whole Yeast	Autolysate	Extract	Phosphorylated Protein Concentrate
Protein (Nx5.8)	39.6	40.4	50.7	62.4
Dietary fibre total	31.4	31.2	3.3	6.2
Soluble	30.3	30.4	3.3	ND
Insoluble	1.1	1.0	0.0	ND
Ash	4.6	6.2	11.7	13.0
Total lipids	0.5	1.2	0.4	8.5
Ribonucleic Acid	9.0	5.6	8.3	9.8
Not determined	14.9	15.4	25.6	0.1

Source: Yamada et al. (2003)

The cells of the yeast *S. cerevisiae* adsorb the grape pigments, especially at the end of the fermentation and, when dead, they are deposited in the barrels, forming the wine lees (Echeverrigaray et al. 2020). This behavior can be explained by the following reasons: the chemical modifications of anthocyanins during fermentation, increasing their absorbability by yeast cells; the structural or metabolic changes that increase the absorption capacity of the yeast; the combined effect of both factors (Morata et al. 2016).

Non-Saccharomyces yeast

Recently, mixed fermentations between *S. cerevisiae* and *non-Saccharomyces* yeasts, such as *Torulaspora delbrueckii and Hanseniaspora*, have been applied to diversify flavor and aroma profiles in wine, making it necessary to search for new volatile compounds that have been produced by new yeast strains to enhance the sensory profile of alcoholic beverages (Rêgo et al. 2020).

Among the *non-Saccharomyces* used as bioprotective agents or in sequential application, the species *Torulaspora delbrueckii and Metschnikowia pulcherrima* were considered, with emphasis on the former which, in association with *Saccharomyces cerevisiae* in sequential inoculation, has been shown to release esters and thus increase the intensity of the fruitiness of red wines (Benito 2018).

Non-*Saccharomyces yeasts*, especially *Torulaspora delbrueckii*, have proven to be good candidates to colonize the must and limit wine defects. Notably, inoculation time and dosage of non-*Saccharomyces* impact the chemical and sensory perception of sulphite-free red wines (Rossouw & Bauer 2016). Compared to the use of non-Saccharomyces in sequential applications, which aggravates the fruitiness of the wine, its use in bioprotection has a significant impact on the aromatic profile of wines, with a tendency to be perceived as fruitier in sensory analysis (Windholtz et al. 2021).

The compounds produced by yeasts are intermediates of the metabolic pathways of catabolism of the components of the medium, such as sugars, nitrogenous compounds and sulfur compounds, used for the production of factors necessary for cell growth as amino acids, proteins, nucleic acids, among others (Nedović et al. 2015). During fermentation, the factors causing selective pressure in the environment (acidity, high concentrations of sugar and ethanol) favor the yeasts that have the most efficient fermentative catabolism, particularly the *S. cerevisiae* strains, one of their main roles being to catalyze quickly, completely and efficiently the conversion of the

sugars to ethanol, carbon dioxide and aromatic compounds without the development of undesirable sensory compounds (Swiegers & Bartowsky 2005).

Lactic bacteria

Lactic bacteria are characterized by the production of lactic acid as a product of metabolization from glucose. They are gram-positive, aerotolerant, acid-tolerant, non-sporulated, strictly fermentative rods or cocci (Petri et al. 2013).

Most of the lactic bacteria present in wine lees belong to the genera *Lactiplantibacillus, Lactobacillus*, *Leuconostoc oenococcus*, and can have a negative or positive impact (Zheng et al. 2020). These microorganisms are part of the microbiota of grapes, musts and wines, but in some cases, inoculation of them occurs with the purpose of improving some aspects (Tristezza et al. 2016).

The use of these bacteria is directly related to the conduction of malolactic fermentation, since this process improves the sensory characteristics and increases the microbiological stability of the wine (Virdis et al. 2021). Commonly, the hydrolysis of grape glycosides, synthesis and the hydrolysis of esters are reactions performed by the lactic bacteria through several metabolic pathways (García-Ruiz et al. 2015).

Regarding the negative aspects, lactic bacteria can contribute to the reactions that produce biogenic amines, volatile phenols and ethyl carbamate, generating serious consequences on wine quality and safety (Inês & Falco 2018). Homofermentative *Pediococcus* and heterofermentative *Lactobacillus* are the main lactic bacteria responsible for wine spoilage (Cappello et al. 2017).

Wine lees components

Wine lees composition shows relevant values of proteins, ashes, moisture and fibers, as made known later in Table 1. The wine lees sugar content found is lower than the parameters mentioned before, especially when compared to other winery by-products, and this fact can be justified by the alcoholic fermentation, when there is a conversion of sugars into alcohol (Rivas et al. 2021). Also, it was found an amount of lipids in wine lees. Some yeast cell wall components are capable of associating with the lipids present in wine (Gómez et al. 2004).

In recent years, due to the studies related in the formation of wine agro-industrial waste, it has become widely known the presence of relevant amounts of bioactive compounds in wine lees (Rivas et al. 2021).

Phenolic compounds

Phenolic compounds are products of the secondary metabolism of grapevines that, in general, are formed by the interaction of the plant with the external environment and have a significant function in protecting against the attacks of pathogenic microorganisms, as well as favoring the attraction of pollinating insects and microorganisms beneficial to the plant (De Iseppi et al. 2020).

The variety in the phenolic content present in grapes depends on factors such as: ultraviolet (UV) radiation, fraction of irrigated water, lighting levels and shortage of nutrients also cause interference, showing the influence of external factors of cultivation in its composition (Del-Castillo-Alonso et al. 2021). Figure 1 shows the main phenolic compounds found in wine lees, in general, according to previous studies.

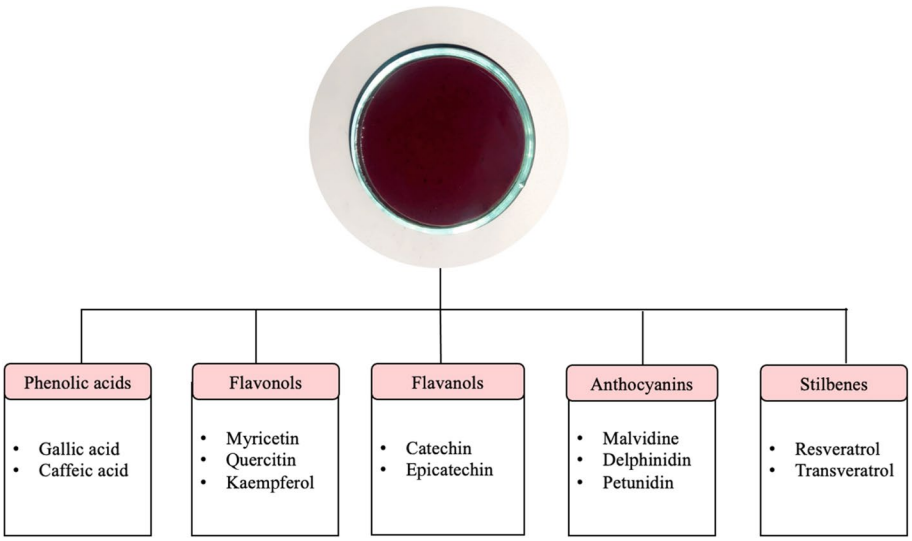


Fig. 1 Main bioactive compounds in wine lees. Source: Elaborated by the authors

Wine lees can be considered a raw source for phenolic compounds extraction due to the ability of yeasts used during the fermentation process to interact with phenolic compounds and adsorb them (Jara-Palacios 2019; Mena et al. 2014). A study using wine lees obtained by raking after alcoholic fermentation of Syrah grapes showed a phenolic content of 36.8% in their dried extract (Pérez-Serradilla & Luque de Castro 2011). During the analyses of red wine lees of the Tempranillo variety, it was found phenolic content between 26 and 245 mg GAE/g (Romero-Díez et al. 2018).

Among the phenolic compounds present in wine lees is the group of flavonoids, characterized by their structure of linked aromatic rings which, due to their oxidation-reduction capacity, performs relevant antioxidant actions in the inhibition of free radicals in the human organism (Romero-Díez et al. 2018). Between the main flavonoids present in wine lees, the following stand out: anthocyanins; catechins and epicatechins belonging to the flavanols; and quercetin and myricetin that make up the subgroup of flavonols (Pérez-Serradilla & de Castro 2008).

Some studies have determined up to 26 anthocyanins present in samples of wine lees: derivates of the anthocyanidins delphinidin, cyanidin, petunidin, peonidin and malvidin (Jara-Palacios 2019). In a recent study about wine lees formed by grapes of Cabernet variety, malvidin was the compound from anthocyanins group with the highest value (López-Fernández-Sobrino et al. 2021). A similar result was observed in another study, which pointed out wine lees as an important source of anthocyanins, detecting in their composition the presence of malvidin-3-O-glucoside and malvidin-3-(6″-p-coumarylglucoside) in higher concentrations (Romero-Díez et al. 2018).

Stilbenes, especially resveratrol, are phenolic compounds of wide scientific interest due to their antioxidant activity, ability to modulate the reduction of low-density lipoprotein (LDL) levels and increase high density lipoprotein (HDL) the levels. Despite being widely identified in grape skins, these compounds are found in lower concentrations in wine lees (Akinwumi et al. 2018; Teixeira et al. 2014).

Phenolic acids, widely found in grape lees, are divided into two groups: hydroxybenzoic and hydroxycinnamic acids, characterized by a benzene ring, carboxylic group, and may have one or more hydroxyl groups (He et al. 2022). The p-hydroxybenzoic and vanillic acids are the main hydroxybenzoic acids found in sour grape lees, while tartaric, ferulic, *p*-coumaric and caffeic acids are the main hydroxycinnamic acids identified in lees (Stefenon et al. 2014).

In the Supplementary table, these bioactive compounds are observed in some studies of different cultivars of *Vitis vinifera*, where they revealed that the contents present in wine lees are mostly constituted of gallic acid, trans and resveratrol, malvidin, while the other compounds were less frequent in the analyzed studies (López-Fernández-Sobrino et al. 2021).

Aromatic compounds

In general, volatile compounds are formed during malolactic fermentation and have the function of enriching the aromatic quality of wines, as well as modifying their color and phenolic composition (Izquierdo-Cañas et al. 2012). Some of these compounds are the volatile phenolics, derived from the thermal degradation of oak wood lignin during toasting of staves (Jiménez Moreno & Ancín Azpilicueta 2007).

The wine lees formed during malolactic fermentation promote the binding of compounds important to the wine's aroma and help to reduce the impact of aromatic compounds originating from the place where the wine ages (Chassagne et al. 2005). One of the reasons for this event is the autolysis of the yeasts present in the lees, offering the must macromolecular components that stimulate malolactic fermentation and, therefore, improve the sensorial characteristics of the wines (Antón-Díaz et al. 2016).

Two articles were used to demonstrate the contribution of wine lees in the amplification of aromatic compounds during the wine aging process. During the wine aging process using lees in different concentrations (10 and 50 g/l), it was possible to note the changes in the aromatic compounds (Jiménez Moreno & Ancín Azpilicueta 2007). The types of grapes used in the study were *Vitis vinifera* grapes of the Cabernet Sauvignon, Tempranillo and Merlot varieties. By increasing the concentration of lees added to the wine, the retention of these aromatic compounds also rises, although not always proportional to the concentration added. The study also states that volatile wine compounds from oak wood that showed the greatest affinity for lees were eugenol, 4-propylguaiacol, 4-methylguaiacol, furfural and 5-methylfurfural. Other compounds important for the aroma of oak-aged wine such as oak lactones and vanillin also bound to the lees, although to a lesser degree.

A study using Chardonnay grapes, reported a lower concentration of furfural and 5-methylfurfural in the samples, suggesting that these compounds have a high affinity for the lees (Liberatore et al. 2010). It was also described that vanillin and syringaldehyde have lower affinity for lees compared to the previous compounds, which is also discussed in the article (Jiménez Moreno & Ancín Azpilicueta 2007).

Sustainability and applications

It is estimated that by 2050, the world's population will consume three times more than what is available on planet Earth. In order to avoid such an event, the European Union plans to implement measures capable of neutralizing this effect, including the circular economy (Perra et al. 2022). Among the main objectives of the circular economy is the reduction and recycling of food waste, issues still present in the agro-industrial sector (Morseletto 2020; Perra et al. 2022).

The agro-industrial residue is one of the main waste generators in the world, and when managed incorrectly can cause serious environmental impacts, such as: production of greenhouse gases and oxygen depletion (Yaashikaa et al. 2022). The winemaking process encompasses some critical points that represent a problem to the environment, and among them there is the generation of by-products (Beres et al. 2017). An example is the fact that wine lees are a matter with high biological (BOD) and chemical oxygen demand (COD) (De Iseppi et al. 2021). BOD and COD concentrations of domestic sewage analyzed were between 25 and 500 g/L and 73-773.3, respectively, a range that encompasses the values found for wine lees, highlighting the importance of enabling new sustainable alternatives for the use of wine lees (Dacewicz 2019).

When reused, wine lees are generally applied in activities of low economic value, such as the production of fertilizer, due to the presence of elements such as Ca, Mg, Fe, and Zn in the winery by-products composition (Kalli et al. 2018) and animal feed (Giacobbo et al. 2019). However, studies state that these applications reaffirm the undervaluation of wine lees, since compounds of high interest present are not widely exploited, remaining the need for disposal at times (Aristizábal-Marulanda et al. 2017).

Wine lees are also used in one of the most traditional methods of recovering tartaric acid, which consists of drying, grinding and diluting the wine lees with potassium bicarbonate in hot water. The residues formed in this process are precipitated with calcium salts, forming calcium tartrate. Tartaric acid is found in wine lees, mostly in potassium bitartrate and in lesser amounts together with dead yeast, solid particles, organic substances and calcium tartrate crystals (Kontogiannopoulos et al. 2016).

Despite the small scientific and technological production related to the use of wine lees, some research shows that it is possible to reuse them in order to add commercial value to wine lees in applications such as food additives, pharmaceuticals, cosmetics and chemical industry (Kokkinomagoulos & Kandylis 2020).

Sodium ascorbate was replaced by wine lees in the condition of natural preservative in wild deer meat hamburger. The lees were previously freeze-dried and added in different concentrations in the hamburger mixture. Benefits were verified from the application of wine lees, such as reduction in pH, modification in color parameters, decrease in psychotropic bacteria count, as well as improvement in antioxidant function, juiciness, and tenderness (Alarcón et al. 2020).

In another research, wine lees were evaluated as a natural antioxidant with added value to improve the rheological properties of ice creams. The results from the analysis were compared the values obtained to the control sample and observed positive effects, since the ice cream showed a decrease in pH, firmness, lightness, and the amount of freezable water, as well as an increase in viscosity and fat destabilization. Furthermore, the ice creams with wine lees showed satisfactory concentrations of anthocyanins and phenolic compounds (Hwang et al. 2009). Wine lees was also used for the homogenization of ice cream with the purpose of generating a product of higher market value. The results were satisfactory in terms of physicochemical characteristics, rheological activities of the product, increased amounts of phenolic compounds and antioxidant activity. The sensory analysis showed that the ice cream prepared with wine lees, in general, showed better acceptability by consumers (Sharma et al. 2015).

Due to the high content of polyphenols, especially anthocyanins, and the antioxidant activity, wine lees can be applied for the cosmetic formulation in order to promote the health of human skin. Grape lees extract, when used in cosmetic products, has skin whitening and anti-aging effects (Matos et al. 2019). In another study, it was seen that phenolic extraction from the wine lees solid fraction by enzymatic hydrolysis was efficient for obtaining wine lees rich in antioxidant and antihypertensive properties. The fraction resulting from this process was rich in flavanols, anthocyanins, phenolic acids and flavonols. The authors claim that numerous benefits have been associated with phenolic compositions, including antihypertensive properties (López-Fernández-Sobrino et al. 2021).

In an approach based on the example of biorefineries, which represent the transition from traditional refineries to sustainable systems based on the valorization of waste streams in order to enhance market value, wine lees can also be used for more sustainable purposes (Bustos et al. 2004). Wine lees as well as wastes from the food supply chain can be used as feedstock to produce fuels, chemicals, biopolymers, food additives and value-added products (Pérez-Bibbins et al. 2015, b).

A study showed that wine lees can be used to produce poly-3-hydroxybutyrate by bacterial strain *Cupriavidus*

necator DSM 7237, after extraction of value-added components with diversified markets. Synergistic use of renewable resources, such as the use of crude glycerol and hydrolysates derived from wine lees, can lead to highly efficient bioprocesses (Dimou et al. 2015).

Technological research into the use of wine lees

As observed in Table 3, the crossing of the words "wine*" and "lee*" in the Espacenet found 216 patent documents of products related to the reuse of wine lees. However, 51 were with accordance with the research theme. Using the same combination in Orbit®, 88 documents were recovered and 46 of them applied to this research for the same reason mentioned.

Regarding the annual evolution, the first patent was filed in 1899 and between the years 2016 and 2018 the average of 4 documents per year were deposited, with the peak of deposits related to this theme was in 2016. In 2019, there was a decrease in the quantity of patents, which is possibly associated with the 18-month secrecy of the documents before they are published in the patent bases. However, it was found that there is a low number of patent documents, highlighting the importance and need for further studies about this theme.

Furthermore, the number of patent documents classified by the filing country or international organization was evaluated. The results showed that China holds the highest number of deposits, with 31 patents, representing 60.80%, followed by Japan 27.45%, Patent Cooperation Treaty 5.88%, United Kingdom 3.92%, and Australia 1.96%. These data are expected, since China is the second grape producing country, contributing 12% of world production, however most of the production is exported to other countries (International Organization of Vine and Wine 2009).

After the update of the Patent Law of China leading the ranking of patent deposits, in addition, the strong government incentive, the search for recognition of universities and institutions, and obtaining certification as high-tech companies are factors that contribute to the development of new technologies in the country (Hu & Jefferson 2009). In the 1990s there were significant increases in patent deposits of Japanese origin, due to the Japanese government's pro-patent policy, in order to stimulate technological innovation and promote international competitiveness.

Also, according to the International Organization of Vine and Wine (International Organization of Vine and Wine 2009), Brazil is the fifteenth grape producer in the world, producing up to 1.6 tons, with 53.5% destined for fresh grape consumption and 46.5% for wine production. However, in the European Patent Office (EPO) database there were no patent applications related to the reuse of wine lees in the Brazilian territory.

The main International Patents Classification (IPC) codes found in the patent bank on wine lees and the number of citations is shown in Fig. 2. The most cited classes were "C - chemistry; metallurgy" and "A - human needs". It was possible to observe that, among the subclasses, the highest number of patents is concentrated in code C05G3/80, referring to mixtures of one or more fertilizers with additives without special fertilizing activity, with 6 records. The subclasses with the second and third largest number of patents are represented by the patent documents registered with classification codes C12G1/022 and C05F17/00, both with 4 registrations, referring to fermentation processes for beer and wine and fertilizer preparation characterized by biological or biochemical treatment steps, composting or fermentation, respectively.

Table 3 Scope of the scoping table on the use of wine lees

Grape*	Wine*	Lee*	A23	A61	C12	Total
x						35.284
	x					89.315
		x				31.568
x	x	x				93
x		**x**				**216**
x		x	x			98
x		x		x		47
x		x			x	54
x	x	x	x			25
x	x	x		x		18
x	x	x			x	45

Source: Prepared by the authors on the basis of Espacenet. A23: Food or foodstuffs and treatment thereof, not covered by other classes; A61: Medical or veterinary science; hygiene; C12: Biochemistry: beer, spirits, wine, vinegar, microbiology, enzymology, mutation or genetic engineering

*was used to find derivations of the keywords

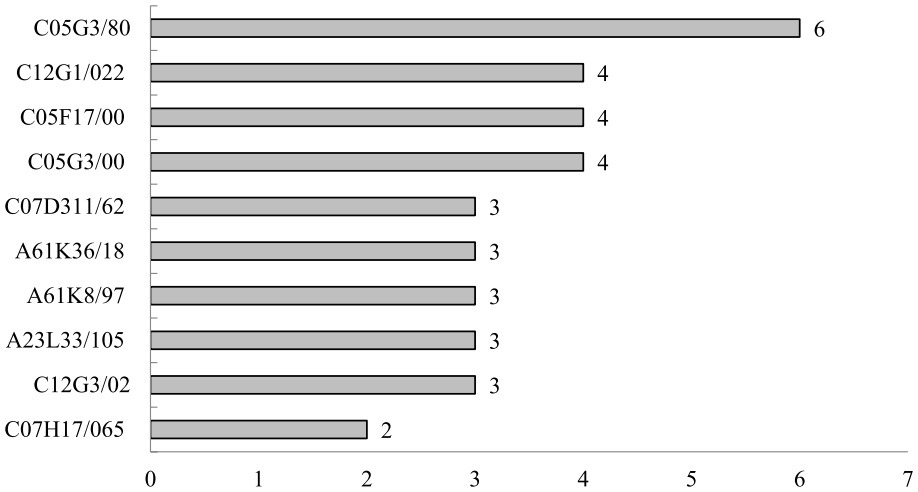


Fig. 2 Distribution of patents related to wine lees by international classification codes (IPC). Source: Elaborated by the authors based on Espacenet

The main inventors about the theme are of Asian origin, corroborating the results previously discussed regarding the distribution of patents per country. The high frequency of patent dominance, by Asian inventors, is probably related to the high investment of these countries in various stages of education and technological research (Tian et al. 2020).

The main applicants of patent on the application and research of wine lees in the world are companies, with 31 deposits, followed by independent researchers, with 14 deposits, and finally, universities with 6 deposited patents. It is noticed that companies (60.7%) were the largest applicants of patent applications in the World, pointing out that the technology under study is promising, since several foreign companies protect their technologies in the country.

Among the patent families by technology domain showed in Fig. 3, it can be seen: food chemistry, basic material chemistry, organic fine chemistry, pharmaceuticals, other special machines. The main technological family of the object of study is food chemistry, represented by 44.07% of patent applications in the world, that includes themes as food products or alcoholic and non-alcoholic beverages; their preparation or treatment; preservation of food or foodstuffs. An example of patent is Health Grape Wine Added With Non-Active Dry Yeasts and Brewing Process Thereof (Document: CN105754776A), the invention refers to grape wine with the presence of non-active dry yeasts and a brewing process, the advantage of this invention is that the precipitate and turbidity caused in the brewing process are effectively avoided and the polysaccharide content is improved. Also, it is described in the document that the yeast autolysate is rich in amino acids, vitamins, and minerals.

The second largest patent family for wine lees is basic material chemistry, which can be justified by the facts

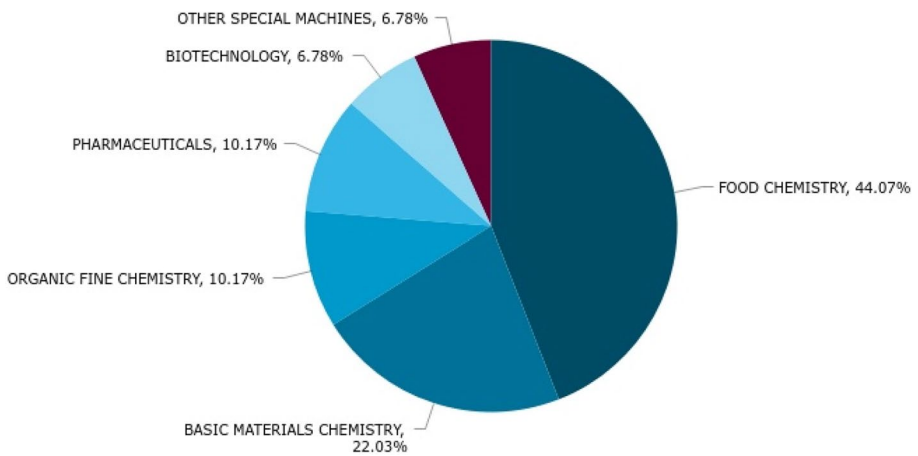


Fig. 3 Patent documents based on reuse of wine lees in different technological domain. Source: Q. Orbit®

that the lees are extremely rich in organic matter, polyphenols, and minerals, these characteristics, combined with its low pH, make raw wine lees compatible with agricultural applications, such as natural additives, antioxidants, antimicrobials, for the enrichment of soil nutrients, composting, preservation in cultivation. This area represents 22.03% of the patent applications and an example of a patent in this area is Germination Accelerating Fertilizer For Muscat Grape Varieties (Document: CN102850106A). According to this document, the organic fertilizer developed with wine lees is rich in organic matter content, which provides nutrients, reduces amount of sulfur and potassium added and is capable to improve soil quality and germination rate. Despite the high bioactive content, wine lees are still underused, being commonly used in low-value activities such as fertilizer (Giacobbo et al. 2019).

Pharmaceuticals family also have patents (10.17%), because of tartaric acid, predominantly found in grapes and wines, and very uncommon in other plant materials. Tartaric acid is an important acidifier used for different applications not only in food and beverage production, but also in the pharmaceutical, cosmetics and chemical industries. One example is the document CN113546020A which describes a facial mask developed with wine lees. According to this invention, wine lees present bioactive substances, such as amino acids, peptides, functional polysaccharides, etc. These components have antioxidant and whitening effects. The lees are also rich in tannins, capable of scavenging free radicals and inhibiting elastase enzyme activity. These activities are related to aging prevention and skin elasticity enhancement. A study about winemaking by-products with cosmeticeutical potential showed great results for antioxidant activity, using the hydroalcoholic red wine lees extract. This result was associated with the high content of phenolic compounds and anthocyanins present in the sample (Matos et al. 2019).

The clusters of keywords related with the reuse of wine lees can be seen in the Fig. 4. Analyzing all groups, is noticed that some concepts are repeated in more than one agglomerate. For example: fertilizer; wine lees organic fertilizer; lees organic fertilizer; and most of them are in the orange agglomerate entitled grape, associated to grape juice. In the blue cluster named red wine can be found the keyword related to polyphenols, it converges with is observed in the literature that red wine is an important source of polyphenols, containing on average 900 - 1400 mg of polyphenols per liter of young red wine (Cueva et al. 2016). Document CN101845036A describes an extraction method of procyanidin from wine lees by using an alcohol solution. According to the invention, the technology used can transforming waste in a valuable source of flavonoid, while also controlling the amount of solvent used, extraction time and production costs comparing with traditional methods.

In the same red wine blue agglomerate, the words associated to extract (unrefined lees extract, grape seed extract, red wine crushing extract) and it can be explained by the interesting about the recovery of polyphenols, once they are considered a high value compound (Domínguez-Rodríguez et al. 2022).

Conclusion

Despite representing an important fraction of winemaking by-products and containing several high-value components with potential to be exploited in industrial sectors, such as phenolic compounds, wine lees are still one of the least studied and exploited residues.

Fig. 4 Clusters of keywords related to patent documents about wine lees reuse. Source: Q. Orbit®

Through the Technological Prospection, it was possible to observe that wine lees are still little studied, with only 51 and 46 patents filed on the technological/nutritional properties of wine lees available to study, in Espacenet and Orbit® (respectively). China is the largest patent applicant on wine lees, 60.80% of the deposits, being one of the largest producers of grapes and the largest exporter in the world.

Food chemistry is the main technological family of the object of study, representing 44.07% of patent applications in the world, that includes themes as food products or alcoholic and non-alcoholic beverages; their preparation or treatment; preservation of food or foodstuffs. In the second place, wine lees are used as basic material chemistry, which can be justified by the facts that the lees are extremely rich in organic matter, polyphenols, and minerals. These characteristics, combined with its low pH, make raw wine lees compatible with agricultural applications.

Therefore, the study suggests that different applications should aim at developing an integrated approach aimed at extracting from wine lees the highest number and quantities of compounds with possible applications in different sectors. The development of this model could contribute to improve the tools available for the valorization of wine lees and would give the wine industry a new and important means to improve its environmental and economic sustainability.

Abbreviations

BOD	Biological Oxygen Demand
COD	Chemical Oxygen Demand
EPO	European Patent Office
EEC	European Regulation
HDL	High Density Lipoprotein
IPC	International Patents Classification
LDL	Low-Density Lipoprotein
OIV	Organization of Vine and Wine

Supplementary Information

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Additional file 1: Supplementary Table. Main phenolic compounds in wine lees from different scientific studies.

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Authors' contributions
RBAB, MAUG and COS designed the study, wrote the manuscript and revised the manuscript. FGP, CMG and PPLGT researched and evaluated prospection data, as well as produced all figures and tables. All the authors approved the final manuscript.

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Availability of data and materials
The authors confirm that all data underlying the findings described in this manuscript are fully available without restriction (all relevant data are within the manuscript).

Declarations

Ethics approval and consent to participate
This article does not contain any studies with human participants or animals performed by any of the authors.

Consent for publication
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Competing interests
The authors declare no conflict of interest.

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