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Review

Value Added Alternatives of Winemaking Process Residues: A Health Based Oriented Perspective

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Abstract

Consumer increasing demand for the use of natural derived compounds and not the chemical synthesized counter parts, the awareness that agricultural practices should become more eco-friendly coupled with the increasing interest of producers to manage surplus waste streams, since the imposed fines and fees imposed to unauthorized discharges are very high, force suppliers and scientists to seek alternatives in waste handling practices, focusing in revalorizing waste streams. Winemaking is one of the most significant agricultural activities forming high volumes of different residues consisted of plant remains characterized of high contents of biodegradable compounds and suspended solids. Grape marc, pomace and wine lees contain high concentrations of major classes of bioactive phytochemicals. There is a vast array of applications for wine bioactive compounds such as functional ingredients (dietary fiber, sugars, antioxidants, grape seed oil, minerals and vitamins), pharmaceutical/biomedical (pullulan) and nutraceuticals or supplements (grape pomace powder). To date, there has been no or almost none assessment as to the market potential for value-added usage neither for grape leaves, mark and grape pomace or wine lees. This paper highlights alternative valorization routes for phytochemicals derived from solid vinery waste, seeking to address health benefits associated with winery bioactive compounds and possible applications as functional ingredients.

Keywords: Grape Pomace; Grape Leaves; Wine Lees; Grape Mark; Bio actives; Valorization of Winery Residues; Dietary Fiber; B-Glucan; Phenolics; Antioxidant; Linoleic Acid; Functional Ingredients; Chronic Vitamin C; Tocopherols; Chronic Diseases; Value Added Products; Bioactive Compounds.

Introduction

Wine is the product obtained from the total or partial alcoholic fermentation of fresh grapes whether or not crushed or of must. Winemaking is a complex multistep process carried out during the elaboration of wine from grapes, considered one of the most significant industrial sectors world widely, with high economic importance. The species most commonly cultivated for wine production is *Vitis vinifera*. Wine world production in 2015, reached 275.7 million hectoliters [1], generating large volumes of residues, arising huge waste management issues and environmental problems (ranging from surface and groundwater pollution to full odours), and attributed mainly to their seasonal character and their improper disposal in open areas. Nowadays European legislation, (EC) 479/ 2008, on the common organization of the wine market indirectly recalls the obligation of distillation enforced by (EC) 1493/1999. Thus, efficient utilization and recycling of these organic residues is of high importance minimizing environmental impact and increasing profits [2].

The main solid residues generated throughout the winemaking process are grape stalks (GS), grape pomace (GP) or grape mark (GM) and wine lees (WL) (figure-1) [3].Grape stalks are produced after destemming, grape pomace or grape mark after pressing in white wine technological process and after fermentation and pressing, in white wine vinification process. Wine lees is the residue that forms at the bottom of recipients containing wine, after fermentation, during storage or after authorized treatments, as well as the residue obtained following the filtration or centrifugation of this product [4].

Grape stalks or the grape skeleton of red grapes comprised mainly of cellulose (30.3%), hemicelluloses (21.0%), lignin (17.4%) and proteins (6.1 %) [5]. Apart from fibers, grape stalks also contain phenolic compounds and some nutritive mineral elements [6].

Grape pomace constitutes 20% approximately of the grapes used to produce wine, considered the most significant by-product of winemaking with an estimated 10,930,834 Mtn [7]. Naziri et al. (2014) stated that 62% of the organic waste is attributed to pomace [8]. Grape pomace contain: 1) skin and pulp (10-12 %) 2) seeds (2-6%) and a part of stalks (2.5-7.5 %). Grape seeds are comprised of: phenolics, oil, proteins, non digestable fibers and minerals [9]. The composition of grape pomace and its constituents depends on several parameters, the grape variety they derive from, the technological process followed throughout winemaking process,

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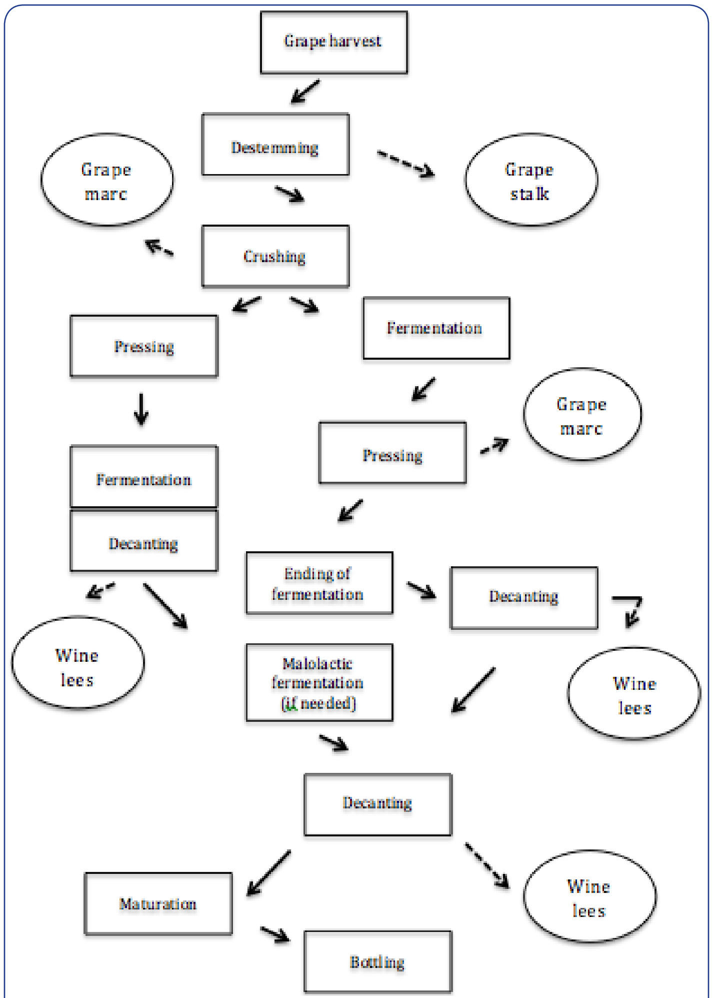

Figure 1: Process flowsheet of white and red winemaking, highlighting the steps that major solid by-products are generated

the maturity of the collected grapes used, the production size and the separation process step followed before and after crushing.

Wine lees (WL) represent 2-6% of the total volume of wine produced and it mainly contains spent yeasts and secondary phenolic compounds, tartrates and ethanol [4]. WL might be used as a source of bioactive compounds such as phenolic compounds and b-glucans.

Grape leaves contain functional ingredients such as catechins, flavonoids, tannins, malic, silicic, citric, tartaric and succinic acids, and resveratrol [10]. Oganesyants et al. (2015), comparing the biochemical composition of red vine leaves of autochthonous and European varieties, using bioassay systems in vitro, revealed that red vine leaves extracts of autochthonous varieties had a marked effect on the rate of glutathione reductase and pyruvate kinase reactions, demonstrating their angioprotective and energizing properties [11].

The aim of the present study was the reviewing of the basic bioactive compounds derived as by-products from wine making, enhance their possible health effects and underline their potential use as functional ingredient (e.g. novel and functional foods production, supplements etc.).

Grape Waste Bioactive Compounds and Associated Health Related Effects

Dietary Fibers

According to AACC (2001) dietary fiber (DF) is defined as "edible parts of plants or analogous carbohydrates that are resistant to digestion and absorption in the human small intestine with complete or partial fermentation in the large intestine". Dietary fiber may promote beneficial physiological effects. The most significant of them are laxation, and blood cholesterol and glucose attenuation [12]. It is well known, that increased consumption of dietary fiber is associated with reduced risks of developing: 1) coronary heart disease 2) stroke 3) hypertension 4) diabetes 5) obesity, and 6) certain gastrointestinal diseases. It has been demonstrated that, in both non-diabetic and diabetic individuals, increasing fiber consumption had advantageous effects in blood pressure and serum cholesterol levels decreasing and glycemia and insulin sensitivity improvement [10,13]. The recommended dietary fiber intake for males, females and children vary from 10.5 to 14g/1000kcal (Table-1) [14]. Since vinification process leads to the production of rich in fibers residues such as pomace (especially skin), stems, leaves and wine lees it might be possible that these by-products could partially substitute other traditional fiber rich products in order to cover the recommended total fiber daily intake.

Table 1: Fiber intakes for males and females, adolescents and children grouped by age

Gender(Male, Female)	Age(year)	Fiber intake (g/1000kcal)
Male	2-5	11.3
	6-11	13.7
	12-19	14.9
Female	2-5	10.5
	6-11	12.0
	12-19	13.3

**Adopted from [13]*

Insoluble dietary fiber in grape pomace comprised mainly of cellulose and hemicellulose and in minor quantities lignin. As for the soluble fraction of dietary fiber pectin is predominant. Llobera et al. (2007) measured dietary fiber by gravimetric-enzymatic method with sugar profiling by High Performance Liquid Chromatography-Evaporative Light Scattering detection (HPLC-ELSD) of skins of two white grape pomace and three red wine pomace varieties [15]. According to their findings red grape skins had higher DF concentration (95% of total) than white ones. Total dietary fiber is the main component of grape stems, exceeding 77 % of the total dry matter (comprised of neutral sugars, uronic acids and Klason lignin) [15]. Grape stalks also contain dietary fibers in high concentrations, as it can be seen in Table-2.

Table 2: Chemical composition of grape stalk

Components	Ping et al. (2011) [61]	Spigno et al. (2008)[62]	Lorenzo et al. (2002)[63]
Klason lignin	39.6	47.3	22.9
Soluble lignin	1.0	-	-
Glucans	36.3	25.3	29.9
Hemicelluloses	14.9	13.9	35.3
Xylans	3.7	10.0	-
Arabinans	2.0	3.7	-
Mannans	3.9	-	-
Ash	3.9	-	-
Tannins	6.4	-	-

**All data are expressed as g per (100) g of grape stalk, on dry basis*

Wine lees may become an innovative way to produce β-glucans, which are major structural compounds (30%) of yeast cell walls. Glucans has been identified as biological response modifiers (BRMs) owning to their ability of enhancing and stimulating the human immune system. Till now, exist in literature more than 6000 publications investigating the immune-modulating effects of β-glucans, such as anti-inflammatory or antimicrobial abilities. Health effects were found not only in humans but also in animals (invertebrates, rodents, fishes as well as farm animals such as cows or pigs) [16]. Also, (1→3)-β-D-glucans, trigger the production of pro-inflammatory molecules such as complement components, IL-1α/β, TNF-α, IL-2, IFN-γ, IL-10, and IL-4 [17,18]. Furthermore, the protective action of β-glucan against oxidative stress has also been reported, using (1→3)-, (1→6)-β-D-glucan prepared from *Saccharomyces cerevisiae* yeast. β-glucans has been associated with other health benefits such as hepato-protective, wound healing, weight loss, antidiabetic and cholesterol lowering functions [10,17,18]. Yeast β-glucan extract is considered as safe for oral applications and recognized as GRAS (Generally Recognized As Safe). For that reason, thinking the health benefits of intake, β-Glucans derived from the cell wall of yeasts, can be efficiently employed as fat replacers, emulsifiers and dietary fibers in food industry [19,20].

The use of dietary fibers derived from wine making may be important in order to produce relative functional foods, giving the fact that the role of dietary fiber in human health is well established, especially in cardiovascular diseases risk decreasing.

Polyunsaturated Fatty acids

Grape seed oil, have been examined for promoting health and preventing disease due to its high content of saturated fatty acids and mainly the polyunsaturated fatty acid (PUFA) fraction. HPLC analysis coupled with ELSD of grape seed oils (extracted via supercritical CO_2 followed by Saponification, since a large amount of fatty acids exists in the form of triglycerides), revealed that the main fatty acids contained in grape seed oil are linoleic acid, oleic acid, palmitic acid, and stearic acid while the most abundant is linoleic acid [21].

It has been reported that the fatty acid composition of grape pomace are similar to the oils of safflower, sunflower, soybean, maize and cotton seed, which belong to the linoleic type. Wine lees unsaturated fatty acid composition has been determined in order to evaluate the potential use of lees as food or food additive [22]. The major components of fatty acids contained in sherry wine lees were those having 16 and 18 carbon atoms and more specifically palmitic acid (about a 33%) followed by linolenic acid (about 21%) and stearic acid (10%) (Table-3). Baydar et al. (2007) reported that the major fatty acid in grape seed and pomace oil was linoleic acid. In the same study it was reported that the major fatty acid contents of the grape seed oils were palmitic (7.42 to 10.24%), stearic (2.95 to 4.68%), oleic (16.15 -21.63%), linoleic (63.33 - 71.37%) and linolenic acid (0.14 - 0.35%) [23]. It should be pointed out that in edible oils, derived from grape waste streams, the fact that linolenic acid concentration is low is rather advantageous for increasing the stability and the shelf life of these oils, since linolenic acid owning to the three double bonds on its hydrocarbon chain is rapidly oxidized. If that fact is properly exploited, then the produced grape waste oil based products, would be not only functional, owning to their fatty acid content, but also stable, concerning shelf life.

Table 3: Fatty acids composition of wine lees

Fatty acid		Relative amount %
Capric acid	C10:0	2.32
Lauric acid	C12:0	4.42
Miristic acid	C14:0	1.98
Palmitic acid	C16:0	33.29
Palmitoleic acid	C16:1	1.8
Margaric acid	C17:0	0.3
Stearic acid	C18:0	10.4
Oleic acid	C18:1	7.82
Linoleic acid	C18:2	21.26
Linolenic acid	C18:3	5.88
Araquidonic acid	C20:0	2.10
Erucic acid	C22:0	6.10
Lignoceric acid	C24:0	2.32

**Adopted from [23]*

Yi et al. (2009) evaluating FA profiles of finely ground pomace flour derived from two red varieties (*Cabernet Sauvignon* and *Royal Rouge*), revealed that both varieties contained high concentrations of: 1) polyusaturated fatty acids, PUFA, (60.9%-64.4%), 2) ratios of PUFA/SFA (2.80 - 3.11) and 3) n-6/n-3 ratios (20.8 - 36.9). High levels of linoleic acid (C18-2, n-6, 60 %), while a lower level of α-linoleic acid (C18-3, n-3, 2.3%) was identified. Regarding SFA (saturated fatty acids) palmitic acid (16:0) and stearic acid (18:0) were the most abundant. From a nutrition point of view, it can be deducted that *Royal Rouge* pomace flour was a better nutrient source since the ratio of n-6/n-3 was lower than the one derived from *Cabernet Sauvignon* [24]. In contrast to plants, mammals are not able to convert oleic acid into linoleic acid, linoleic acid

Table 4: Mineral composition (mg/100g) in grape pomace

Macro & Micro elements		Concentration of grape seed (g/Kg) [60]	Concentration of grape pomace (mg/100g) [54]
Calcium		5.208 ± 0.793	0.44 ± 0.715
Magnesium		1.385 ± 0.209	0.13 ± 0.255
Sodium (Na)	0.192 ± 0.087	0.044 ± 0.056	
Potassium (K)	5.904 ±1.432	1.40 ±0.313	
Phosphorus (P)	3.736 ±0.654	0.183 ± 0.255	
Sulfur	-	0.089 ±0.336	
Iron (Fe)	51.63 ±17.56	18.08 ± 0.03	
Copper (Cu)	7.524 ± 1.467	-	
Zinc (Zn)	11.27± 5.708	0.95 ± 0.702	
Manganese (Mn)	14.94 ± 5.708	0.817 ± 0.550	

into a-linoleic acid or convert n-6 to n-3. Therefore, linoleic acid and n-3 PUFAs are well known as essential fatty acids [25]. n-3 PUFAs has been associated with the prevention of heart disease and certain types of cancer, while improving immune functions. n-6 PUFAs are precursors of prostaglandins E_2, E_{2a}, thromvoxane A_2 and leukotrienes A_4, B_4, C_4 and E_4, which are responsible for arthritis and inflammation. On the other hand n-3 PUFAs, like EPA (eicosipentanoic acid) compete with arachidonic acid for cyclooxygenase and lipoxygenase that produce eicosanoids, inhibiting their production. n-3 PUFAs produce prostaglandins E_3, F_{3a}, thromvoxane $A_3$and leukotrienes A_5, B_5, C_5. The effects of excess of n-6 precursors are rather disadvantageous for health, since have been associated with thrombosis, immune suppression, arthritis and inflammation. It seems that n-3 PUFAs can decrease the n-6 PUFAs concentrations in phosphor lipid pools. Thus, changing n-6 to n-3 ratio may have several effects in the pathophysiology of chronic diseases. Decreasing n-6 to n-3 ratio may act beneficial in decreasing the risk of development chronic diseases such as nonalcoholic fatty liver disease (NAFLD), cardiovascular disease, obesity, inflammatory bowel disease (IBD), rheumatoid arthritis, Alzheimer's disease (AD), and cancer [26, 27]. On the other hand recently epidemiological studies trying to determine the optimum ratio of n-6 to n-3 PUFAs, inadvertently established the irrelevance of dietary ratio and reaffirming the benefits of n-3 PUFAs to reduce cardiovascular disease risk [28].

Grape waste oil derived from seeds can be used for the production of conjugated linoleic acid (CLA), a mixture of positional and configurational of $C_{18:2}$ fatty acids that could be used as functional ingredient. CLA is considered an anti-obese agent, impacting lipid metabolism and body composition [29], leading to body mass reduction. Briefly, the most studied possible health benefits of CLA are: 1) body fat reduction, 2) improvement of resistance to insulin, 3) anti-thrombogenic and anti-carcinogenic action 4) reduction of atherosclerosis 5) improvement of lipid profile 6) modulation of the immune system 6) triggering of bone mineralization, 7) reduction of blood levels of glucose 8) increment of lean mass and reduction of fatty mass [29,30,31,32].

More research should be done in that area trying to valorize grape waste oil, exploiting fatty acids as functional ingredients with multiple applications.

Phenolic compounds

The main groups of phenolic compounds found in winery residues are: 1) phenolic acids (hydroxybenzoic acids and hydroxycinnamic acids), 2) simple flavonoids (flavanols or flavan-3-ols, proanthocyanidins, flavones, and flavonols), 3) stilbenes, 4) tannins and proanthocyanidins [33].

In grape skin, flavonols are the most abundant phenolic compounds. Though existing the most abundant phenolic compounds in grape seeds, are flavan-3-ols monomer, such as (+)-catechin and (−)-epicatechin, as well as dimers, trimers and polymeric forms, otherwise called procyanidins (2–10 units), and not flavonols. Most times, procyanidins are linked with an inter flavan bond with subunits of gallic acid and epigallocatechin of epicatechin gallate. The main phenolic compounds (pigments) existing in red grape skins are anthocyanins, known to be responsible for the color of red wine. Anthocyanins may be present in winery waste as glycosides and acylglycosides (most abundant is malvidin-3-O-glucoside), originated from cyanidin, peonidin, delphinidin, petunidin and malvidin [33,34]. Also, the presence of low molecular weight phenolic compounds, released free flavonol aglycones and pyranoanthocyanins, having functional and bioactive properties, was recently reported by Barcia et al. (2014) [35]. Seradilla et al (2011) determined that the total phenols index in the spray dried microwave extracted phenolics of wine lees was 36.8% (expressed as gallic acid), showing an oxygen radical absorbance capacity (ORAC) value of 3930 μmol trolox equivalents per g (TE/g). Additionally, malvidin 3-glucoside (Mv3G), Cm-Mv3G, myricetin, quercetin, quercetin-3-b-glucoside, caffeic acid and p-coumaric acid were quantified in the dry extract by HPLC with diode array detection (DAD) (Figure-2) [36].

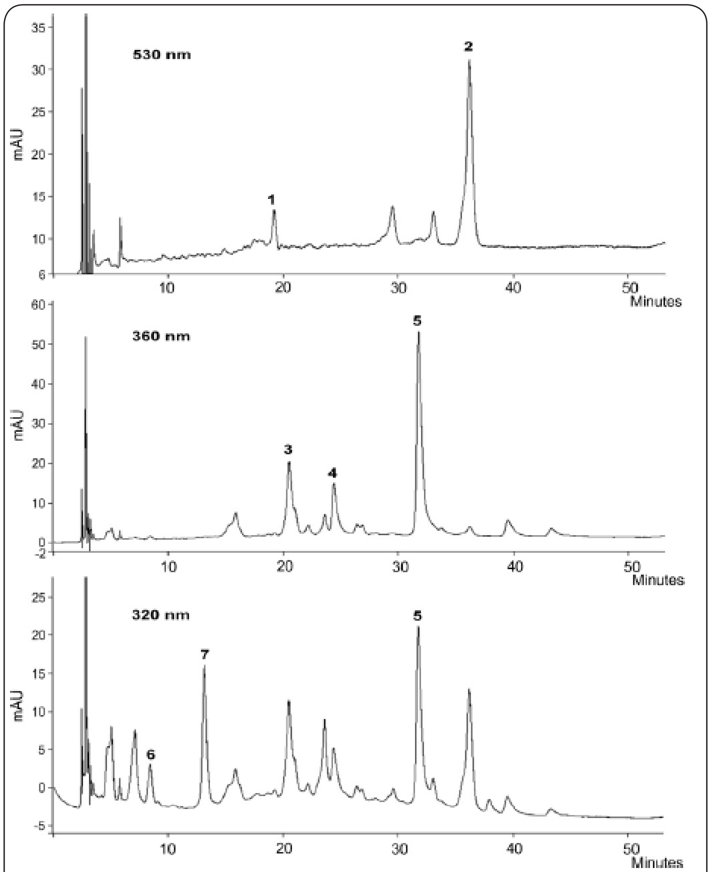

Figure 2: HPLC–DAD chromatograms of the wine lees spray-dried extract. Identified phenolic compounds by HPLC-DAD in wine less 1. Mv3G, 2. Cm-Mv3G (tentatively identified), 3. quercetin-3-b-glucoside, 4. Myricetin 5 quercetin, 6.caffeic acid, 7. p-coumaric acid) (Adopted by [36]).

Phenolic compounds contained in grape seeds, skin and lees may exert, if extracted properly, several health benefits due to their possible antioxidant, anticancer, antimicrobial, hepatoprotective, anti-aging and anti-inflammatory activities and activation of apoptosis signal [37]. Reactive oxygen and nitrogen species contribute to the development of many degenerative pathologies (Figure-2), either by damaging biological structures or changing redox cellular status or taking part in intracellular signaling.

It is opined that phenolic compounds not only suppress the production of reactive oxygen and nitrogen but also act in cells and tissues enhancing antioxidant capacity endogenously (glutathione synthesis) and generally may affect the expression of specific genes [38]. It should be mentioned that the cardio-protective action of polyphenols is likely to be considered as the synergistic outcome of several biological activities including endothelial functionality improvement, LDL uptake decrease, LDL oxidation diminution and aggregation, blood pressure reduction and platelet aggregation inhibition [39,40]. Lazzè et al. (2009) determined that the grape extract possess a strong antiradical activity in the in vitro 2,2-diphenyl-1 picrylhydrazyl radical assay and protects against reactive oxygen species production in human colon adenocarcinoma cells (Caco-2). On the contrary, no positive effects noted in the citronellal thermo oxidation, implying a power less protective action against lipid peroxidation in Caco-2 cells. However, the clonogenic assay and the cell cycle distribution analysis evinced that the waste polyphenolic extract had a notable anti-proliferative effect in tumor cell line [41]. Ali et al. (2015) investigating the antioxidant effect of grape seed and grape skin against Ehrich solid tumor (EST) in mice, opined that supplementation of grape seed and skin in the standard diet in EST bearing mice, potentially recovered liver function enzymes, reduced lipid peroxidation level, augmented antioxidant parameters, normalized liver protein and DNA contents and improved the pathologically examined hepatic lesions. That study in other words, revealed that grape seeds and skins, forming a dietary supplement, possibly are capable of augmenting the antioxidant defense system and in that manner protect liver against oxidative stress induced by Ehrlich solid carcinoma tumors. Interestingly, proanthocyanidins have gained special interest since these phenolic compound emerged 50 times greater antioxidant power than vitamin C and 20 times greater than vitamin E [42]. Grape seed extract might be employed as a novel alternative treatment to limit both dietary fat absorption and fat accumulation in adipose tissue. That is attributed to the fact that grape seed extracts may inhibits fat-metabolizing enzymes pancreatic lipase and lipoprotein lipase [43]. Also, preclinical in vivo studies in rats have revealed that winery residues prevent Low Density Lipoproteins (LDL) oxidation. It has been demonstrated that a 15% grape pomace supplementation in a cholesterol diet (0.3%) resulted in reducing the rat liver and serum levels of cholesterol by half, while high-density lipoproteins (HDL) increased by 26% [44].

Numerous reports suggest that resveratrol inhibit cellular events associated with tumor initiation, promotion and progression as a result of anti-inflammatory, proapoptotic, antiangiogenic, chemo-, and radio-sensitizing properties [45,46,47]. Trans-resveratrol may prevent carcinogenesis in the three stages of tumor development [48]. It seems that this bioactive compound enhances apoptosis and tumor cells death, vascularizing the micro-tumors via blocking metalloproteases and reducing inflammation via inhibiting the action of cyclooxygenase 2 (inflammation biomarker) [49]. Zoberi et al. (2002) suggested that resveratrol may plays a significant role in the regulation of cell cycle progression since pretreatment with resveratrol, in cervical cancer cell lines, inhibits cell division and induces an early S-phase arrest [50]. Gomez et al., (2013) reported that resveratrol is capable of inhibiting the enzyme 6-phosphofructo-1-kinase (PFK), which is critical for glycolysis, and its activity is directly associated with intracellular glucose consumption, decreasing viability, glucose consumption and ATP content in the human breast cancer cell line MCF-7. Thus, may act as preventing factor from breast cancer [51].

Polyphenols, as one of the basic functional ingredients derived from grape processing, could be used in a variety of applications with aim to produce foods with added biological role.

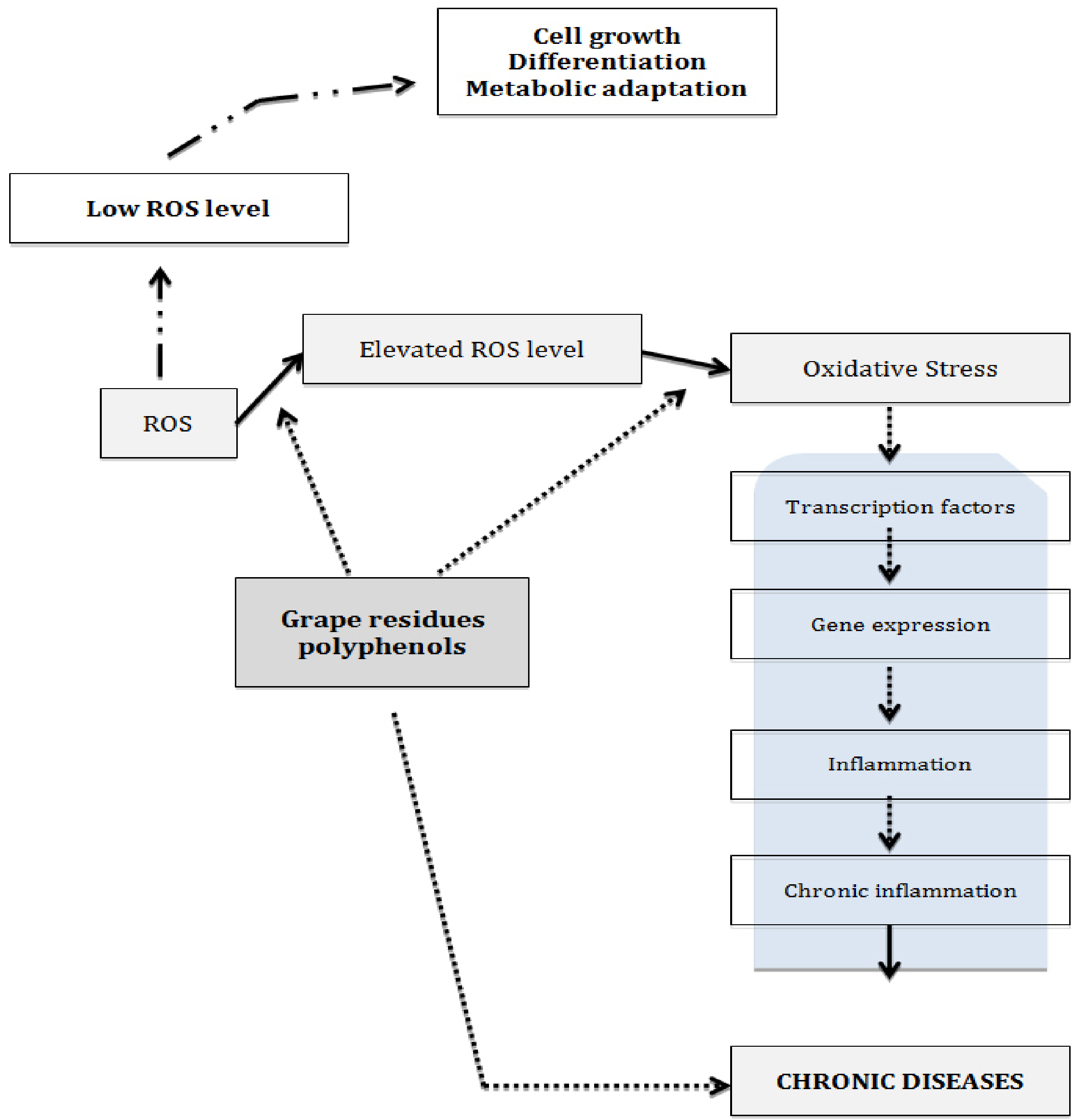

Figure 3: Polyphenols derived of winery waste potential mechanism action against ROS and chronic induced diseases.

Vitamins C and E and Minerals

The average concentration of Vitamin C in grapes is 10.8 mg/100 g edible part [52]. Average grape pomace flour concentration of 26.25 mg/100g Vitamin C has been determined by Sousa et al. (2014) [53]. It has been determined that grape skins contain also Vitamin C, but in lower quantities (4.9 - 12.2 mg/ 100 g), indicating possible challenges in the area of employing Vitamin C derived from winery residues in the production of functional food [54]. Ascorbic acid has been associated with many possible health benefits such as: (1) modest reduction of the cold period, (2) contribution to wound repair and regeneration by stimulating collagen synthesis (3) protection against LDL oxidation and plasma lipid peroxidation as well possible cardiovascular disease development (4) prevention of cancer either by neutralizing free radicals, before they damage DNA and initiate tumor growth, and or by their possible action as a pro-oxidant factor promoting body's own free radicals to destroy tumors in their early stages [55]. It is obvious that this antioxidant vitamin is fundamental ingredient for humans since the body cannot synthesize it. On the other hand, though this nutraceutical has been discovered in 17th century there are many controversies in literature cited publications, regarding cancer treatment and pro-oxidant action. One of the earliest symptoms of Vitamin C deficiency is a general fatigue, explained by the fact that vitamin C is involved in the biosynthesis of carnitine, a compound essential for producing energy by transporting long-chain fatty acids into the mitochondria. Vitamin C deficiency is strongly correlated with many symptoms related to collagen, an essential element in tendon, cartilage, bone and skin function [56]. Overdose effects of vitamin C are rather scarce, since it is water soluble vitamin exerted by urine efficiently. The most recent recommendations for ascorbic acid in healthy individuals is 90 mg/L for men and 75 mg/L for women [57].

Apart from vitamin C also the presence of vitamin E or tocopherol has been reported in grape seed and pomace extracts. Tocopherol is considered one of the most effective natural fat-soluble antioxidant. Baydar et al (2007) found out that pomace oil extract gave higher individual tocopherol contents than the seed oil extract, among five different types of cultivars tested. More specifically, in pomace oil extract, α-tocopherol concentrations ranged from 198.66 to 925.69 mg/kg, γ-tocopherol from 27.53 to111.42 mg/kg and δ-tocopherol ranged from 2.17 to13.59 mg/kg. As far as considered seed oil extracts contents varied from 128.14 to 325.39 for α , 14.37 to 31.73 for γ , 0.62 to 1.63 mg/kg for δ-tocopherol, indicating that a-tocopherol was the most abundant tocopherol and β-tocopherol was absent in both extracts. The variations in concentrations were attributed to different genotypes [23]. Gliszczynska-Swiglo et al. (2004) analyzing individual tocopherols concentrations in grape seed oil found out that a-tocopherol of 100.55 mg/kg was the most abundant. Also found out that also β-tocopherols along with γ-tocopherols existed in seed oil extract (γ+ β 17.14 mg/kg) as well as δ-tocopherols (3.89 mg/kg) [58]. Tocopherols are considered as one of the most effective lipid-soluble antioxidants, protecting cell membranes from peroxyl radicals and mutagenic nitrogen oxide species. Apart from acting as antioxidant, it has been proposed of acting as "gene regulator". The effects have been observed at m-RNA and protein level, propably as a consequence of regulating gene transcription, mRNA stability, protein translation, protein stability and post-translational events [59].

The presence of minerals has also been determined in grape pomace and seed. Iron, potassium, zinc, manganese and sodium have been measured in grape pomace flour (Table-3). The presence of higher levels of potassium than sodium can lead to a balance diet, lowering blood pressure and decreasing the risks of cardiovascular morbidity and mortality. According to dietary reference intake the amount of iron detected in grape pomace (18.8 mg/100 g) could cover the adult daily requirements of both women, which are 8 to 18 mg of iron per day and men (8 mg/day). Considering pomace derived zinc concentrations (0.98 mg/100g) could partially cover recommended daily intake (11mg zinc/day for women and 8 mg/day for men). Lahman et al. (2013) comparing essential elements concentrations contained in grape seeds, derived from white and red varieties winemaking, found out that red varieties contained higher levels of macro elements. Red varieties contained higher Fe, Cu, Zn and comparable Mn levels [60].

Results herein from different research papers revealed the considerable potential of grape waste as a valuable inexpensive source of vitamins and essential elements which are vital to sustain good health.

Conclusion

Vinery by-products (grape pomace, wine lees, grape leaves and grape stems) are capable of interfering in the human metabolism and physiology yielding several beneficial health effects. Moving in that frame the extraction of bioactive ingredients could lead to several diversified opportunities such as adding value to food commodities, improving dietary patterns of population and providing natural means in preventing diseases such as cancer, cardiovascular disease, Alxheimer , and other degenerative diseases, along with decreasing environmental impact and economic losses from waste management strategies. It should be highlighted that the composition of bioactive compounds in grape residues varies and depends on grape cultivar, growth climates, and processing conditions. The extraction methodology followed to obtain each phytochemical compound is vital for the production of possible functional products with diversified health benefits. The use of pomace, lees, stems, leaves, containing several bioactive compounds if used in the food industry can create some opportunities to lower production costs and give rise to new food sources enriched with functional ingredients with pivotal biological action suitable for human consumption. Though more research should be carried out, trying to specify the benefits in health of every specific bioactive compound contained in different grape wastes, it should be noted that grape waste rich in antioxidants, vitamins, unsaturated fatty acids, fibers are really nutritional highlights.

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