Grape Wine and Juice: Comparison on Resveratrol Levels
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Abstract—Resveratrol is a polyphenol found mainly in grape seeds, as well in the peel of red grape berries. As a consequence, it is present also in the grape wine and juice. It is a metabolite produced in the secondary plant metabolism in part as a response to bacteria, fungus or virus infection, as well as to mechanical damages and ultraviolet radiation. Resveratrol is known mainly for its antioxidant, anti-inflammatory and antitumoral properties. Thus, this study aimed to evaluate the effects of the vinification process on the variation of resveratrol levels in wine, comparing to the grape juice manufacturing processes and its consequent resveratrol content. Its bio-availability and metabolic pathways should still be more deeply studied, in order to draw conclusions about the real effect of this compound. During the winemaking process, there is an increase in the extraction of phenolic compounds, while in the production of grape juice, the concentration of these compounds occurs.

Keywords—Vitis spp., byproducts, functional properties.

I. INTRODUCTION
The search for foods capable of helping reducing oxidative process rates in the organism has been subject of numerous researches. This protective effect comes from substances found in some foods, as grapes, also highlighted as source of several polyphenols. This group includes a heterogeneous set of substances from several classes, with antioxidant activity (Vargas et al., 2008).

Grapes present different characteristics, such as flavor and coloring, which is directly related to their polyphenols composition and content, as function of the cultivar group (Vedana, 2008). The phenolic content of raw grape fruits exerts strong influence on the quality of derived products such as juices and wines (ABE et al., 2007).

Grapes and their by-products are rich in phenolic compounds, aromatic substances commonly found in foods of plant origin. Several studies have demonstrated that these substances have anticarcinogenic and antioxidant action (Pimentel et al., 2005).

According to Law No. 7,678, dated November 8, 1988, wine is the beverage obtained by alcoholic fermentation of the simple grape must, healthy and fresh, while the grape juice is the unfermented beverage, obtained from the simple, sulphited or concentrated grape must.

In addition to the in natura grape, its by-products such as grape juice and wine also contain various combinations of phenolic compounds (Torres and Bobet, 2001). Regular consumption of products derived from grapes, as well as fresh fruits, brings benefits such as chemo-preventive activity and cardiovascular protection (Pezzuto, 2008).

As a result of the "French Paradox" (Goldberg et al. 2003), stilbenes as resveratrol and trans-pterostilbene were identified in Vitis vinifera. The French paradox motivated research on the presence and effectiveness of resveratrol because, through the MONICA program, an organized system of data on coronary heart disease (CHD) of the World Health Organization (WHO), it was observed a low incidence of CHD, even with a high-fat diet, smoking and alcohol consumption, by the French population (Castelli, 2001). This fact was partially elucidated by the discovery of high concentration of phenolic compounds present in the wine, as well as resveratrol, described as natural antioxidants (Melzoch et al., 2001).

Being a biologically active substance classified as phytoalexin, resveratrol (3, 5, 4-trihidroxystilbene) is a metabolite produced in the secondary plant metabolism; in part as a response to bacteria, fungus or virus infection, as well as to mechanical damages and ultraviolet radiation (Oliveira, 2010).

According to Freitas et al. (2010), the amount of resveratrol found in wine is supposed to be lower than that found in grape juice. In general, significant concentrations of resveratrol are found in wines and grape juice, but these concentrations vary according to grape origin and type, vinification or juice extraction processes, and fungal infection occurring in wines.

Considering the assumptions previously described, this study aimed to evaluate the effects of the vinification process in comparison to the effects of the grape juice
manufacturing process, on the variation of resveratrol content in the wine and grape juice, respectively.

II. POLYPHENOLS: FUNCTIONAL PROPERTIES OF GRAPES

Functional foods are part of a new food concept, launched in Japan in the 1980’s, through a government program that aimed to develop healthy food for a population that was aging and had a long-life expectancy (Anjo, 2004). In addition to the basic nutritional properties of foods, relevant results obtained in recent years attribute the influence of secondary compounds on human health. For example, high concentrations of polyphenolic compounds with biological activity are found in alcoholic and non-alcoholic fruit products, classifying them as nutraceuticals or functional foods (Machado, 2010).

Thus, the antioxidant capacity of phenolic compounds is due to the ease with which a hydrogen atom of the aromatic hydroxyl group can be donated to a free radical and the ability of the phenolic group to support an unpaired electron (Pimentel, 2005). This action reduces the oxidation, for example, of LDL by free radicals decreasing the possibility of atherogenicity. Vitis labrusca grapes, used for the production of commercial juices and wines, are rich in polyphenolic compounds (Ashraf-Khorassani and Taylor, 2004).

Chemopreventive activity and cardiovascular benefits resulting from regular grapes and their products consumption, are highlighted in several studies (Pezzuto, 2008). According to Signorelli and Ghidoni (2005), there are also protective effects against the occurrence of Alzheimer’s disease associated to consumption of phenolic compounds, due to the occurrence of a potential cholinesterase activity, since the disease is associated with cholinergic deficiency.

The performance of wine in different pathologies, such as atherosclerosis, LDL reduction has already been verified by several authors. The beverage decreases the formation of free radicals and increases the resistance of the collagen fibers (Souza et al., 2006).

The antioxidant activity which characterize the grape and its derivatives as functional foods, as already mentioned, is directly related to the presence of phenolic compounds. The generic term “phenolic compound” encompasses all phenolic core substances, and phenols are compounds that contain a single aromatic ring with one or more hydroxyl groups, while those with multiple phenolic rings in their structure are called polyphenolic (Silva, 2010).

III. CLASSIFICATION OF PHENOLIC COMPOUNDS

Flavonoids and derivatives of benzoic acid and cinnamic acid are the two major groups of phenolic compounds. Flavanols (catechin, epicatechin and epigallocatechin), flavonols (kaempferol, quercetin and myricetin) and anthocyanins, are part of flavonoids, while phenolic, hydroxybenzoic and hydroxycinnamic acids belong to the group of benzoic acid and cinnamic acid derivatives. Another class is that of the stilbenes, to which the polyphenol resveratrol is framed (Abe et al., 2007).

Grape is one of the largest fruit sources of phenolic compounds. According to Malacrida and Motta (2005), the main concerned components of grape are flavonoids (anthocyanins, flavanols and flavonols), stilbenes (resveratrol), phenolic acids (derived from cinnamic and benzoic acids) and a wide variety of tannins.

3.1. Stillbenes

Stilbenes make up another class of phenolic compounds, among which the cis- and trans-resveratrol and cis- and trans-piceid monomers stand out. Compounds named phytoalexins, precursors of viniferous oligomers, are synthesized by the grapevine plant in response to stress, as previously stated (Gris, 2010).

3.2. Resveratrol

Compound originating from a family of molecules including glycosides and polymers called viniferins, resveratrol exists in the cis- and trans- configurations (Figure 1). According to Copelli (2005), this component is included in the class of antibiotics known as phytoalexins, since it has the capacity to inhibit the progression of infections caused by fungi.

According to Sautter (2003), resveratrol can be found in nature in glycosidic or aglycosidic forms, and the former can be found under several denominations according to the glycone involved and the isomeric form, as shown in Figure 2.
Resveratrol was found by Tyukavkina (1972), in Pinus sibirica bark, while looking for the presence of another stilbene, the pinitilbene. Langcake and Pryce (1976) for the first time reported the presence of the trans-resveratrol isomer in Vitis vinifera and other species of the Vitaceae family, and in 1977 they synthesized ε-viniferin in vitro, and after two years identified the trans-pterostilbene. As early as 1995, Jayatilake et al. (1995) identified a new stilbene derivative, which was named resveratrol triacetate (3,4',5-triacetoxy hydroxy stilbene, l) in a Porifera species of the Anchinoidae family, Kirkpatrickia varilosa.

Resveratrol content decreases drastically, which hinders the detection of the compound. However, the compound is present throughout the vine plant and not only in the fruit, although in different concentrations. A study developed by Melzoch et al. (2001), with wines from the "Mikulovská" region in the Czech Republic, shows significant concentrations of resveratrol in leaves and especially in engage (Table 1).

The concentration of resveratrol in the grape berry is higher in the peel than in the pulp or seed, since the peel suffers mechanical, chemical or metabolic disorder damage by sun radiation (Jeandet et al., 1991).

Malonyl-CoA, one of the precursor coenzymes to the synthesis of resveratrol, is derived from a combination of the acetyl-CoA units formed from phenylalanine, a compound synthesized in plants from sugars via the chiquimic acid route (Copelli, 2005). This occurs through oxidative deamination catalyzed by phenylalanine ammonia biase, which converts phenylalanine to cinnamic acid which is subsequently enzymatically hydroxylated to c-coumaric acid; in the final step, p-coumaril CoA is then formed by free coenzymes.

The biosynthesis of resveratrol occurs through the repetitive condensed decarboxylation of the p-coumaril residue of p-coumaril-CoA with 3 units of malonyl-CoA, these reactions being catalyzed by stilbene synthetase (Dias, 2009). Subsequently, reactions combine native resveratrol, which can give rise to chalcone, glucosyl or sulfate residues in position 3 of the biphenolic ring, the first form of resveratrol being susceptible to oxidation degradation, while the piccoid form or glycosylation is resistant (Signorelli and Ghidoni, 2005).

In the formation of chalcone, the chalcone synthase converts the unstable molecule, called native resveratrol to the respective compound, and during the process of resveratrol formation the release of 4 molecules of carbon dioxide for each mol of said synthesized compound (Sautter, 2003).

Environmental factors, such as mineral nutrition, may influence the synthesis of phytoalexins, modifying the expression of the genetic characteristics of the plant (Copelli, 2005). This author also reports the effects of the main macronutrients as nitrogen and potassium, showed that when the grapevine is fertilized with high potassium compared to nitrogen, resveratrol synthesis is increased in both viniferous and hybrid varieties.
Resveratrol is known mainly for its antioxidant, anti-inflammatory and antitumoral properties (Soleas et al., 1997; Baxter, 2008). The compound acts on an enzyme called lipoygenase, which has independent activities, which are dioxygenase related to oxidation induction and hydroperoxides, involved in xenobiotic detoxification (Sautter, 2003). According to Pinto et al. (1999), resveratrol acts inhibiting the dioxygenase activity of lipoygenase, however, without interfering with the hydroperoxidase activity of this same enzyme.

Studies by Fuhrman et al. (1995) have shown that the consumption of grape juice and wine is able to reduce lipid peroxidation (Halliwel and Gutteridge, 2000). Resveratrol, in addition to other biological properties previously mentioned, have been reported by Baxter (2008) and David et al. (2007), as reducing symptoms of menopause due to the structural similarity of stilbene to synthetic estrogen; improves tolerance in diabetics to glucose, protects against osteoporosis, cancer and Alzheimer's disease.

Regarding its anti-inflammatory action, resveratrol inhibits the transcription and activity of cyclooxygenase 1 and 2 (COX-1 and COX-2), responsible for the catalysis of the oxidative pathway of arachidonic acid, thus interrupting the production of prostaglandins, inflammatory agents, besides interfering with the cascade of arachidonic acid and the genesis of tumors (Subbaramaiah et al., 1998).

Resveratrol can act as an anti-proliferative agent, promoting apoptosis in tumors in a controlled manner in some types of tumors (Sautter, 2003). Apoptosis or programmed cell death, requires energy and protein synthesis for this to occur (Sautter, 2003); in this process, there is no release of the cellular content to the interstitium, so there is no inflammation around the dead cell, thus differing from necrosis. Resveratrol exhibits antitumoral activity due to its ability to induce apoptosis. It inhibits cell transformation, inducing tumor cells to apoptosis (Soleas et al., 1997).

Resveratrol does not exhibit toxicity at concentrations present in foods, acting in a beneficial manner as previously described. Resveratrol is a competitive antagonist of dioxin and other AhR ligands, having low toxicity and high potency as a prophylactic agent against aryl hydrocarbon-induced pathologies (Casper et al., 1999).

### 4.2. Functions

#### Table 1: Resveratrol distribution on grapefruit plant and wine at Mikulovská region, Czech Republic.

| Wine Type | Resveratrol Content |
|-----------|---------------------|
|           | Leaves mg Kg\(^{-1}\) dry | Engage mg Kg\(^{-1}\) dry |
|           | Total | Trans | Cis | Total | Trans | Cis |
| Cabernet  | 5.0   | 1.3   | 6.3 | 7.0   | 7.0   |
| Pinot noir| 1.6   | 1.2   | 2.8 | 13.  | 13.0  |
| Laurot    | 4.4   | 1.6   | 6.0 | 15.0  | 2.0   | 17.0 |
| Tintet    | 3.6   | -     | 3.6 | 440   | 6.8   | 446  |
| Neronet   | 9.9   | -     | 9.9 | 209   | 2.3   | 212  |
| Merlot    | 7.1   | 3.0   | 10.1| 15.0  | 1.8   | 16.8 |
| Erilon    | 44.2  | 2.2   | 46.2| 482   | 9.9   | 491  |
| Rubikon   | 14.6  | 2.6   | 17.2| 6.0   | 6.0   |
| Hibernal  | 5.4   | 1.3   | 6.7 | 63.0  | 3.4   | 66.4 |

According to Boliani et al. (2008), the production of resveratrol and other stilbenes is also induced by solar radiation. In order to evaluate the production capacity of different grape varieties, irradiation methods applied in the post-harvest period allowed the detection of varieties with potential for producing wines with higher contents of these compounds (Bertagnolli et al., 2007).

In order to increase resveratrol content in white wines, a pilot study was conducted to investigate the feasibility of developing yeasts with the ability to produce resveratrol during wine fermentation by altering the metabolic pathway of phenylpropanotes in *Saccharomyces cerevisiae*, since red wine has much higher levels of resveratrol compared to white wine, as the peel of red grape berries is much richer in resveratrol compared to peel from white grape berries (Becker et al., 2003).
glucoside may be absorbed from grape juice by the small intestine, such as flavonoid glucosides, in sufficiently biologically active amounts. In in vivo experiments, Kuhnle et al. (2000) and Andlauer et al. (2000) observed that resveratrol is absorbed as resveratrol glucuronide in the small intestine at a ratio of 96.5% and 16.8%, respectively.

Despite all the benefits to human health promoted by resveratrol, reported in numerous researches, bioavailability and metabolic pathways should still be more deeply studied, in order to draw conclusions about its real effect of this compound (Frémont, 2000; Bhat et al., 2004).

Pinto et al. (1999) state that resveratrol can be used as a natural lipid antioxidant in foods, influencing the formation of desired aroma and flavor in animal and vegetable products; however, the authors remarks that off-flavors can be generated.

Gambini et al. (2015) state that resveratrol presents antioxidant properties and ability to bind to organic compounds such as hormone receptors and enzymes; this interaction with biological molecules confers to resveratrol beneficial effects against tumors and cardiovascular issues. Paiva (2018) remarks that flavonoids, flavonols and anthocyanins, associate to non-flavonoid compounds as resveratrol and phenolic acids to improve the efficiency on health improvement and conservation.

V. COMPARATIVE – RESVERATROL LEVELS

All food goes through physico-chemical modifications that can be beneficial or not to nutrients maintenance during the process of transformation, industrialization or even during the simple home food preparation.

During the winemaking process, there is increase in the extraction of phenolic compounds, while in the production of grape juice, the concentration of these compounds occurs. Thus, a comparison on the levels of resveratrol in grape wine and juice are significant to guide consumers on the decision of using alcoholic or non-alcoholic beverages regarding the consumption of adequate levels of resveratrol for its benefits to the organism.

5.1. Grape Juice

Depending on the production method, the final chemical composition of the wine or juice will be influenced. In grape juice production by the pressing method, there is great effect on the extraction of resveratrol, although the cultivar has a significant influence on resveratrol concentration (Sautter et al., 2005). According to Freitas et al. (2010), in wine the amount of resveratrol is usually lower than that found in grape juice, because the juice passes through cooking and hot packing, which promotes the concentration of several compounds, including resveratrol.

In a study developed by Sautter (2003), which aimed to quantify the levels of resveratrol (Table 2 and Table 3) in grape juice, it is observed the presence of trans- and cis-resveratrol, varying according to juice type and processes used for formulation, such as dilution of the juice and type of packaging.

Table 2: Trans-resveratrol contents in distinct grape juice types.

| Juice Type            | Trans-resveratrol (mg L⁻¹) |
|-----------------------|----------------------------|
| Integral              | Min | Max | Mean | SD¹ | CV²  |
| Reprocessed           | 0.39 | 0.44 | 0.41 | 0.035 | 4.26 |
| Reconstituted         | 0.61 | 0.90 | 0.75 | 0.205 | 13.5 |
| Sweetened             | 0.19 | 0.32 | 0.25 | 0.053 | 84.0 |
| Nectar                | -    | -    | 0.41 | 0.0004 | 0.97 |

¹ Standard deviation of the mean; ² Coefficient of variation around the mean (%). Source: Sautter (2003).

Table 3: Cis-resveratrol contents in distinct grape juice types.

| Juice Type            | Cis-resveratrol (mg L⁻¹) |
|-----------------------|--------------------------|
| Integral              | Min | Max | Mean | SD¹ | CV²  |
| Reprocessed           | 0.07 | 0.26 | 0.16 | 0.134 | 40.71 |
| Reconstituted         | 1.22 | 1.59 | 1.40 | 0.261 | 9.31 |
| Sweetened             | 0.07 | 0.67 | 0.38 | 0.330 | 86.84 |
| Nectar                | -    | -    | 1.24 | 0.001 | 0.08 |

¹ Standard deviation of the mean; ² Coefficient of variation around the mean (%). Source: Sautter (2003).

Among the types of grape juice evaluated, reconstituted and sweetened grape juice presented the highest coefficient of variation for trans-resveratrol (CV = 84.0%), due both to the type of cultivar and processing method. Grape nectar had higher trans-resveratrol concentration than simply extracted juice, because nectar, according to the Ministry of Agriculture and Livestock (MAPA) Regulation 1, is obtained from the dilution in drinking water of the edible part of the vegetable or its extract, holding 51% of juice, while the extracted juice is in its natural concentration, not added with sugar. According to Sautter (2003) this can be explained by the processing of the nectar, which undergoes smaller losses of the trans-resveratrol, since in extracted juice processing, there is filtration and stabilization.

Sautter (2003) reports that hot processes such as pasteurization, pressure and maceration increase the concentration of trans-resveratrol, as they also favor the
The phenolic compounds are extracted during the maceration of the grape in the vinification process, transferring them to the must. However, most of these substances remain in the grape residue at different concentrations, depending on the process applied or the variety of the raw material (Campos, 2005).

According to Roggero (1996), the cis- isomer, which is not detected in grape peel, is formed from the isomerization of trans-resveratrol or from the breakdown of resveratrol polymers during wine fermentation. According to Soleas et al. (1995), during wine clarification, the predominant form of resveratrol in wine is trans-, the cis- form being found in lower concentrations, which is probably formed during vinification.

According to Frankel et al. (1995), during wine manufacturing, when grapes are crushed with stalk, peel and seed, more phenolic compounds are incorporated in the wine. Jeandet et al. (1995) and Roggero (1996) verified that both plant diseases caused by *Botrytis cinerea* (grey mould), as well as the wine aging, modify the concentration of resveratrol in wines. The authors found that resveratrol is relatively stable in wine, and even in older wines, these may have higher concentrations compared to young wines.

The difficulty in identifying most of the factors responsible for the variation in resveratrol concentration in wines, is mainly associated to problems in the execution of controlled experiments with alcoholic fermentation. These factors need specific investigation, because during the processing a range of interferences occurs (Trevisan, 2003).

According to Frémont (2000), variations in the concentration of resveratrol were detected in red wines from countries such as the United States, France, Spain and Japan. These variations depend on plant infection by gray mould, grape variety, geographical origin and winemaking process. However, subsequent studies have shown that a high contamination by gray mold is not favorable to the formation of resveratrol, since grapes with 10% infection originates wines with high resveratrol contents, but wines obtained from grapes with 40% or 80% infection resulted in wines with lower resveratrol concentration. This result lead researchers to believe that high levels of contamination by *Botrytis* causes resveratrol degradation by the fungus enzymes (Frémont, 2000).

Evaluating the content of resveratrol in Japanese white and red wines, it can be verified that the former presented 0.027 mg L⁻¹, while the latter resulted in 0.175 mg L⁻¹. Wines from Spain showed average values of 0.13 mg L⁻¹, and Portuguese wines 0.21 mg L⁻¹ for white and 1.25 mg L⁻¹ for red wines (Trevisan, 2003). Due to the alterations caused by vinification on resveratrol concentrations, studies were conducted to understand the influence of the steps of maceration, fermentation and clarification on the content of this important wine component (Copelli, 2005).

The extraction of resveratrol is strongly influenced by the maceration process. When comparing wines that underwent longer maceration with those that went through the same process during a shorter time (short maceration), they presented 1.84 mg L⁻¹ and 0.81 mg L⁻¹, respectively (Trevisan, 2003). Most significant concentration is in red wines in part because they remain for a longer time in contact with the berry peel, whereas in white wines, the peel is separated at the beginning of the process. However, too much maceration may lead to the extraction of phenolic compounds that provide undesirable characteristics in wines, such as excessive astringency and bitter taste, which can be removed later (Copelli, 2005).

A study reported by Copelli (2005) revealed that the maximum level of resveratrol in the must was found between three and eleven days after maceration, where the extraction of resveratrol from the peel is facilitated by the production of ethanol during fermentation, since the compound is more soluble in ethanol than in water, and is consequently more easily extracted from the peel during fermentation, which do not occur during juice production.

Phenolic compounds have their values frequently reduced during clarification, through the addition of clarifying agents that aid in wine clarification and stability (Copelli, 2005). The use of bentonite, egg albumen and diatomaceous earth as clarifying agents exert no influence on resveratrol content of wines, and non-significant amounts of resveratrol are removed by using gelatin and silica gel. However, the addition of high levels of activated carbon reduces resveratrol content by about 50%, while its isomers are reduced in about 80%.
and the use of PVPP (polyvinypolyprrolidone) reduces resveratrol levels by 33 % (Trevisan, 2003).

According to Bertagnolli et al. (2007), trans-resveratrol content increases during fermentation, regardless of the vinification technique used. Samples of wines from carbonic maceration resulted in slight decline due to the atmosphere rich in CO₂ where the must was stored, which inhibited the route of formation of resveratrol at the end of the main alcoholic fermentation.

VI. CONCLUSION
In grape juice, the variation of cis-resveratrol in the reconstituted and sweetened grape juices, may be associated with juice exposure during industrial processing. High concentration of cis-resveratrol in the reprocessed juice were also observed due to the shelf life of the elaborated juice packaged in a PET-type package and the consequent transformation of trans-resveratrol to cis-resveratrol.

In red wine, phenolic compounds have their values frequently reduced during clarification, through the addition of clarifying agents. However, bentonite, egg albumen and diatomaceous earth as clarifying agents exert no influence on resveratrol content of wines, and non-significant amounts of resveratrol are removed by using gelatin and silica gel. However, the addition of high levels of activated carbon or PVPP reduces resveratrol content.

During the winemaking process, there is an increase in the extraction of phenolic compounds, while in the production of grape juice, the concentration of these compounds occurs.

Overall, the resveratrol content, and its isomers, tend to be similar in grape juice and wine, although with large variation ranges in both of them, depending on the manufacturing procedures. These differences are mainly attributed to the juice processing or reprocessing procedures; the clarifying agents for wine; grape variety, edaphoclimatic and cultivation conditions; and harvesting and post-harvesting procedures. The interferent factors on resveratrol level that are controllable, need to be correctly adjusted to maximize resveratrol levels in the final product.

REFERENCES
[1] Abe, L. T., Da Mota, R. V., Lajolo, F. M., Genovese, M. I. (2007). Compostos Fenólico e Capacidade Antioxidante de Uvas Vitis labrusca e Vitis vinifera L. Ciência e Tecnologia de Alimentos, 27, 394-400.
[2] Adrian, M., Jeandet, P., Bessis, R., Joubert, J. M. (1996). Induction of phytoalexin (resveratrol) synthesis in grapevine leaves treated with aluminium chloride (AlCl₃). Journal of Agricultural and Food Chemistry, 44, 1979-1981.
[3] Ali, K., Maltese, F., Choi, Y., Verpote, R. (2010). Metabolic constituents of grapevine and grape-derived products. Phytochemistry Reviews, 9(3), 357-378.
[4] Andlauer, W., Kolb, J., Siebert, K., Fürs, P. (2000). Assessment of resveratrol bioavailability in the perfused small intestine of the rat. Drugs under Experimental and Clinical Research, 26, 47-55.
[5] Anjo, D. L. C. (2004). Alimentos funcionais em angiologia e cirurgia vascular. Jornal Vascular Brasileiro, 3, 145-154.
[6] Ashraf-Khorassani, M., Taylor, L. T. (2004). Sequential Fractionation of Grape Seeds into Oils, Polyphenols, and Procyanidins via a Single System Employing CO₂– Based Fluids. Journal of Agriculture and Food Chemistry, 52, 2440-2444.
[7] Baxter, R. A. (2008). Anti-aging properties of resveratrol: review and report of a potent new antioxidant skin care formulation. Journal of Cosmetic Dermatology, 7, 2-7.
[8] Becker, J. V. W., Armstrong, G. O., Van Der Merwe, M. J., Lambrechts, M. G., Vivier, M. A., Pretorius, I. S. (2003). Metabolic engineering of Saccharomyces cerevisiae for the synthesis of the wine-related antioxidant resveratrol. FEMS Yeast Research, 4, 79-85.
[9] Bertagnolli, S. M. M., Rossato, S. B., Silva, V. L., Cervo, T., Sautter, C. K., Hecktheuer, L. H., Penna, N. G. (2007) Influência da maceração carbônica e da irradiação ultravioleta nos níveis de trans-resveratrol em vinhos de uva cabernet sauvignon. Revista Brasileira de Ciências Farmacêuticas, 43, on-line.
[10] Bhat, K. P. L., Kosmeder, J. W., Pezzuto, J. M. (2004). Biological effects of resveratrol. Antioxidants & Redox Signaling, 3, 1041-1064.
[11] Boliani, A. C., Fracaro, A. A., Corrêa, L. S. (2008). Uvas rústicas: cultivo e processamento em regiões tropicais. Iales: Universidade Gráfica e Editora.
[12] Campos, L. M. A. S. (2005). Obtenção de extratos de bagaço de uva Cabernet Sauvignon (Vitis vinifera): parâmetros de processo e modelagem matemática. Florianópolis: UFSC, 2005. Dissertation (Master in Food Engineering), Federal University of Santa Catarina.
[13] Casper, R. F., Quesne, M., Rogers, I. M., Shirotá, T., Jolivet, A., Milgrom, E., Savouret, J. F. (1999). Resveratrol has antagonist activity on the aryl hydrocarbon receptor: Implications for prevention of dioxin toxicity. Molecular Pharmacology, 56, 784-790.
[14] Castelli, T. (2001). Ecologie et systematique des kevres du vin. In: Aquarone, E., Borzane, W., Schemedell, W., Lima, U. A. *Biotecnologia industrial: biotecnologia na produção de alimentos*. São Paulo: Élgard Blucher.

[15] Copelli, E. V. (2005). Avaliação de trans-resveratrol em vinhos da cv. Cabernet Sauvignon tratado com Fitofos K. Plus. *Monography (Technology in Winemaking and Enology)*, Federal Center for Technological Education, Bento Gonçalves, Brazil.

[16] David, J. M. P., David, J. P., Santos, V. L. C. S., Santos, M. L. S., Mota, M. D. (2007). Resveratrol: Ações e Benefícios à Saúde Humana. *Diálogos & Ciência*, 5, 14-23.

[17] Dias, J. F. (2009). Determinação dos conteúdos de resveratrol em vinhos tintos de duas regiões brasileiras. Dissertation (Master in Food Science), Federal University of Rio de Janeiro.

[18] Dixon, R. A. (2001). Natural products and plant disease resistance. *Nature*, 411, 843-847.

[19] Frankel, E. N., Waterhouse, A. L., Teissedre, P. L. (1995). Principal phenolic phytochemical in selected California Wines and their antioxidante activity in inhibiting oxidation of human low-density lipoproteins. *Journal of Agricultural and Food Chemistry*, 43, 890-894.

[20] Freitas, A. A., Detoni, A. M., Clemente, E., Oliveira, C. C. (2010). Determinação de resveratrol e características químicas em sucos de uvas produzidas em sistemas orgânico e convencional. *Ceres*, 57, 1-5.

[21] Frémont, L. (2000). Minireview: Biological effects of resveratrol. *Life Sciences*, 66, 663-673.

[22] Fuhrman, B., Lavy, A., Aviram, M. (1995). Consumption of red wine with meals reduces the susceptibility of human plasma and low-density lipoprotein to lipid peroxidation. *American Journal of Clinical Nutrition*, 61, 549-554.

[23] Gambini, J., Inglês, M., Olaso, G., Lopez-Gruelo, R., Bonet-Costa, V., Gimenno-Mallench, L., Mas-Bargues, C., Abdelaziz, K. M., Gomez-Cabrera, M. C., Vina, J., Borras, C. (2015). Properties of resveratrol: in vitro and in vivo studies about metabolism, bioavailability, and biological effects in animal models and humans. *Oxidative Medicine and Cellular Longevity*, 2015, 837042.

[24] Goldberg, D. M., Yan, J., Soleas, G. J. (2003). Absorption of three wine-related polyphenols in three different matrices by healthy subjects. *Clinical Biochemistry*, 36, 79-87.

[25] Gris, E. F. (2010). Perfil fenólico e atividades antioxidante e hipolipemiante de vinhos de variedades *Vitis vinifera* cultivadas em São Joaquim – SC – Brasil. 1thesis (Doctorate in Food Science), Federal University of Santa Catarina, Florianópolis.

[26] Halliwell, B., Gutteridge, J. C. (2000). Free radicals and antioxidant in the year 2000. *Annals of the New York Academy of Sciences*, 899, 136-147.

[27] Jayatilake, G. S., Baker, B. J., McClintock, J. B. (1995). Isolation and identification of a stilbene derivative from the Antarctic sponge *Kirkpatrickia variolosa*. *Journal of Natural Products*, 58, 1958-1960.

[28] Jeandet, P., Bessis, R., Gautheron, B. (1991). The production of resveratrol (3,5,4’ – trihydroxystilbene) by grape berries in different developmental stages. *American Journal of Enology and Viticulture*, 42, 41-46.

[29] Jeandet, P., Bessis, R., Shaghi, M., Meunier, P., Trollat, P. (1995). Resveratrol content of wines of different ages: relationship with fungal disease pressure in the vineyard. *American Journal of Enology and Viticulture*, 46, 1-4.

[30] Krikorian, R. et al. (2012). Concord grape juice supplementation and neurocognitive function in human aging. *Journal of Agricultural and Food Chemistry*, 60, 5736-5742.

[31] Kuhnle, G., Spencer, J. P. E., Chowmimoott, G., Schoeter, H., Debnan, E. S., Srai, S. K. S., Rice-Evans, C., Hahn, U. (2000). Resveratrol is absorbed in the small intestine as resveratrol glucoronide. *Biochemical and Biophysical Research Communications*, 272, 212-217.

[32] Langcake, P., Pryce, Ca. (1976). The production of resveratrol by *Vitis vinifera* and other members of Vitaceae as a response to infection or injury. *Physiological Plant Pathology*, 9, 77-86.

[33] Machado, M. M. (2010). Desenvolvimento de uma bebida nutracêutica a partir de resíduos da produção do suco de uva: avaliação de propriedades antioxidantes e físico-bioquímicas. Thesis (Doctorate in Biological Sciences), Federal University of Santa Maria, Brazil.

[34] Malacrida, C. R.; Motta, S. Compostos fenólicos totais e antocianinas em suco de uva. Ciência e Tecnologia de Alimentos, Campinas, v. 25, n. 4, p. 659-664, 2005.

[35] Melzoch, K., Hanžlíková, I., Filip, V., Buckiová, D., Šmidral, J. (2001). Resveratrol in parts of vine and wine originating from Bohemian and Moravian vineyard regions. *Agriculturae Conspectus Scientificus*, 66, 53-57.

[36] Merck. (2001). *The Index Merck: an encyclopedia of chemicals, drugs, and biologicals*. 13th ed. Merck & C.O. 1462.
[37] Nakaune, R., Hamamoto, H., Imada, J., Akutsu, K., Hibi, T. (2002). A novel ABC transporter gene, PMR5, is involved in multidrug resistance in the phytopathogenic fungo Penicillium digitatum. Molecular Genetics and Genomics, 267, 179-185.

[38] Oliveira, D. A. (2010). Caracterização fitoquímica e biológica de extratos obtidos de bagaço de uva (Vitis vinifera) das variedades merlot e syrah. Dissertation (Master in Food Engineering), Federal University of Santa Catarina, Florianópolis.

[39] Paiva, A. P. M. (2018). Fenologia, produção e qualidade de uvas para processamento. Thesis (Doctorate in Agronomy), State University of São Paulo, Brazil.

[40] Pezzuto, J. M. (2008). Grapes and human health: a perspective. Journal of Agriculture and Food Chemistry, 56, 6777-6784.

[41] Pimentel, C. V. M. B., Francki, V. M., Gollücke, A. P. B. (2005). Substâncias bioativas em alimentos funcionais. São Paulo: Varelus, 2005.

[42] Pinto, M. C., García-Barrado, J. A., Macáis, P. (1999). Resveratrol is a potent inhibitor of the dioxygenase activity of lipoxygenase. Journal of Agricultural Food Chemistry, 47, 4842-4846.

[43] Roggero, J. P. (1996). Changes in resveratrol and piceid contents in wines during fermentation or ageing: Comparison of Garnacha and Mourvedre varieties. Sciences des Aliments, 16, 631-642.

[44] Sautter, C. K. (2003). Avaliação da presença de resveratrol em suco de uva. Dissertation (Master in Food Science and Technology), Federal University of Santa Maria, Santa Maria.

[45] Sautter, D. S., Alves, A. O., Mallmann, C. A., Penna, N. G., Hecktheuer, L. H. (2005). Avaliação da presença de resveratrol em sucos de uva. Ciências e Tecnologia de Alimentos, 25, 437-442.

[46] Signorelli, P., Ghidoni, R. (2005). Resveratrol as an anticancer nutrient: molecular basis, open questions and promises. Journal of Nutritional Biochemistry, 16, 449-466.

[47] Silva, A. D. F. (2010). Análise de compostos fenólicos e potencial antioxidante de amostras comerciais de sucos de uva e produtos derivados de uvas vinícolas. Dissertation (Master in Food Science and Technology), Federal University of Paraíba, João Pessoa.

[48] Sokas, G. J., Diamandis, E. P., Goldberg, D. M. (1997). Wine as a biological fluid: history production, and role in disease prevention. Clinical Laboratory Analysis, 287-313.

[49] Sokas, G. J., Goldberg, D., Karumanchiri, A., Diamandis, E. P., Ng, E. A. Influences of viticultural and oenological factors on changes in cis- and trans-resveratrol. Journal of Wine Research, 6, 107-121.

[50] Souza, G. G., Meneghin, L. O., Coelho, S. P., Maia, J. F., Silva, A. G. (2006). A uva roxa, Vitis vinifera L. (Vitaceae) – seus sucos evinhos na prevenção de doenças cardiovasculares. Natureza on line. On-line.

[51] Subbaramiah, K., Chung, W. J., Michaluart, P., Telang, N., Tanabe, T., Inoue, H., Jang, M., Pezzuto, J. M., Dannenberg, A. J. (1998). Resveratrol inhibits cyclooxygenase-2 transcription and activity in phorbol ester-treated human mammary epithelial cells. Journal of Biological Chemistry, 273, 21875-21882.

[52] Torres, J. L., Bobet, R. (2001). New flavanol derivatives from grape (Vitis vinifera) byproducts: antioxidant aminoethylthio-flavan-3-ol conjugates from a polymeric waste fraction used as a source of flavanols. Journal of Agricultural Food Chemistry, 49, 4627-4634.

[53] Trevisan, V. (2003). Influência do tempo de maceração na extração de compostos fenólicos e determinação do trans-resveratrol em vinhos brasileiros. Caixas do Sul: UCS.

[54] Tyukavkina, N. A. (1972). Hydroxyestilbene from the bark of Pinus sibirica. Khim Prir Soedin, 8, 600-603.

[55] Vargas, P. N., Hoelzel, S. C., Rosa, C. S. (2008). Determinação do teor de polifenóis totais e atividade antioxidante em sucos de uva comerciais. Alimentos e Nutrição, 19, 11-15.

[56] Vedana, M. I. S. (2008). Efeito do processamento na atividade antioxidante da uva. Dissertation (Master in Food Technology), Federal University of Paraná, Curitiba.