

Review Article

Wine phenolics: looking for a smooth mouthfeel

Alice Vilela^a, António M. Jordão^b, Fernanda Cosme^{a*}^aCQ-VR - Chemistry Research Centre, University of Trás-os-Montes and Alto Douro, School of Life Science and Environment, Edifício de Enologia, 5001-801 Vila Real, Portugal.^bPolytechnic Institute of Viseu (CI&DETS), Agrarian Higher School, Estrada de Nelas, Quinta da Alagoa, Ranhados, 3500-606 Viseu, Portugal.*E-mail: fcosme@utad.pt (Fernanda Cosme)

Received date: 29-11-2015; Accepted date: 22-12-2015 ; Published date: 04-01-2016

Abstract: Each grape variety has its own phenolic profile. However, the concentration of the phenolic compounds present in wine mainly dependson winemaking processes. Phenolic compounds influence wine sensorial characteristics namely taste or mouthfeel, bitterness, astringency and color. Humans can perceive six basic tastes: sweet, salty; sour; umami; fat-taste and bitter taste. This last basic taste is considered as a defense mechanism against the ingestion of potential poisons. Some of the genes,encoding G-protein-coupled receptors - TAS2Rs, which translate for these distinct bitter compounds detectors have been identified. Different phenolic compounds activate distinguished combination of TAS2Rs.Astringency in wine is primarily driven by proanthocyanidins, soluble protein-proanthocyanidins complexes which diminish the protective salivary film and bind to the salivary pellicle; insoluble protein-proanthocyanidins complex and proanthocyanidins are rejected against salivary film and trigger astringency sensation via increasing friction.

Thus, the aim of this review is to expand the knowledge about the role of wine phenolic compounds in wine sensorial properties, namely in bitterness and astringency phenomenon's.

Key words: wine phenolic compounds, proanthocyanidins, bitter taste, astringency,sensorial properties.

Corresponding author: Fernanda Cosme

Address: Chemistry Research Centre, University of Trás-os-Montes and Alto Douro, School of Life Science and Environment, Edifício de Enologia, 5001-801 Vila Real, Portugal.

Tel.: ++351259350567; fax: ++351259350480

Introduction

Wine is a hydroalcoholic acid solution containing various phenolic compounds. They are present in seeds, skins and stems of the grapes; therefore their concentration in wine is highly affected by winemaking process such as fermentation/maceration lengthsin which extraction occurred.However, the grape variety used in winemakingis also an important factor that affects the wine phenolic composition, since each grape variety has its own phenolic profile (Jordão et al., 1998; Bautista-Ortin et al., 2007;Jordão and Correia, 2012; Costa et al., 2015).Wine phenolic compounds have an importantinfluence in wine sensorial characteristics. For example, monomeric (+)-catechins give bitter taste to wine, whereas polymers cause astringent

Taste (Jackson, 2000; Oliveira et al., 2011).In red wine, phenolic compoundslike, coumaric, caffeic, ferulic and vanillic acids are relatively simple structures while others are complex polymeric structures such as tannins, that can combine with numerous substances including polysaccharides, proteins, and other polyphenols,affectingmouthfeel,bitterness, astringency and color. Anthocyanins and tannins influence the color and color stability of wine besides influencing mouthfeel, depth and astringency (Saint-Cricq de Gaulejac et al., 1998). These complex structures change over time; specifically during the wine aging process,becoming more complex due to the increase ofthe mean degree of polymerization(Suriano et al., 2015).

Wine phenolic composition

Wine contains many phenolic substances, their major sources being grape stems, seeds and skins (Jordão et al., 2001; Cheynier, 2005). However, wine phenolic composition is also determined by yeast metabolism, since they can form important wine color components, including anthocyanins adducts and pigmented polymers (Fulcrand et al., 1998; Benabdelljalil et al., 2000; Blazquez Rojas et al., 2012) or by the type of wine aging process, such as the use of oak wood barrels or oak wood fragments (De Coninck et al., 2006; Jordão et al. 2008). According to several authors (Ribéreau-Gayon et al., 2006; Jordão et al. 2012) the levels of polyphenolic compounds in red wine depended from several factors namely the pomace-contact maceration time and the evolution profile of major polyphenol groups.

Wine phenolic compounds can be classified into two groups: flavonoids and nonflavonoids. The major C₆-C₃-C₆ flavonoids in wine include conjugates of the flavonols, quercetin, and myricetin; the flavan-3-ols (+)-catechin and (-)-epicatechin, and malvidin-3-glucoside and other anthocyanins. The nonflavonoids incorporate the C₆-C₁ hydroxy-benzoic acids, gallic and ellagic acids; the C₆-C₃ hydroxycinnamates caffeic, caftaric, and *p*-coumaric acids, and the C₆-C₂-C₆ stilbenes trans-resveratrol, *cis*-resveratrol, and *trans*-resveratrol glucoside (Waterhouse, 2002; Cosme and Jordão, 2014).

Total phenol content ranged in red wine from 1850-2200 mg/L and in white wine from 220-250 mg/L, being the flavonoid compounds the main phenols in red wine, extracted from grape skins and seeds during the fermentation/maceration process (Waterhouse and Teissedre, 1997; Cristino et al., 2013).

Non-flavonoid phenolic compounds are present in wine at low concentration, and their origin could be from the grape pulp or oak wood barrels used in wine aging. The three main hydroxycinnamates in grapes and wine are those based on coumaric acid, caffeic acid and ferulic acid. In grapes hydroxycinnamic acids exist as esters of tartaric acid and are *p*-coumaric acid, caftaric acid, and fertaric acid, respectively (Somers et al., 1987; Waterhouse, 2002). At the concentration found in wines, the hydroxycinnamates seem to have no perceptible bitterness or astringency, since they are present below their sensory threshold (Verette et al., 1988). Hydroxybenzoic acids comprise *p*-hydroxybenzoic acid, syringic acid, vanillic acid and gallic acid. Gallic acid could be also originated from the hydrolysis of gallate esters of hydrolyzable tannins and condensed tannin (Waterhouse and Teissedre, 1997; Waterhouse, 2002).

Total monomeric flavan-3-ols in red wine ranged from 40–120 mg/L, depending on the extraction process during vinification. However, condensed flavan-3-ol units the so called condensed tannins or proanthocyanidins (0.5 g/L–1.5 g/L in red and 10–50 mg/L in white wine) are the main phenolic compounds in red wine (Waterhouse, 2002). In terms of

sensorial perception, flavan-3-ols ((+)-catechin, (-)-epicatechin, (-)-epicatechin-3-*O*-gallate) can be both bitter and astringent, however in polymer form bitterness is slight, but astringency remains (Su and Singleton 1969, Robichaud and Noble, 1990). Thus, tannins have an important role in wine astringency and also contribute to impart bitterness sensation.

Monomeric anthocyanins extracted from grapes are the main compounds responsible for the color of young red wines (Boulton, 2001). There are five anthocyanidins: cyanidin, peonidin, delphinidin, petunidin and malvidin, which could be at the six-hydroxyl of the glucose, acyl substituted, with ester linkages connecting an acetyl group, a coumaryl group, and a lesser amount of caffeoyl group. There are also derivatives of anthocyanins that result by the interaction of anthocyanins with other molecules such as, vinyl catechol, pyruvic acid, vinyl phenol, acetone, α -ketoglutaric acid, 4-vinylguaiacol or glyoxylic acid (Pinho et al., 2012). For example, pyranoanthocyanins namely, vitisin-A and vitisin-B, are formed by the condensation of anthocyanin, malvidin-3-glucoside with the fermentation by-products pyruvic acid and acetaldehyde, respectively. These compounds are more stable and originate at pH 4.0 deeper colors than monomeric anthocyanins (Morata et al., 2007; Cano-López et al., 2008). During wine aging, polymerization reactions take place and polymeric pigments became responsible for wine color. It was observed that wine color changed from a bright red to a reddish-brown hue. This is associated to the formation of new and more stable polymeric pigments resulting from reactions between anthocyanins and other phenolic compounds, for example, flavan-3-ol monomers and proanthocyanidins (Somers, 1971, Kantz and Singleton, 1991, Singleton and Trousdale, 1992; He et al., 2012). These reactions are based on acetaldehyde mediated condensation, co-pigmentation and self-association reactions (Boulton 2001, Castillo-Sánchez et al., 2008). It is known that anthocyanins do not contribute to mouthfeel sensations; however they are able to contribute to mouthfeel when combined with other species in the form of polymers (Haslam, 1998).

Winemaking technology, including, fermentation temperature and lengths, as well as pH and alcohol concentration influence the wine phenolic concentration. Also, clarification and stabilization techniques used to achieve wine limpidity and stability result in a potential decrease of phenolic content (Mira et al., 2006; Gonçalves and Jordão, 2009; Lasanta et al., 2013; Guise et al., 2014; Ribeiro et al., 2014; Ibeas et al., 2015). For example, the use of fining agents such as gelatin, egg albumin, isinglass and casein/potassium caseinate also could reduce specific phenolic compounds in function of the protein fining agent applied and could lead to changes in color, bitterness and astringency in some wines (Cosme et al., 2007; Braga et al., 2007; Cosme et al., 2008; Cosme et al., 2009; Gonçalves and Jordão, 2009).

Bitterness or astringency?

Phenolic compounds are responsible for bitterness and astringency of many foods and beverages, including wine (Bravo, 1998; Gawel, 1998). Whereas lower-molecular-weight phenolic compounds tend to be bitter, higher-molecular-weight polymers are more likely to be astringent (Noble, 1994). Astringency (drying or puckering mouth feel detectable throughout the oral cavity), may be due to a complexing reaction between polyphenols and proteins of the mouth and saliva (Noble, 1994).

High-molecular-weight polyphenols or tannins have long been regarded as antinutrients because they interfere with protein absorption or reduce iron availability, they complex with proteins, starches, and digestive enzymes and are thought to reduce the nutritional value of foods (Chung et al., 1998).

Phenolic compounds in wine range from low-molecular weight-catechins to high-molecular-weight tannins (Blanco et al., 1998). As referred by Drewnowski and Gomez-Carneros (2000) perceived bitterness and astringency increased as a linear function of concentration for (+)-catechin and for grape seed tannin. Flavonoid monomers such as (+)-catechin and (-)-epicatechin were rated as more bitter than astringent (Thorngate and Noble, 1995). At higher molecular weights, (+)-catechin polymers became progressively more astringent. Thus, wine polyphenols with molecular weights >500, such as grape-seed tannin, were more astringent than bitter (Peleg et al., 1999).

Kallithraka et al. (1997) realized a sensory study of (+)-catechins in a wine model system similar, in composition, to a dry table wine. The results obtained showed that (-)-epicatechin was significantly more bitter and astringent than (+)-catechin. In this study, tasters associated bitterness and astringency with perceived mouth drying and with mouth roughening, especially in higher concentrations of (-)-epicatechin.

Phenols in wine are largely derived from grape skins (30%) and seeds (70%) that remain in contact with fermenting grape juice from 24 to 36 hours for rosé wines and from 4 to 21 days for red wines. Phenolic content of red wines can thus reach 1000–3.500 mg/L, depending on processing conditions (Chandrashekar et al., 2000; Blanco et al., 1998). However, the bitterness of phenolics is reduced by sucrose and is substantially enhanced by ethanol (Noble, 1994). In fact, Lanier et al. (2005) found that some people experience more bitterness when drinking more alcoholic beverages. This phenomenon is directly related to the genes they've inherited and, individual differences in bitterness and sweetness are predictors of alcohol liking and intake in young adults (Lanier et al., 2005). Actually, as previously reviewed by Jordão et al. (2015), consumers know that wines with high alcohol content can cause a gustatory disequilibrium affecting wine sensory perceptions leading to unbalanced wines. Multiple studies (Wooding et al., 2004; Drayna et al., 2003) have linked

variation in TAS2R (taste receptor, type 2) bitter receptor genes, to alcohol intake.

Mechanism of bitter taste perception

The primary organ responsible for the sense of taste is the tongue, which contains the taste receptors to identify non-volatile chemicals in foods and beverages. Taste-stimuli are typically released when food is masticated and dissolved into saliva (pre-digested by oral enzymes, such as amylase, lipase, and proteases (Pedersen et al., 2002)). The taste buds, in the tongue, are located in structures called 'papillae'. These structures are the first stage of gustatory signal processing. Cells within a bud communicate with one another, including electric coupling via gap junctions and cell to cell chemical communication via glutamate, serotonin, and ATP (Breslin and Spector, 2008; Roper, 2013).

Humans perceive nutrients and toxins qualitatively as sweet (elicited by sugars); salty (elicited by sodium ion - Na^+ , and other ions reflecting mineral content); sour (elicited by free hydrogen ions - H^+); savory or umami (elicited by glutamate and other amino acids), fat taste - elicited by products of fats and fatty acids (Keast and Costanzo, 2015) and bitter tasting - reflecting potential toxins in foods (Breslin and Spector, 2008). This last basic taste modality (bitter taste) may be considered as a defense mechanism against the ingestion of potential poisons, since numerous harmful compounds, including inorganic ions and rancid fats, secondary plant metabolites like alkaloids, synthetic chemicals do taste bitter (Meyerhof et al., 2005).

The chemical detectors of the bitter compounds in the tongue can recognize thousands of different chemicals. Some of the genes that translate for these distinct bitter compounds detectors have been identified (Adler et al., 2000; Bufe et al., 2002). These genes encoding G-protein-coupled receptors, TAS2Rs (previously referred to as T2Rs or TRBs), have been suggested to represent bitter taste receptors and are responsible for bitter taste transduction mechanism. An important gene contributing to PTC (the ability to taste the bitterness of phenylthiocarbamide) TAS2R38—taste receptor, type 2, member 38, perception has been identified. The gene located on chromosome 7q36, is a member of the bitter taste receptor family (Duffy et al., 2004).

Recently, it was evidenced by Soares et al. (2013) that different phenolic compounds activate distinguished combination of TAS2Rs: (-)-epicatechin stimulated three receptors (TAS2R4, TAS2R5, and TAS2R39) while pentagalloylglucose activated two receptors (TAS2R5 and TAS2R39). Only one receptor was responded to malvidin-3-glucoside and procyanidin trimer.

The bitterness transduction mechanisms is schematized in Figure 1: Initially, bitter ligands activate TAS2Rs causing a conformational change. The active G-protein, transducin, activates enzyme phospholipase C (PLC- β 2) to generate from to breakdown of phosphatidylinositol

biphosphate (PIP_2) the second messenger - inositol triphosphate (IP_3), initiating the release of Ca^{2+} from intracellular stores (vacuoles). TrpM5 is activated by elevated Ca^{2+} to flow in Na^+ , resulting in depolarization of receptor cell. The combined action of elevated Ca^{2+} and membrane depolarization opens the pannexin 1 hemichannel to release transmitters to brain. Adenosine triphosphate (ATP) is secreted to gustatory afferent glossopharyngeal nerve fibers and ultimately generates a nerve signal in the brain recognized as a bitter taste (Ma et al., 2014).

In wines, in contrary to astringency, a gradual reduction of bitterness is perceived as their molecular weight augments (Noble, 1994). In grape there are evidences of different proportions of galloyl group between the seed and skin fraction. The seed fraction with a higher proportion of galloyl group and a lower mean degree of polymerization (mDP) seems to be perceived as more bitter than the skin fraction (Brossaud et al., 2001).

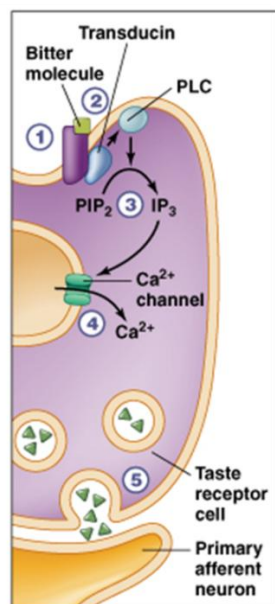


Figure 1 - Bitter taste receptor cell and bitter taste transduction mechanism. Adapted from Moyes and Schulte (2008).

Mechanisms for astringency

Astringency refers to "the complex of sensations due to shrinking, drawing or puckering of the epithelium as a result of exposure to substances such as alums or tannins" (ASTM, 2004). Astringency could be stimulated by salts of multivalent metallic cations, dehydrating agents like ethanol, mineral and organic acids, tannins and small polyphenols (Bajec and Pickering, 2008). However, in wine, astringency is primarily driven by proanthocyanidins, also called condensed tannins (Sáenz-Navajas et al., 2012; Brandão et al., 2014).

The mechanism for astringency was first proposed by Bate-Smith (1954) and is believed to be due to the ability of tannins to bind and precipitate salivary proteins. The loss of

lubrication in the oral cavity, including the tongue, occurs when tannins pass by and they bond to salivary proteins forming insoluble tannin-protein precipitates in the mouth, increasing friction which results in the sensation of astringency (Baxter et al. 1997). The general accepted mechanism for protein-tannin interaction was proposed by Siebert et al. (1996). Concerning this mechanism, a protein has a fixed number of sites to which a tannin can bind. According to the ratio of protein or tannin used, different protein-tannin complexes are formed. According to Charlton et al. (2002), proteins and polyphenols combine to form soluble complexes, but when they grow to colloidal size particles, they become larger, leading to sediment formation.

Charlton et al. in 2002 proposed a 3-stage model of the interaction between tannins and proteins: Initially, hydrophobic associations (π - π) occur between the planar surfaces of the tannin aromatic rings and hydrophobic sites of proteins such as pyrrolidine rings of prolyl residues. Simultaneously, hydrogen bonding effect assists to stabilize the complexes, occurring between the hydroxyl group of tannins and H-acceptor sites (carbonyl and $-\text{NH}_2$ groups) of proteins. Next, the protein-tannin complexes self-associate via further hydrogen bonding to produce soluble larger protein-tannin complexes and then aggregate. Finally, the aggregated complexes are large enough to form insoluble sediment and precipitate from solution.

However, several authors supported the idea that "tannin-protein interaction" is more closely associated with astringency than "tannin-protein precipitation" (Obrique-Slier et al., 2010). Recently, Lee et al. (2012) demonstrated that PRPs (proline-rich proteins) precipitated tannins and alum except for hydrochloric acid while mucins mainly consisting the coating of epithelium tissues were able to precipitate acid and alum except for tannins. Thus, a disturbance of oral lubricating coatings may contribute to the increase of astringency. The loss of oral lubricating films/pellicle allows soluble tannin-protein aggregates or free astringent stimuli to interact directly with oral tissue possibly through receptors. The disturbance of the protective salivary film, could also be the explanation for the dry mouth perception usually associated with the astringent mouth-feel (Ma et al., 2014). According to Brandão et al. (2014), salivary proteins families have relative discriminatory functions in rating the perception of astringency depending on the type of astringent stimuli used. They show that repeated stimulations with procyanidins may differently affect the several families of salivary proteins, suggesting that they could be involved in different stages of the development of astringency. Furlan et al. (2014) recently studied the interaction between monomeric flavan-3-ols and lipid liposomes, indicating that astringency sensation may also implicate the binding between red wine tannins and oral cavity membrane. Gibbins and Carpenter (2013) showed a multiple-modal system by which implicates several possible astringency mechanisms. In Figure

2, is a schematic representation of a possible astringency mechanism.

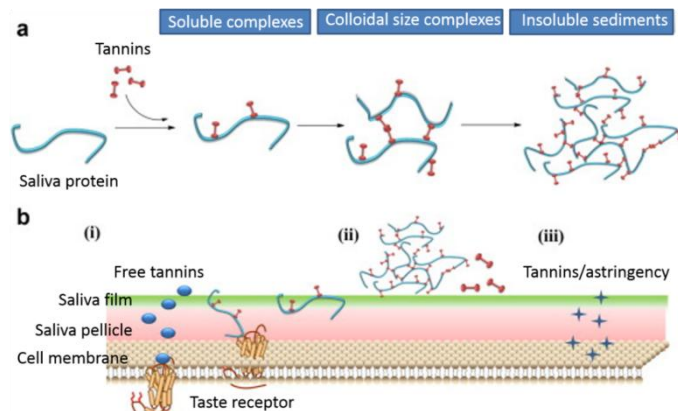


Figure 2 - (a) A 3-stage model of the interaction between tannin and proteins; (b) Astringency stimulation: (i) "Free" tannins and soluble protein-tannin complexes deplete the protective salivary film and eventually bind to the pellicle or even to the receptors exposed; (ii) Insoluble protein-tannin complex and tannins are rejected against salivary film. Insoluble protein-tannin complexes trigger astringency sensation via increasing friction. (iii) Tannins interact with oral cavity membrane causing astringency. Adapted from Ma et al. (2014).

Although it is commonly accepted that interaction between tannins and saliva proteins play an important role in astringency perception in wine (Ma et al., 2014), the physiological and physicochemical mechanisms for this phenomenon are not fully understood and more studies focusing this subject must be done.

Final remarks

This review evidenced the important role of phenolic compounds on the wine sensory characteristics. Therefore, tannin and anthocyanin management during grape-growing by following phenolic maturity of red grapes and during winemaking is a very important factor, for tailoring the wine sensorial characteristics namely taste or mouthfeel, bitterness, astringency and color.

References:

- Adler, E., Hoon, M.A., Mueller, K.L., Chandrashekar, J., Ryba, N.J., Zuker, C.S. (2000). A novel family of mammalian taste receptors. *Cell*, 100, 693–702.
- ASTM. (2004). Standard definitions of terms relating to sensory evaluation of materials and products. In *Annual book of ASTM standards*. Philadelphia: American Society for Testing and Materials.
- Bajec, M.R., Pickering G.J. (2008). Astringency: Mechanisms and Perception. *Critical Reviews in Food Science and Nutrition*, 48, 858-875.
- Bate-Smith, E.C. (1954). Astringency in foods. *Food Chemistry*, 23, 124-135.
- Bautista-Ortin, A.B., Fernandez-Fernandez, J.I., Lopez-Roca, J.M., Gomez-Plaza, E. (2007). The effects of enological practices in anthocyanins, phenolic compounds and wine color and their dependence on grape characteristics. *Journal of Food Composition and Analysis*, 20, 546–552.
- Baxter, N.J., Lilley, T.H., Haslam, E., Williamson, M.P. (1997). Multiple interactions between polyphenols and a salivary prolinerich protein repeat result in complexation and precipitation. *Biochemistry*, 36, 5566-5577.
- Benabdeljalil, C, Cheynier, V, Fulcrand, H, Hakiki, A, Mosaddak, M, Moutounet, M (2000). Evidence of new pigments resulting from reaction between anthocyanins and yeast metabolites. *Sciences des Aliments*, 20, 203–220.
- Blanco, V.Z., Auw, J.M., Sims, C.A., O'Keefe, S.F. (1998). Effect of processing on phenolics of wines. *Advances in Experimental Medicine and Biology*, 434, 327–40.
- Blazquez Rojas, I., Smith, P.A., Bartowsky, E.J. (2012). Influence of choice of yeasts on volatile fermentation-derived compounds, colour and phenolics composition in Cabernet Sauvignon wine. *World Journal of Microbiology and Biotechnology*, 28, 3311–3321.
- Boulton, R. (2001). The copigmentation of anthocyanins and its role in the colour of red wine: A critical review. *American Journal of Enology and Viticulture*, 52, 67–87.
- Braga, A., Cosme, F., Ricardo-da-Silva, J., Laureano, O. (2007). Gelatine, casein and potassium caseinate as wine fining agents: effect on colour, phenolic compounds and sensory characteristics. *Journal International des Sciences de la Vigne et du Vin* 41, 203-214.
- Brandão, E., Soares, S., Mateus, N., Freitas, V. (2014). In Vivo Interactions between Procyanidins and Human Saliva Proteins: Effect of Repeated Exposures to Procyanidins Solution. *Journal of Agricultural and Food Chemistry*, 62, 9562–9568.
- Bravo, L. (1998). Polyphenols: chemistry, dietary sources, metabolism, and nutritional significance. *Nutrition Reviews*, 56, 317–33.
- Breslin, P.A., Spector, A.C. (2008). Mammalian taste perception. *Current Biology*, 18, R148–R155.
- Brossaud, F., Cheynier, V., Noble, A.C. (2001). Bitterness and astringency of grape and wine polyphenols. *Australian Journal of Grape and Wine Research*, 7, 33-39.
- Bufe, B., Hofmann, T., Krautwurst, D., Raguse, J.D., Meyerhof, W. 2002. The human TAS2R16 receptor

- mediates bitter taste in response to beta-glucopyranosides. *Nature Genetics*, 32, 397–401.
17. Cano-López, M., Pardo-Mínguez, F., Schmauch, G., Saucier, C., Teissedre, P.-L., López-Roca, L. M., Gómez-Plaza, E. (2008). Effect of micro-oxygenation on color and anthocyanin-related compounds of wine with different phenolic contents. *Journal of Agricultural and Food Chemistry*, 56, 14, 5932–5941.
 18. Castillo-Sánchez, J.X., García-Falcón, M.S., Garrido, J., Martínez-Carballo, E., Martins-Dias, L.R., Mejuto, X.C. (2008). Phenolic compounds and colour stability of Vinhão wines: Influence of wine-making protocol and fining agents. *Food Chemistry*, 106, 18–26.
 19. Chandrashekar, J., Mueller, K.L., Hoon, M.A., Adler, E., Feng, L., Guo, W., Zuker, C.S., Ryba, N.J. (2000). T2Rs function as bitter taste receptors. *Cell*, 100, 703–11.
 20. Charlton, A.J.; Baxter, N.J.; Khan, M. L.; Moir, A.J.G.; Haslam, E.; Davies, A.P.; Williamson, M.P. 2002. Polyphenol/peptide binding and precipitation. *Journal of Agricultural and Food Chemistry*, 50, 1593–1601.
 21. Cheynier, V. (2005). Polyphenols in food are more, complex than often thought. *American Journal of Clinical Nutrition*, 81, 223S–229S.
 22. Chung, K.T., Wong, T.Y., Wei, C.I., Huang, Y.W., Lin, Y. (1998). Tannins and human health: a review. *Critical Reviews in Food Science and Nutrition*, 36, 421–64.
 23. Cosme, F., Jordão, A.M. (2014). Grape phenolic composition and antioxidant capacity. In: *Wine: Phenolic Composition, Classification and Health Benefits*. Editor Youssef El Rayess. Nova Science Publishers, ISBN: 978-1-63321-048-6. pp: 1-40.
 24. Cosme, F., Ricardo-da-Silva, J. Laureano, O. (2007). Protein fining agents: characterization and red wine fining assay. *Italian Journal of Food Science*, 19, 39–56.
 25. Cosme, F., Ricardo-da-Silva, J. Laureano, O. (2008). Interactions between protein fining agents and proanthocyanidins in white wine. *Food Chemistry*, 106, 536–544.
 26. Cosme, F., Ricardo-da-Silva, J., Laureano, O. (2009). Behavior of Various Proteins on Wine Fining: Effect on Different Molecular Weight Proanthocyanidin Fractions of Red Wine. *American Journal of Enologia and Viticultura*, 112:197–204.
 27. Costa, E., Cosme, F., Rivero-Pérez, M.D., Jordão, A.M., González-SanJosé, M.L. (2015). Influence of wine region provenance on phenolic composition, antioxidant capacity and radical scavenger activity of traditional Portuguese red grape varieties. *European Food Research and Technology*, 241, 61–73.
 28. Cristino, R., Costa, E., Cosme, F., Jordão, A.M. (2013). General phenolic characterization, individual anthocyanin and antioxidant capacity of matured red wines from two Portuguese appellations of origins. *Journal of the Science of Food and Agriculture*, 93, 2486–2493.
 29. De Coninck, G., Jordão, A.M., Ricardo-da-Silva, J.M., Laureano, O. (2006). Evolution of phenolic composition and sensory properties in red wine aged in contact with Portuguese and French oak wood chips. *Journal International des Sciences de la Vigne et du Vin*, 40, 25–34.
 30. Drayna, D., Coon, H., Kim, U.K., Elsner, T., Cromer, K., Otterud, B., Baird, L., Peiffer, A.P., Leppert, M. (2003). Genetic analysis of a complex trait in the Utah Genetic Reference Project: A major locus for PTC taste ability on chromosome 7q and a secondary locus on chromosome 16p. *Human Genetics*, 112, 567–572.
 31. Drewnowski, A., Gomez-Carneros, C. (2000). Bitter taste, phytonutrients, and the consumer: a review. *American Journal of Clinical Nutrition*, 72, 1424–35.
 32. Duffy, V.B., Davidson, A.C., Kidd, J.R., Kidd, K.K., Speed, W.C., Pakstis, A.J., Reed, D.R., Snyder, D.J., Bartoshuk, L.M. (2004). Bitter receptor gene (TAS2R38), 6-n-propylthiouracil (PROP). Bitterness and alcohol intake. *Alcoholism Clinical and Experimental Research*, 28, 1629–1637.
 33. Fulcrand, H., Benabdeljalil, C., Rigaud, J., Cheynier, V., Moutounet, M. (1998) A new class of wine pigments generated by reaction between pyruvic acid and grape anthocyanins. *Phytochemistry* 47, 1401–1407.
 34. Furlan, A. L., Castets, A., Nallet, F., Pianet, I., Grelard, A., Dufourc, E. J., Géan, J. (2014). Red wine tannins fluidify and precipitate lipid liposomes and bicelles. A role for lipids in wine tasting? *Langmuir*, 30, 5518–5526.
 35. Gawel, R. (1998). Red wine astringency: a review. *Australian Journal of Grape and Wine Research*, 4, 74–95.
 36. Gibbins, H. L., Carpenter, G. H. (2013). Alternative mechanisms of astringency - what is the role of saliva? *Journal of Texture Studies*, 44, 364–375.
 37. Gonçalves, F.J., Jordão, A.M. (2009). Influence of different commercial fining agents on proanthocyanidin fraction and antioxidant activity of a red wine from *baga* grapes. *Journal International des Sciences de la Vigne et du Vin*, 43, 111–120.
 38. Guise, R., L. Filipe-Ribeiro, D. Nascimento, O. Bessa, F.M. Nunes, F. Cosme. (2014). Comparison between different types of carboxymethylcellulose and other oenological additives used for white wine tartaric stabilization. *Food Chemistry*, 156, 250–257.
 39. Haslam, E. (1998). Practical polyphenolics from structure to molecular recognition and physiological action. Cambridge University Press, Cambridge.

40. He, F., Liang N.-N., Mu, L., Pan, Q.-H., Wang, J., Reeves, M.J., Duan, C.-Q. (2012). Anthocyanins and Their Variation in Red Wines II. Anthocyanin Derived Pigments and Their Color Evolution. *Molecules*, 17, 1483-1519.
41. Ibeas, V., Correia, A.C., Jordão, A.M. (2015). Wine tartrate stabilization by different levels of cation exchange resin treatments: impact on chemical composition, phenolic profile and organoleptic properties of red wines. *Food Research International*, 69, 364-372.
42. Jackson, R.S. (2000). *Wine Science Principles, Practice, Perception* (Second ed.). San Diego: Academic Press.
43. Jordão, A.M., Correia, A.C. (2012). Relationship between antioxidant capacity, proanthocyanidin and anthocyanin content during grape maturation of Touriga Nacional and Tinta Roriz grape varieties. *South African Journal of Enology and Viticulture*, 33, 214-224.
44. Jordão, A.M., Ricardo-da-Silva, J.M., Laureano, O. (1998). Evolution of anthocyanins during grape maturation of two varieties (*Vitis vinifera* L.): Castelão Francês and Touriga Francesa. *Vitis*, 37, 93-94.
45. Jordão, A.M., Ricardo-da-Silva, J.M., Laureano, O. (2001). Evolution of catechin and procyanidin composition during grape maturation of two varieties (*Vitis vinifera* L.) Castelão Francês and Touriga Francesa. *American Journal of Enology and Viticulture*, 52, 230-234.
46. Jordão, A.M., Ricardo-da-Silva, J.M., Laureano, O., Mullen, W., Alan, C. (2008). Effect of ellagitannins, ellagic acid and some volatile compounds from oak wood on the (+)-catechin, procyanidin B1 and malvidin-3-glucoside content of model wine solutions. *Australian Journal of Grape and Wine Research*, 14, 260-270.
47. Jordão, A.M., Simões, S., Correia, A.C., Gonçalves, F.J. (2012). Antioxidant activity evolution during Portuguese red wine vinification and their relation with the proanthocyanidin and anthocyanin composition. *Journal of Food Processing and Preservation*, 36, 298-309.
48. Jordão, A.M., Vilela, A., Cosme, F. (2015). From Sugar of Grape to Alcohol of Wine: Sensorial Impact of Alcohol in Wine. *Beverages*, 1, 292-310.
49. Kallithraka, S., Bakker, J., Clifford, M.N. (1997). Evaluation of bitterness and astringency of (+)-catechin and (-)-epicatechin in red wine and in model solutions. *Journal of Sensory Studies*, 12, 25-37.
50. Kantz, K., Singleton, V.L. (1991). Isolation and determination of polymeric polyphenols in wines using Sephadex LH-20. *American Journal of Enology and Viticulture*, 42, 309-316.
51. Keast, R.S.J., Costanzo, A. (2015). Is fat the sixth taste primary? Evidence and implications. *Flavour*. 4:5 (<http://www.flavourjournal.com/content/4/1/5>), 7 pages.
52. Lanier, S.A., Hayes, J.E., Duffy, V.B. (2005). Sweet and bitter tastes of alcoholic beverages mediate alcohol intake in of-age undergraduates. *Physiology & Behavior*, 83, 821-31.
53. Lasanta, C., Caro, I., Pérez, L. (2013). The influence of cation exchange treatment on the final characteristics of red wines. *Food Chemistry*, 138, 1072-1078.
54. Lee, C.A., Ismail, B., Vickers, Z.M. (2012). The role of salivary proteins in the mechanism of astringency. *Journal of Food Science*, 77, C381-C387.
55. Ma, W., Guo, A., Zhang, Y., Wang, H., Liu, Y., Li, H. (2014). A review on astringency and bitterness perception of tannins in wine *Trends in Food Science and Technology*, 40, 6-19.
56. Meyerhof, W., Behrens, M., Brockhoff, A., Bufer, B., Kuhn, C. (2005). Human Bitter Taste Perception. *Chemical Senses*, 30 (suppl 1), i14-i15.
57. Mira, H., Leite, P., Ricardo-da-Silva, J., Curvelo-Garcia, A.S. (2006). Use of ion exchange resins for tartrate wine stabilization. *Journal International des Sciences de la Vigne et du Vin*, 40, 223-246.
58. Morata, A., Calderón, F., González, M.C., Gómez-Cordovés, M.C., Suárez, J.A. (2007). Formation of the highly stable pyranoanthocyanins (vitisins A and B) in red wines by the addition of pyruvic acid and acetaldehyde. *Food Chemistry*, 100, 1144-1152.
59. Moyes, C.D., Schulte, P.M. (2008). *Principles of Animal Physiology* (2nd Edition), Pearson/Benjamin Cummings, 754 pp.
60. Noble, C.A. (1994). Bitterness in wine. *Physiology and Behavior*, 56:1251-5.
61. Obreque-Slier, E., López-Solís, R., Peña-Neira, Á., Zamora-Marín, F. (2010). Tannine-protein interaction is more closely associated with astringency than tannine-protein precipitation: experience with two oenological tannins and a gelatin. *International Journal of Food Science and Technology*, 45, 2629-2636.
62. Oliveira, C.M., Ferreira, A.C.S., De Freitas, V., Silva, A.M.S. (2011). Oxidation mechanisms occurring in wines. *Food Research International*, 44, 1115-1126.
63. Pedersen, A.M., Bardow, A., Jensen, S.B., Nauntofte, B. (2002). Saliva and gastrointestinal functions of taste, mastication, swallowing and digestion. *Oral Diseases*, 8, 117-129.
64. Peleg, H., Gacon, K., Noble, A.C. (1999). Bitterness and astringency of flavan-3-ol monomers, dimers

- and trimers. *Journal of the Science of Food and Agriculture*, 79, 1123–8.
65. Pinho, C., Couto, A. I., Valentão, P., Andrade, P., Ferreira, I.M.P.L.V.O. (2012). Assessing the anthocyanic composition of Port wines and musts and their free radical scavenging capacity. *Food Chemistry*, 131, 885–892.
66. Ribeiro, T., Fernandes, C., Nunes, F. M., Filipe-Ribeiro, L., Cosme, F. (2014). Influence of the structural features of commercial mannoproteins in white wine protein stabilization and chemical and sensory properties. *Food Chemistry*, 159:47–54.
67. Ribéreau-Gayon P, Glories Y, Maujean A, Dubourdieu D. 2006. *Handbook of Enology. The Chemistry of Wine Stabilization and Treatments*. (2nd ed.). (Vol. 2). France: Bordeaux. Wiley & Sons Ltd., Chichester, England
68. Robichaud, J.L., Noble, A.C. (1990). Astringency and bitterness of selected phenolics in wine. *Journal of the Science of Food and Agriculture*, 53: 343–353.
69. Roper, S.D. (2013). Taste buds as peripheral chemosensory processors. *Seminars in Cell and Developmental Biology*, 24, 71– 79.
70. Sáenz-Navajas, M. P., Avizcuri, J.M., Ferreira, V., Fernández-Zurbano, P. (2012). Insights on the chemical basis of the astringency of Spanish red wines. *Food Chemistry*, 134, 1484–1493.
71. Saint-Cricq de Gaulejac, N., Glories, Y., Vivas, N. (1998). Recherche des composés responsables de l'effet antiradicalaire dans les vins. *Journal des sciences et techniques de la tonnellerie*, 4, 147–161.
72. Siebert, K.J., Troukhanova, N.V., Lynn, P.Y. (1996). Nature of polyphenol-protein interactions. *Journal of Agricultural and Food Chemistry*, 44, 80–85.
73. Singleton, V.L., Trousdale, E.K. (1992). Anthocyanin-tannin interactions explaining differences in polymeric phenols between white and red wines. *American Journal of Enology and Viticulture*, 43, 63–70
74. Soares, S., Kohl, S., Thalmann, S., Mateus, N., Meyerhof, W., De Freitas, V. (2013). Different phenolic compounds activate distinct human bitter taste receptors. *Journal of Agricultural and Food Chemistry*, 61, 1525–1533.
75. Somers, T.C. (1971). The polymeric nature of wine pigments. *Phytochemistry*, 10, 2175–86
76. Somers, T.C., Verdet, E., Pocock, K.F. (1987). Hydroxycinnamate esters of *Vitis vinifera*: Changes during white vinification and effects of exogenous enzymatic hydrolysis. *Journal of the Science of Food and Agriculture*, 40, 67–78.
77. Su, C.T., Singleton, V.L. (1969). Identification of three flavan-3-ols from grapes. *Phytochemistry*, 8, 1553–1558.
78. Suriano, S., Alba, V., Tarricone, L., Di Gennaro, D. (2015). Maceration with stems contact fermentation: Effect on proanthocyanidins compounds and color in Primitivo red wines. *Food Chemistry*, 177, 382–389.
79. Thorngate, J.H., Noble, A.C. (1995). Sensory evaluation of bitterness and astringency of 3R (-)-epicatechin and 3S (+)-catechin. *Journal of the Science of Food and Agriculture*, 67, 531–35.
80. Verette, E., Noble, A.C., Somers, C. (1988). Hydroxycinnamates of *Vitis vinifera*: sensory assessment in relation to bitterness in white wine. *Journal of the Science of Food and Agriculture*, 45, 267–272.
81. Waterhouse, A. L. (2002). *Wine Phenolics*. *Annals New York Academy of Sciences*, 957, 21–36
82. Waterhouse, A.L., Teissedre, P.L. (1997). Levels of phenolics in California varietal wine. In *Wine: Nutritional and Therapeutic Benefits*. T. Watkins, Ed.: 12–23. American Chemical Society. Washington, DC.
83. Wooding, S., Kim, U.K., Bamshad, M.J., Larsen, J., Jorde, L.B., Drayna, D. (2004). Natural Selection and Molecular Evolution in PTC, a Bitter-Taste Receptor Gene. *The American Journal of Human Genetics*, 74, 637–646.