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Wine as Food and Medicine

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“Wine is the most civilized thing in the world.” - Ernest Hemingway

1. Introduction

The name “Wine” is derived from the Latin word vinum, “wine” or “(grape) vine”. Wine is the earliest domesticated fruit crops and is defined as an alcoholic beverage which is produced by the fermentation of grape juice. Grapes are small berries with a semi-translucent flesh, whitish bloom and a smooth skin, whereby some berries contain edible seeds and others are seedless. Grape berries have a natural chemical balance which allows a completely fermentation without the addition of sugar, acid, enzymes or other nutrients. It is a rich source of vitamins, many essential amino acids, minerals, fatty acid and others. Grapevine, botanically called *Vitis vinifera*, has a wide range of different species whereby wine is a mixture of one or more varieties (Bouquet et al. 2006). Pinot Noir, Chardonnay, or Merlot for example are predominated by grapes with a minimum of 75 or 85% grape by law and the result is a varietal as opposed to a blended wine. Nevertheless, blended wines are not of minor value compared to varietal wines. Wines from the Bordeaux, Rioja or Tuscany regions are one of the most valuable and expensive wines which are a mixture of many different grape varieties of the same vintage. Wines of high quality are not permitted to be labeled as varietal names because of the ‘cépage’ (grape mix) which is restricted by law. Red Bordeaux wines are a composition of four different grapes including, but not exclusively, Cabernet Sauvignon and Merlot. Red and white Burgundy are made from a single grape variety and they use their regional label because of marketing strategies and historical reasons. To name some few native North American grapes like *Vitis labrusca, Vitis aestivalis, Vitis rupestris, Vitis rotundifolia* and *Vitis riparia* which are usually used for eating as fruit or made into grape juice, jam, or jelly sometimes into wine for example Concord wine (*Vitis labrusca species*). The most common vineyards worldwide are planted with the European vinifera vines that have been grafted with native species of North America. This is because grape species from North America are resistant against phylloxera (Granett et al. 2001). The theory of “terroir” is defined by the variety of the grape, orientation and topography of the vineyard, elevation, type and chemistry of soil, the climate and seasonal conditions under which grapes are grown. Among wine products, there is a high variety which is due to the fermentation and aging processes. Many winemakers with small production volume prefer growing and using production methods that preserve the unique sensory properties like aroma and the taste of their terroir.
The main challenge of the producers is to reduce differences in sources of grapes by using wine making technology such as micro-oxygenation, tannin filtration, cross-flow filtration, thin film evaporation, and spinning cone. Grapese is one of the major fruits in the world which is grown in temperate regions on the northern and southern hemisphere mostly between the 30th and 50th parallel. Grapevine is cultivated in large fields because of their economic value (Bouquet et al. 2006). The most popular wine regions of the world are France, Italy, Northern California, Germany, Australia, South Africa, Chile and Portugal respectively. The genus grape (Vitis vinifera) contains around 60 species which are common in the temperate zones with some species growing in the tropical region. In 2009 the production of grape was about 69 million tons (especially for wine, juice and raisins) compared to data from 1995 with only 55 million tons (Data from the Organisation Internationale de la Vigne et du Vin (OIV)). Grapes need a minimum of 1500 hours of sunshine to ripen fully, red wine needs more radiation than white.

1.1 Some historical facts of wine
Wine and grape are one of the oldest fruits and the traditional winemaking processes are an ancient art, which began as early as 1,000 B.C. Archaeological investigations and discoveries attest that the wine production by fermenting processes, took place from early as 6000 BC. Other studies from China show that grapes were used together with rice to produce fermented juices as early as 7000 BC. Some research studies document the origin home countries of wine to the Balkan Range along the coast of the Black Sea. Wine is mentioned in historical literature documents as Iliad and Odyssey by Homer. In Greco-Roman mythology, Dionysius is adored as the god of wine. He is also known as Bacchus whereby Dionysius is regarded as the patron of vine events. One of the most important grape wine producers in Europe is Turkey as well as other neighboring countries around the Mediterranean Sea. Especially Anatolia was described as the origin place of viticulture and wine making. One of the first traces of the cultivation of grape wine was in the Early Bronze Age around the Mediterranean basin (Gorny 1996). Many archaeological investigations prove the early domestication of wine in the East (This et al. 2006). During the Bronze Age in the Mediterranean were olive, fig and grape the most common fruits. Scientists discovered many evidences like grape pips in a shrine, wine shop with jars and cups from the Bronze Age (Refai 2002). In Europe around the Mediterranean area between Black Sea and Caspian Sea grape was cultivated and used for winemaking 4000 BC (Monti 1999). The wild grapevine specie Vitis vinifera ssp. Sylvestris Gmelin was grown from Portugal to Turkmenistan and the north of Tunisia. About 8400 years seeds of the oldest wild grape in Turkey were discovered in a valley near Urfa (This et al. 2006). Specific investigations of the chlorotype showed a higher diversity of the wild grape population in the central and eastern parts than in the western areas of the Mediterranean (Arroyo-Garcia et al. 2006). All domesticated grapevine species originated from the wild type Vitis vinifera ssp. sylvestris whereby Vitis vinifera L. is the only native species of Eurasia and appeared 65 million years ago. To enhance the yield of grapevine hermaphrodite genotypes were selected for domestication procedures with intensive pigmentation and techniques for propagation (Terral et al.).Nowadays the skills of the winemaking process are considered for intellectual persons. Special famous events only about wine are exhibits, expos, and auctions worldwide. The Boston Wine Expo is one major annual convention where top wine producer exhibit, sell their goods and show new technologies. Such expos serve as venue for the world’s top producers to exhibit and sell their good. Persons with high interests as well
as wine collectors attend such exhibitions to exchange ideas and share their passions for wine. Wine is associated with education, lifestyle and class and that is the reason why wine is always included in special occasions. What did early wine producers start out with, and how did they change grapevines in the course of domesticating them? How does the evolutionary history of grapevines affect grape growers today?

2. Classification of wine

The naming of wines has a long tradition and is based on their grape variety or by their place of production. European wines are labeled after their place of production like Bordeaux, Rioja and Chianti as well as the type of grapes used such as Pinot, Chardonnay and Merlot. All other wines from all over the world are generally named for the grape variety. Non-European wine labels become more and more famous and the market recognition get more stability. Some examples include Napa Valley, Barossa Valley, Willamette Valley, Cafayate, Marlborough, and Walla Walla just to name a few. Sensory properties like the taste of a wine depends on the grape species and the blend, and furthermore on the ground and climatic conditions (terroir).

2.1 Red wine

The color of wine is caused by the presence or absence of the grape skin during the fermentation process. Grapes with colored juice like Alicante Bouchet became popular as colorants so called “teinturier”. The basic natural products of red wine are red or black grapes, but the intensive red color originates from maceration, which is a process whereby the skin is left in contact with the juice during fermentation. In the following table 1 are listed some red wine varieties, their country origin and characteristics.

| Wine variety       | Country of origin | Characteristics                                      |
|--------------------|-------------------|------------------------------------------------------|
| Aleatico           | Italy             | Dark skinned grape, fragrant, very rare               |
| Alicante Bouschet  | France            | Red skinned grape                                    |
| Cabernet Sauvignon | France (Bordeaux) | principal component of Bordeaux reds                 |
| Concord            | America           | Most important variety in US, belongs to Vitis labrusca |
| Dolcetto           | Italy             | Wine is soft and fruity                              |
| Pinotage           | South Africa      | Wild grown hybrid variety                            |

Table 1. Varieties of Red Wine

Dependent on the grape specie, climatic conditions during the ripening process and many other external factors can influence the sugar and alcohol content of the wine. In the following table 2 is shown the nutritional value of red table wine.

| Energy 80 Kcal, 360 KJ |
|------------------------|
| Carbohydrates 26 g     |
| Sugar 0.6 g            |
| Fat 0.0 g              |
| Protein 0.1 g          |
| Alcohol 10.6 g         |

Table 2. Nutritional value of red table wine per 100 g
2.2 White wine
White wine can be produced from any color of grape as the skin is separated from the juice during fermentation. The following table 3 shows some examples white wine, their country origin and characteristics.

| Wine variety    | Country of origin | Characteristics                        |
|-----------------|-------------------|----------------------------------------|
| Chardonnay      | France            | Widely grown throughout the world.     |
| Frontignac      | Greece            | highly fragrant                        |
| Gewürztraminer  | France (Alsace)   | highly fragrant and spicy              |
| Muscadelle      | France (Bordeaux) | An aromatic variety.                   |
| Picolit         | Italy (Friuli region) | Used to make sweet white wine.        |
| Riesling        | Germany           | noble variety producing some of the world’s greatest wines. |
| Sauvignon Blanc | France (Bordeaux) | A highly aromatic variety.             |

Table 3. Varieties of White Wine

2.3 Rosé wine
Rosé wine is produced from different very dark red grape-varieties whereby it is not a blending of red and white wine. In recent times many wine dressers mix a special amount of white wine with red wine.

2.4 Sparkling wines
Sparkling wines contains carbon dioxide which is naturally made due to the fermentation process; champagne for example. To achieve this sparkling effect, the wine has to ferment two times. The first time in an uncovered container that carbon dioxide can escape into the environment. In a second step the wine is in a sealed fermentation container so that the gas remains in the wine. In the following table 4 are listed some famous sparkling wines from different countries.

| Wine variety             | Country of origin | Characteristics                                      |
|--------------------------|-------------------|-----------------------------------------------------|
| Chardonnay               | France            | Basic component of champagne                        |
| Macabeo                  | Middle East       | Basic component of the Spanish sparkling wine Cava. |
| Muscat Blanc À Petits Grains | Greece            | Used for Italian sparkling wines known as Asti.    |
| Prosecco                 | Italy (Veneto)    | Used for Prosecco, an Italian sparkling wine.       |

Table 4. Varieties of Sparkling Wines

2.5 Table wine
The characteristic of table wines is that the alcohol content is not higher than 14% in the U.S. whereas in Europe, the alcohol range of light wine must be between 8.5% and 14% by volume. Depending on the color of the wine, table wines are classified as “white”, “red” or “rosé”.

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2.6 Dessert wine
The sugar range in dessert wines can be from slightly sweet (less than 50 g/L sugar) to very sweet wines (more than 400 g/L sugar). For example, wines such as Spätlesen are produced from grapes harvested after they reached the maximum ripeness. Dried grape wines like Recioto and Vin Santo are made from partially raisined grapes after harvesting. Botrytized wines are produced from grapes infected with Botrytis cinerea; some examples include Sauternes from Bordeaux, Bonnezeaux and Quarts de Chaume, Tokaji Aszú from Hungary, and Beerenauslese from Germany and Austria.

2.7 Fortified wine
Fortified wines are sweet with high alcoholic content because their fermentation process stopped by the addition of spirit like brandy. To popular fortified wines belong Port, Madeira, Tokay and Banyuls.

3. Social and cultural aspects of wine
Wine has a long tradition as cultural beverage and is a popular social gathering since ancient times. Wine was a favorite drink among Roman emperors, Greek scholars, monks living in monasteries and other civilizations. Monks and royalty preferred to drink wine, while beer was only used from the workers. Egyptians investigated the wine regardlessly in that quality and developed the first arbors and pruning methods. One path of wine history could follow the developments and science of grape growing and wine production; another might trace the spread of wine commerce through civilization, but there would be many crossovers and detours between them. However the timeline is followed, clearly wine and history have greatly influenced one another. Fossil vines, 60-million-years-old, are the earliest scientific evidence of grapes. The earliest written account of viniculture is in the Old Testament of the Bible which tells us that Noah planted a vineyard and made wine. As cultivated fermentable crops, honey and grain are older than grapes, although neither mead nor beer has had anywhere near the social impact of wine over recorded time. This unique alcoholic drink is enjoyed by people from all walks of life up until contemporary times. The social background of wine includes gatherings, parties, religious rites, special occasions, and even casual events. Wine experts believe that wine is more than a product, it is a culture. It is not just a commodity; it is a collector’s item. The main reason why wine is strict regarded to social tools is because of historical distingue purpose. Wine has special characteristics and qualities that make it a favorite among works of art, poems, and other literary pieces. Winemaking and oenophilists investigate technological novelties and processes are constantly being invented to reach the perfection in wine production.

4. Grapevine in food industry
There are many different ways in which grape fruits can be used and they include; fresh, preserved, dried into raisins or crushed for juice or wine (Wellness Encyclopedia of Food and Nutrition, 1992). Grape berries are sensitive fruits and should be carefully handled during the winemaking process because once in a bottle, it will develop with time. The long period of wine process is affected by different external factors which are listed below. The optimal temperature during the ripening process of the wine should be between 12 and 15 °C as well as the humidity should be between 70 and 80%. The circulation of fresh air in the wine cellar
The cultivation and winemaking process needs a long term experience and optimal conditions for the production of a high quality wine. The quality of wine depends on the maturity of berries or the so called “sugar ripeness”, that is the content of soluble substances in the fruit as well as sugar/acid balance (Kliwer 1964, Coombe 1960). Thanks to new investigations with the use of analytical chemistry like gas chromatography, volatile compounds most especially aromas which are typical for Sauvignon blanc wine can be analyzed. As earlier mentioned, grape is a rich source for phenolic substances and these compounds can be measured since the 80s by HPLC. The initial fruit chemistry measurements can be differentiated from the sensory perception of wine because of the biochemical and chemical transformation of compounds during fermentation. Because many factors influence the entire process of winemaking, thus for a good quality a long term experience is needed to go through all the steps of winery and vineyard respectively. Since thousands of years, humans have tried to manipulate the natural growth habits of grapevines to make the plant productive and economically effective for agriculture. The main focus was in breeding new varieties of grapes to maximize production, fruit quality and economic efficient (Coombe 1960, Bogs et al. 2006).

Different kind of factors such as genotype, environment and cultural practices have an influence on the phenolic biosynthesis and accumulation through the ripening process of grape berries. The quantity of phenolic compounds and also the composition has an influence on the wine quality. One characteristic of grape are the high concentrations of anthocyanin which can be used as chemical marker for the classification of red-grape varieties and wines. Furthermore the intravarietal heterogeneity can be used as characteristic which induces a very
different behavior among the different clones. The research interest focuses on high productive clones with a loss of color and phenolic compounds. Rootstock genotypes are associated with water, gas exchange status and canopy growth as well as yield (Koundouras et al. 2006). That is why rootstocks have an influence on the composition of phenolic compounds and also on the time of harvesting (Koundouras et al. 2006).

Grape and the quality of wine is also influences by many different environmental factors such as topography, agro-pedology, climate), which are described as “terroir”. The amount and composition of phenolics depends also on the sunlight exposure and the temperature which acts on the grape berries during the ripening process (Cohen et al. 2008). Low temperatures at night have a positive effect on the anthocyanin accumulation whereas high temperatures cause a decrease of their concentration. Otherwise the accumulation of colored pigments seems to be increased linearly with increasing sunlight exposure. Berries which are exposed ultraviolet light and temperature are related with metabolic reactions and alterations in anthocyanin composition (Joscelyne et al. 2007). Water availability is one of the most important factors which are responsible for the wine quality. Vine water status cause accumulation of phenolic compounds in grape berries with positive reactions of water deficit on berry phenolic composition (Qian et al. 2009). Environmental factors like rainfall, soil water storage capacity, as well as soil characteristics such as soil depth, structure, texture and fertility affect phenolic composition (Mateus et al. 2003). Different agricultural practices during the berry ripening process are also responsible for the synthesis of phenolic substances. Another interesting aspect are cultural aspects such as training system, row vine spacing, pruning, bunch thinning, bud and leaf removal and also the management of fertilization and water irrigation (Poni et al. 2009) with their special influence on phenolic biosynthesis and accumulation. Another interesting effect on the phenolic compounds during the ripening of grape berries are different agronomic techniques and growth conditions such as conventional, organic or biodynamic systems (Vian et al. 2006). Finally, other the vine age and pathogenesis (Amati et al. 1996).

6. Management of fruit quality

Considering the fact that grapes grow in a wide range of temperate climates on the northern and southern hemisphere, special modifications in breeding resistant and tolerant to environmental factors have been achieved to extend the margins of production. However the standard approach to grapes production is intensive agricultural management to balance between climate and site (soil conditions, topography) on one hand and vine biology and preferred fruit quality on the other hand. For high quality end products, the choice of cultivar (clone, rootstock) as well as the genetic potential of the grape plants are from high importance and can influence the quality of fruits. The yield and growth of wine depends on many environmental factors like climate, soil, water, nutrients, just to name a few. In some areas, vineyards have to be watered by irrigation which is by inter-annual changes in soil water. Nevertheless, the yield and fruit quality is inconsistent, most especially red varieties are growing under the principle “regulated deficit irrigation” which suppress the vegetative growth and influence directly the fruit quality. That means water deficit cause smaller berries, early sugar maturity and modifications in phenolic contents. Temperature, solar radiation, intensity of sunlight reaching the fruit and air movement have an influence on the metabolism in grape berries and furthermore the fruit quality. The orientation of the
vineyards should be north-south because of the daily solar cycle. Recent investigations showed that the amount for vines in a loose vertical canopy and under water stress can be about 42 to 45% of the daily total solar radiation. On the other hand fruits of east-west oriented vineyards are either shaded north-facing fruits or south-facing fruits with high sunlight intensities during the day.

### 7. Polyphenolics in wine

Grapevine and their wide range of phenolic compounds represent a large group of biomolecules with an important role in enology. Sensory properties of wine such as taste, astringency, bitterness as well as color are caused by many different phenolic substances accumulated in grape (Kammerer et al. 2004). High antioxidant potential of grapevine is also related with other health promoting compounds and that is why the consumption amounts of red wine is increasing (Pitsavos et al. 2005). Wine “experts” explain this phenomenon as the “French paradox” which describes the high life expectancy of French people in regard to their diets, exceptionally high in fats. Many nutritionists believe that this phenomenon is caused by the high consumption of red wine which contains high amounts of antioxidants and flavonoids (Renaud and de Lorgeril 1992). In a recent study the blood drawn of 20 probands before and after drinking wine were analyzed. After drinking it, higher levels of nitric oxide was found (nitric oxide reduce clots), as well as a reduction in platelet aggregation. Furthermore an increase of alpha-tocopherol, which is connected with the antioxidant vitamin E, and the total amount of antioxidants in blood were found to be 50% higher. The consumption of wine causes other effects like the protection of LDL cholesterol from oxidation. The negative properties of oxidized LDL are responsible for arteries damaging their walls and an increased risk of atherosclerosis (Iriti and Faoro 2006). Actual investigations found that some phenolic compounds which are accumulated in grape skins inhibit protein tyrosine kinases. These enzymes regulate cells, inhibiting production of endothelin-1 which seems to be a key component in several heart conditions (da Luz et al. 1999). Furthermore scientists got a special interest to investigate the composition of phenolic compounds in grape because of their anticarcenogenic properties (Block 1992) as well as neuroprotective effect (Ma et al.). (Monagas et al. 2005)) explains the acidy character of the phenolic function and due to the nucleophilic characteristics of the aromatic group is responsible for their reactivity. Phenolic compounds are a large group of secondary metabolites which can be classified in various ways whereby the most common separation is in flavonoids and non-flavonoids (Table 6). There are more specific and detailed families in each group whereby the chemicals structure of the compound is responsible for properties such as color, aroma and taste (Fournand et al. 2006).

Phenolics are formed from the essential amino acid, phenylalanine within the phenylpropanoid biosynthetic pathway. More than 4,000 phenolic compounds have been identified whereby their role in plants is linked to several functions: protection from UV light, pigmentation, defense against pathogens (antifungal properties), nodule production, attraction of pollinators as well as dispersion of seed (Gould et al. 2000). Grapes accumulate a high variety of polyphenolics as describes below. Phenolic acids are classified into hydroxybenzoic and hydroxycinnamic acids whereby hydroxybenzoic acids derive from benzoic acid. Grapes pulp accumulates high amounts of gallic acid (Lu and Serrero 1999) as well as flavan-3-ols in grape (Singleton and Esau 1969). In the following table 7 are listed more phenolic acids as and their derivates (Monagas et al. 2005, Rentzsch et al. 2007).
Phenolic compounds

| Flavonoids | Non-Flavonoids |
|------------|----------------|
| Phenolic acids |
| Non Flavonoids |
| Benzoic acids |
| Cinnamic acids |

Flavonoids

Flavonols

- Benzoic acids
- Cinnamic acids

Flavanols and flavones

- Catechins
- Condensed Tannins
- Procyanidins
- Prodelphinidins

Table 6. Classification and composition of phenolic compounds in grape (adapted from Kontoudakis et al.)

| Benzoic acid | Hydroxycinnamic acid | Hydroxycinnamic ester |
|--------------|----------------------|-----------------------|
| p-Hydroxybenzoic | Sinapic | Trans-feruloyltartaric acid (fertaric acid) |
| Protocatechuic | p-Cumaric | Trans-p-coumaroyltartaric acid (coutaric acid) |
| Vanillic | Caffeic | Trans-caffeoyltartaric acid (caftaric acid) |
| Gentisic | Ferulic | |
| Syringic | Gallic | Salicilic |

Table 7. Common phenolic acids in grape and derivates

Hydroxycinnamic acids are located and accumulated in the vacuoles of the skin and pulp as tartaric esters (Ribereau Gayon 1965). The highest amounts of principal hydroxycinnamic acids found in grapes are the caftaric, cutaric and fertaric acids in trans form as well as lower contents of the cis form (Singleton and Esau 1969). Further bioactive important compound in grape are stilbenes whereby trans-resveratrol is the most abundant. Stilbenes in grape can occur in oligomeric and polymeric form (Rentzsch et al. 2007). Plants synthesize stilbenes as defense reaction against infections by fungus or UV irradiation especially in leaves, roots and skin. Vitis rotundifolia seeds accumulated high contents of stilbene (Langcake and Pryce 1977, Adrian et al. 2000). Stilbenes play no important role in the organoleptic characteristics of wine but their importance in human health due to their antioxidative, anticarcinogenic potential and neuroprotective effects is from high interest (Nassiri-Asl and Hosseinzadeh 2009). Flavonoids are another large group of compounds synthesizes in grape and are divided in four subclasses. The class name depends on the base of the oxidation state of the pyran ring: the flavonols, the flavanones and flavones, the flavanols and the anthocyanins (Souquet et al. 2000). Flavanols and anthocyanins have the highest concentrations in wine and play an important role of the quality of red wine. Flavonols are yellow colored pigments which are responsible for the protection against UV light and are mainly accumulated in grape skin (Mane et al. 2007) but also detected in grape pulp (Pereira et al. 2006). In table 8 are listed the most abundant flavonols in grape.

The most abundant phenolics of the group flavanones and flavones are astilbin and engeletin. They were found in high amounts in the skin and wine of white grapes, grape
pomace and in stems (Souquet et al. 2000) but also in red wine (Vitrac et al. 2000). The chemical structure of flavones is similar with flavonols. Some examples of flavones in grape are apigenin, baicalein and luteolin (Wang and Huang 2004). Grape contains also high amounts of flavonols or flavan-3-ols in seed, skin and stem (Gomez-Miguez et al. 2006, Souquet et al. 2000). Flavanols were found in the monomeric, oligomeric and polymeric form and are responsible for organoleptic characteristics in grape wine. The common name of flavan-3-ols monomers is “catechin” (Escribano-Bailon et al. 2001). Anthocyanins (greek: purple flower) are a very well investigated large group of phenolics, are mainly accumulated in skin of red grapes and are responsible for red wine color (Castillo-Munoz et al. 2009). Cyanidin, Delphinidin, Peonidin, Petunidin and Malvidin are the most important anthocyanins in grape (Monagas et al. 2005).

| Flavonol             |                 |
|----------------------|-----------------|
| Kaempferol           | Myricetin       |
| Kaempferol-3-O-glucoside | Myricetin-3-O-glucoside |
| Kaempferol-3-O-galactoside | Myricetin-3-O-glucuronide |
| Kaempferol-3-O-glucuronide | Isorhamnetin-3-O-glucoside |
| Quercetin            | Isorhamnetin    |
| Quercetin-3-O-glucoside | Quercetin-3-O-glucuronide |

Table 8. Classification of flavonols

8. Accumulation of metabolic compounds during ripening

Basically, the maturity of grape berries depends on solar radiation which is indirectly by driving temperature of berries. That means that the sugar accumulation of berries is slowly under low temperatures and the ripening process will be slow. Organic acids will be metabolized more slowly and that cause high concentrations of acids. High temperatures cause various biochemical thresholds which limit metabolic reactions and is commonly called “the vine shuts down”. Grape berries are a rich source of phenolic compounds which are important plant secondary metabolites and are produced through photosynthesis (primary metabolites). The composition of phenolic substances is responsible for sensory properties in plant derived food including grapes and wine (Sandhu and Gu). Every wine contains a typical aroma, color, taste and mouth feel. The three major phenolics in grape are anthocyanins and flavonols (Ferrer et al. 2008). Flavonols are useful for UV radiation absorption and anti-microbial properties as response to wounds. The synthesis of these substances in berries is promoted in the vineyard due to solar radiation that is why they are accumulated in the exocarp (surface layer) (Versari et al. 2001). Anthocyanins cause the color modifications of fruits during ripening with variations from red, purple to black what is typical for the color of red wine. Anthocyanins form complexes with tannins and flavonols that contribute in the stability of the pigments. They are also synthesized in darkness but berries exposed for a long time to solar radiation during the ripening period will synthesize and accumulate higher contents of plant pigments. Astringent sensory properties of wine are the consequence of condensed tannins which are typical compounds of seed and skin of grapes. The decision on the optimal harvesting time depends on the climate, fruit developmental stage because high contents of condensed tannins in young berries have a higher biological benefit because of their bitterness and astringency.
9. Health promoting compounds in grape

The interests of scientists in the potential for specific phytochemicals increased in the last years because of their medicinal importance. Actual investigations show that the consumption of fresh fruits and vegetables are important to prevent chronic diseases and provides essential nourishment to humans. Plant geneticists around the world are able to breed special cultivars with higher nutraceuticals value to increase the concentration of health-promoting compounds in grape (God et al. 2007). Grape has many different varieties in health promoting compounds and is rich in bioactive metabolites like phenolic compounds that act as antioxidants or resveratrol which serve as chemo-preventative. Plant phenolics are attractive for researchers and the industry due to their techno-functional and putative beneficial bio-functional properties (Kammerer et al. 2004). The health benefit in wine comes from their high content in flavonoids and phytonutrients which are responsible for the color in grapes. Quercetin and Resveratrol are two important stilbenes in grapes which are responsible for heart-protection effects (Frankel et al. 1993). These bioactive phenolic compounds can reduce blood clotting due to their antiaggregant effect and protect low-density lipoproteins (LDL) cholesterol from oxidative reactions which can cause arterial damage (Albini et al.). The resveratrol (3,4′,5-trihydroxystilbene), is a bioactive secondary metabolite with high importance in medicine and pharmaceutics. Many studies showed that trans-resveratrol has a high antioxidative potential and reduces the risks of coronary heart disease and prevent any formation of cancer cells (Cui et al. 2002). The results of different investigations demonstrated that the concentrations of anthocyanins, phenolics and resveratrol differ significantly among cultivars and breeding lines. Grape (Vitis vinifera L.) has large amounts of phenolic compounds whereby the highest accumulation is in the skins and seeds (Rodriguez et al., 2006; Poudel et al., 2008). The most abundant phenolic compounds in grape skins are flavonols. The seeds contain high amounts of monomeric phenolic compounds like (+)-catechins, (-)-epicatechin and (-)-epicatechin-3-O-gallate as well as dimeric, trimeric and tetrameric procyanidins which do have antimutagenic and antiviral effects (Kammerer et al. 2004).

In in vitro tests, it was verified that phenolic compounds inhibit the oxidation of low-density lipoproteins (LDL) (Fauconneau et al. 1997). Phenolic substances are from high importance in the quality of grapes and wines. They can be classified in two groups: non-flavonoid (hydroxybenzoic, hydroxycinnamic acids, stilbenes) and flavonoid compounds (anthocyanins, flavan-3-ols, flavonols). Anthocyanins are a large group within the family of phenolics which are responsible for the pigmentation-coloration in grapes. Anthocyanins produce in a reaction with flavanols are more stable pigments (Butkup and Samappito 2008). Flavan-3-ols (monomeric catechins and proanthocyanidins) create a further large class of phenolic compounds which are responsible for astringent and bitter properties. They are responsible for the browning process in grape (Macheix et al. 1991). Special phenolic compounds are part in the phenomenon of co-pigmentation. Another large group of flavonoids are flavonols like quercetin, myricetin, kaempferol, isorhamnetin as well as their glycosides which have a high potential such as antioxidants. Grape became very attractant because of their high contents of phenolics especially antioxidant properties and their beneficial effects on human health (Vitseva et al. 2005). Scientific investigations verified the health benefits of catechins and procyanidins and the use of grape extract as an antioxidant supplement in the dietary food (Guendez et al. 2005). Special antioxidants can be used as food preservation due to their protective effects against microorganisms (Vattem et al. 2005). Phenolic compounds which
have microbiological effects are found in seeds, skins and stem extracts of *Vitis vinifera* (Chidambara Murthy et al. 2002). Further phytoneutrient in grape with health benefits are saponins which reduce blood cholesterol by binding its molecules and preventing their absorption, as well as reducing inflammation and cancer-protecting effect. Scientists from the University of California found that alcohol improve the bioavailability of saponins that means making them more easily absorbed in wine. The content of saponins in red wines is 3 to 10 times higher than the amount of saponins contained in white wines. Besides there is a positive association between the alcohol concentration and saponin concentration; that means stronger wines having more saponins. The highest content of saponins was found in red Zinfandel (16% alcohol) followed by Syrah, Pinot noir and Cabernet Sauvignon. White varieties like Sauvignon blanc and Chardonnay contain much less saponins. Furthermore Grape berries contain Pterostilbene with antioxidant activity which has also positive effects against cancer and cholesterol.

10. Resveratrol

Resveratrol is in the human diet and daily life of high importance because of their protection against benzopyrene which is the main substance in cigarette smoke and provokes lung cancer. Resveratrol inhibits the cell receptor aryl hydrocarbon receptor (AhR) on which benzopyrene and carcinogenic polycyclic aromatic hydrocarbons are not able to bind to cell membranes; because by binding they cause an expression of several cancer-promoting genes (Halls and Yu 2008). Researchers found out that Resveratrol inhibits the production of endothelin-1 and influence heart cells by inhibiting angiotensin II which is a very powerful vasocontracting hormone. They are equally known to prevention the differentiation of fibroblasts into myofibroblasts because of the collagen production. Resveratrol is one of the main components in red wine but they contain several other phytochemicals like catechins and epicatechins in high concentrations (Anekonda 2006). These two phenolic compounds have a high potency to reduce the activity of COX-1 and COX-2. The anti-microbial effect of Resveratrol was carried out in Turkey where an extract from grape seeds, skin and stems showed anti-microbial effects against 14 bacteria like Escherichia coli and Staphylococcus aureus with the only resistant bacterium being Yersinia enterocolitica at a concentration of 2.5%.

11. Byproducts of winery

Many byproducts and wastes contain polyphenols with a high potential for the application as food antioxidants and preventive agents against several diseases as well as due to a cost-efficient recovery. Valorization from grape by-products contains different bioactive substances like pigments, flavonoids, stilbenes and phenolic acids which could be used as natural antioxidants or colorants. Polyphenolic substances are extracted into wine, but the highest concentration remains in the vinification waste (pomace, stems, and seeds), which form over 13% of the processed grape weight (Torres et al. 2002). The majority of grape by-products remains in the waste during the vinification process, it is also an animal food as source of some products such as ethanol, alcoholic beverages, tartaric and citric acid, grape seed oil and dietary fiber (Torres et al. 2002). Residues of the winemaking process so called pomace a very attractive residual sources of valuable bioactive compounds, even though it is still underutilized (Kammerer et al. 2004). For example fractions of Parellada grape (Vitis vinifera) containing oligomers with
galloylation ca. 30% which are the most potent free radical scavengers and antioxidants (Torres et al. 2002). Several substances from grape pomace like ethanol, tartaric, malic and citric acids as well as seed oil can be recovered. Winery byproducts are from high importance in the food industry and also for agricultural purposes because pomace is used as soil conditioner or for compost production. Red and white grape varieties were investigated in their phenolic potential of the press residues. The results showed over 35 different compounds especially anthocyanins, phenolic acids, non-anthocyanin, flavonoids and stilbenes. Anthocyanins were found in high concentrations in red grape pomace up to 132 g/kg dry matter. Some compounds found in pomace showed significant differences in their content in dependence of the cultivar-specific differences, grape ripening stage, microclimatic and phytosanitary conditions (Kammerer et al. 2004).

Seed extracts of *Vitis vinifera* contain high contents of flavan-3-ols and their derivatives. The main compounds of pomace and stem extracts are significant amounts of flavonoids, stilbenes, and phenolic acids. Stems contain high concentrations of *trans*-resveratrol and *ε*-viniferin (Anastasiadi et al. 2009). Pomace was also used for the recovery of phenolics on laboratory scale. Until now for the extraction of anthocyanin was acted using acidified and sulfited solvents. Sulfite cannot be quantitatively removed and allergic reaction after the consumption of sulfitted food was visible. A new pectinolytic and cellulolytic method of pomace enhance the release of phenolic compounds (Maier et al. 2006). By the optimization of this extraction process the yields of extracted phenolic acids, non-anthocyanin flavonoids and anthocyanins reaching 91.9, 92.4 and 63.6 %. Pomace is also a rich source for the edible oil from the seed and rich in polyphenols with high antioxidant activity. To obtain the phenolic compounds from the press residues in high contents is very easy, whereby they can be applied as supplements of functional or enriched foods (Maier et al. 2006). A new technology with resin adsorption allows a high level of purification and concentration of anthocyanin extracts from a Cabernet Mitos’ grape pomace. These processes are common in industrial processes, for example to debitter citrus juices or to stabilize and standardize juice concentrates (Kammerer et al. 2004). Furthermore, resin adsorption can be also an effective method to concentrate plant phenolics, to fractionate extracts and to enrich some compounds. This novel technique can also contribute to the production of valuable plant extracts with health-beneficial properties. High-speed countercurrent chromatography (HSCCC) is also a new technique which is useful for the analytical and preparative part in winemaking process as well as for the isolation of bioactive compounds from crude plant extracts. By using the HSCCC method phenolic extracts from a ‘Lemberger’ grape pomace were analyzed and some compounds like caftaric, coutaric and fertaric acids were isolated. Purified extracts of caftaric, coutaric, and fertaric acids were up to 97.0 %, 97.2 % and 90.4 % and the end product from 10 g of grape pomace were 62, 48 and 23 %. These byproducts especially from grape waste can be used for the recovery of bioactive beneficial compounds to increase the profit of conventional processing techniques and to maximize sustainable agricultural production (Pinelo et al. 2005).

Grape has a wide variety of polyphenols whereby flavonoids are the best investigated compounds and known to have antibacterial activities. These metabolites are produced and accumulated due to their interaction with extracellular soluble proteins and/or bacterial cell walls (Cowan 1999). Furthermore catechins inhibit in vitro the action of many bacteria like *Vibrio cholerae, Streptococcus mutans*, and *Shigella*, whereas (-)-epigallocatechin gallate is a potent Gram-positive bactericidal that acts by damaging the respective bacterial membranes (Ikigai et al. 1993).
12. Grape phenolics and their nutritional pharmacological effects

Recent investigations show that the addition of biomolecules in food supports human health. Especially glycosylated, esterified, thiolylated, or hydroxylated forms of bioactive compounds display their health benefit in metabolic activities combined with several diseases. All these bioactive plant food components are mainly found in whole grains, fruits and vegetables (Klotzbach-Shimomura 2001). There are thousands of bioactive food compounds derived from plants like the polyphenols, phytosterols, carotenoids, tocopherols, tocotrienols, isothiocyanates and diallyl- (di, tri)sulfide compounds, fiber, and fruto-oligosaccharide. Grape is a well known and investigated plant because of their social importance and useful metabolites especially flavonoids in humans health. Polyphenols belong to the major substances in grape which are a widely distributed group of biomolecules. Bioflavonoids belong to health promoting compounds in grape and their recent scientific interest confirm the importance in our daily healthy diet. They play an important role in longevity, cancer prevention and heart disease. Many studies investigated the content of phenolics and their effect on human cancer cells. (Yi et al. 2005) reported that muscadine grapes are rich in phenolic compounds and show a high potential on human liver cancer cells HepG2. The phenolic content of four cultivars of muscadine grapes (‘Carlos’, ‘Ison’, ‘Noble’, and ‘Supreme’) were investigated and separated into phenolic acids, tannins, flavonols, and anthocyanins. Extracted phenolic acids of muscadine grapes inhibited the HepG2 cell population growth in about 50% at concentration of 1–2 mg/mL. Anthocyanins showed the greatest positive effects regardingly apoptosis as well as cell viability at concentrations of 70–150 and 100–300 μg/mL.

13. Bioavailability of phenolic compounds

Polyphenols are very important micronutrients in our diet, and play a key role in the prevention of cancer and cardiovascular diseases. The health benefit of polyphenol depends on the consumed amount as well as their bioavailability (Manach et al. 2003). The main interests are the antioxidant properties of polyphenols as well as their appearance in the human diet and their role in the prevention of cancer, cardiovascular and neurodegenerative diseases (Scalbert et al. 2005). Polyphenols are responsible for the activity of a wide range of enzymes and cell receptors (Middleton et al. 2000). Polyphenols are not absorbed with equal efficacy because they are extensively metabolized by intestinal and hepatic enzymes as well as the intestinal micro flora.

14. Wine in biotechnological approach

Plant cell cultures are a potential alternative to traditional agriculture for the industrial production of valuable bioactive secondary metabolites. Especially pharmaceutical compounds and food additives like flavors, fragrances and colorants), perfumes and dyes are produced and accumulated in plant cell cultures (DiCosmo and Misawa 1995). Thereby the anthocyanin production can explain the basic mechanisms of biosynthesis of secondary metabolites, their transport as well as their accumulation in specific plant tissue. Plant pigments like anthocyanins are the large group of water-soluble pigments which are responsible for many colors. These pigments are also used in acidic solutions for the
stabilization of the red color in soft drinks, sugar confectionary, jams and bakery products. As mentioned before grape pomaces is the major source of anthocyanins for commercial purposes and wastes from juice and wine industries (Curtin et al. 2003). Crude preparations of anthocyanins are relatively inexpensive and are used extensively in the food industry. The costs of pure anthocyanins are around US$ 1,250–2,000/kg. Cell suspension cultures of *Vitis vinifera* produce high contents of anthocyanins after cessation of cell division (Kakegawa et al. 2005). Furthermore the external influence and stimulation of the anthocyanin biosynthesis is regulated by the amino acid phenylalanine which is accumulated in the plant cells (Shimada et al. 2005). End products of the flavonoid biosynthesis pathway include anthocyanin pigments. Plant pigment extracts contain mixtures of various anthocyanin molecules, which differ in their levels of hydroxylation, methylation, and acylation. The major anthocyanins which are produced and accumulated in *V. vinifera* cell culture are cyanidin 3-glucoside (Cy3G), peonidin 3-glucoside (Pn3G), malvidin 3-glucoside (Mv3G) as well as the acylated versions of these compounds, cyaniding 3-p-coumaroylglucoside (Cy3CG), peonidin 3-p-coumaroylglucoside (Pn3CG) and malvidin 3-coumaroylglucoside (Mv3CG) (Conn et al. 2003). The production of anthocyanins by plant in-vitro cultures has been estimated in different plant species. Many investigation studies are using a cell line as model system for the production of secondary metabolites especially anthocyanin, because of the color that enables production. (Sano et al. 2005), of Nippon Paint Co. in Japan, investigated the production of anthocyanins. High osmotic potential in *Vitis vinifera* L. (grape) cell suspension cultures caused an increase in the anthocyanin production. By addition of sucrose or mannitol in the medium the osmotic pressure and the anthocyanin concentration accumulated was increased (Zhao et al.).

15. References

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