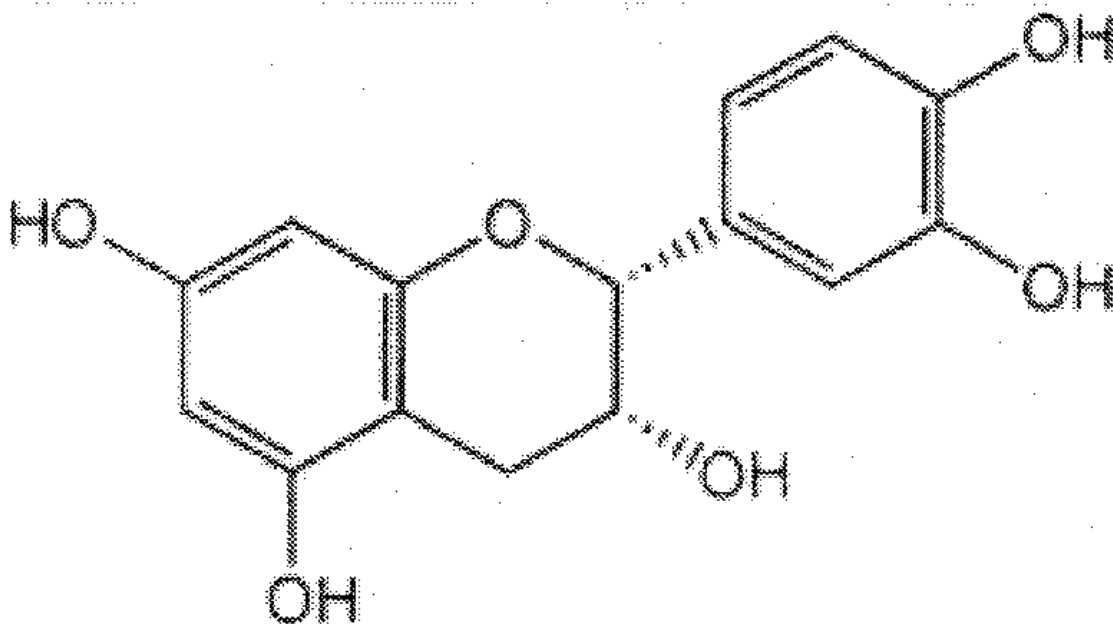


**“ Wine is a food, a medicine, and a poison-it’s just a question of dose”.**

Paracelsus, 16<sup>th</sup> century Swiss physician

Wine, the fermented beverage from grape juice, has hundreds of components. An important group is polyphenols. Polyphenols come in many forms and some more widely studied. Some polyphenols are especially important for health reasons. Research has shown the most abundant polyphenols in young red wines are proanthocyanidins (also called procyanidins).



Epicatechin (EC), one of the possible building blocks of *proanthocyanidins*

There are a host of foods with procyanidins. They are abundant in nature; however modern food processing has a way of eliminating them. Fresh foods high in procyanidins include apples, cranberries, cocoa, chocolate, pomegranates, persimmons, raspberries, walnuts, cinnamon, pinto beans, sorghum grain, Concord grape juice and red wines.

Modern medicine has made fantastic progress over the past fifty years. However, dietary choices often counteract these gains. Societies with some of the healthiest, longest-lived people-Sardinia, Crete, rural southwest France-often lack state-of-the-art health services and clinics. Yet, because they take better care of themselves, their inhabitants still live to ripe old ages.

Recent studies indicate that life expectancy in the US and parts of Europe are decreasing. It is a complicated mix of reasons, but much is due to obesity.

Diets can be a problem and also are tricky. We evolved as a species living off relatively low-calorie foods. We had to eat more of these foods to get the energy to survive. In doing so, we consumed more micronutrients-the vitamins and minerals that keep the cells in our body in a healthy state.

Had Michelangelo been asked to portray 16<sup>th</sup> Century European man, it might have looked like this familiar figure.



Over the past century, the Western diet has become increasingly rich in calories. So now, the calories required to live can be obtained from a smaller quantity of food. But, in eating less, the micronutrients consumed also go down. The Catch 22 is that going on a diet may reduce caloric intake, but it also reduces micronutrient intake.

Other problems exist. Our lifestyles have changed. Energy expenditure has been reduced through jobs that are more sedentary and we don't get as much physical exercise. Our caloric needs have gotten smaller. Also, our food is being processed away from its natural state. This has led to an increase in type B malnutrition. This is not as severe as malnutrition resulting from starvation, but is still important.

Had Michelangelo been asked to portray 21st Century American man, it might have looked like this evolved figure.



Western practices focus on medical or surgical intervention on symptom, rather than on prevention of the ailments. It is now believed that chronic progressive diseases such as heart disease, diabetes, dementia and several forms of sight loss have several common underlying symptoms. The most important of these are blood vessel abnormalities and capillary function.

Diets rich in flavonoids (a type of polyphenol) reduce heart disease and the frequency of cancer. Several reasons are being studied concerning these findings.

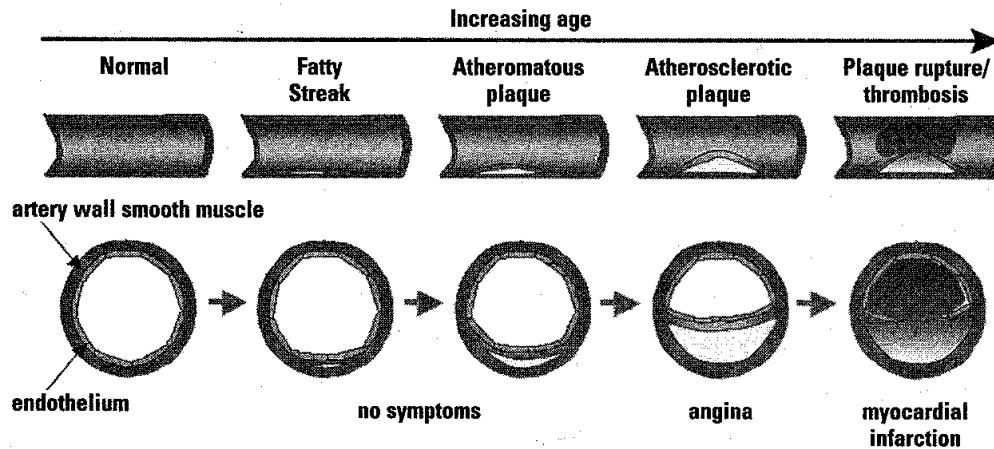
### *What is it about red wine?*

Examining the dozens of studies on alcohol consumption and health, while moderate consumption of any alcoholic beverage is beneficial, red wine is best for long-term well being.

What represents healthy wine drinking? Most "diets" also eliminate alcohol, so we won't look there. Tests show that some red wines contain much higher levels of procyanidins than others. By drinking these wines, maximum benefits, if any, can be gained by drinking less wine. However, red wine does not always show the same benefits as expected in all studies. Is it a particular substance in red wine that leads to health benefits? If so, knowing the active components would make it much easier to do more detailed research.

Some specific research has been done. Experimental studies have shown that alcohol was independent on red wines effect on arteriosclerosis. Grape seed extract at a dose of 1.5 to 2 grams per day has been shown to cut in half the level of cholesterol-induced arteriosclerosis. It has also been shown that purple Concord grape juice could hamper blood vessel wall changes that trigger arteriosclerosis.

## THE SILENT PROCESS OF ATHEROSCLEROSIS



*Coronary heart disease develops gradually. The illustration shows schematically a coronary artery, both lengthways (top) and in cross section (bottom). This shows the natural progression of atherosclerosis from early life through to the formation of a coronary artery blood clot or thrombosis, causing a myocardial infarction (heart attack).*

*Normal healthy arteries can accumulate small fat deposits of bad cholesterol (LDL-cholesterol). This can occur before you are 20 if you eat the wrong diet or have other risk factors. A change of diet and lifestyle can get rid of fatty streaks in the artery wall.*

*If left untreated, these atherosclerotic plaques progress slowly until they obstruct the normal blood flow and cause angina during physical effort. Stable angina, although restricting quality of life, is not necessarily life-threatening: some people live with it for many years. The real danger comes from an atherosclerotic plaque that suddenly becomes unstable and ruptures; this triggers the formation of a blood clot (thrombosis), which, by blocking the blood supply to the heart muscle, can cause the heart to stop beating rhythmically, with drastic consequences.*

Healthy artery walls are made of smooth muscle cells and fibrous connective tissues. Nerves outside the artery walls regulate the muscle cells, causing constriction and dilation. In one effect of high blood pressure (from stress and other occurrences) the nerves constrict the blood vessels. The fibrous tissue must be flexible when this happens. If the arteries are hard, they are less flexible and the blood pressure increases to dangerous levels. Blood vessels get firmer with age, increasing the risk for heart disease.

Blood cells are lined with endothelium. This single layer of cells creates a nonstick coating. The circulating blood won't stick to the wall layers of smooth muscle. The endothelium also responds to inflammation. The endothelium can tell the body's white blood cells where they are needed to fight infection and other inflammations.

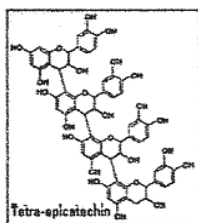
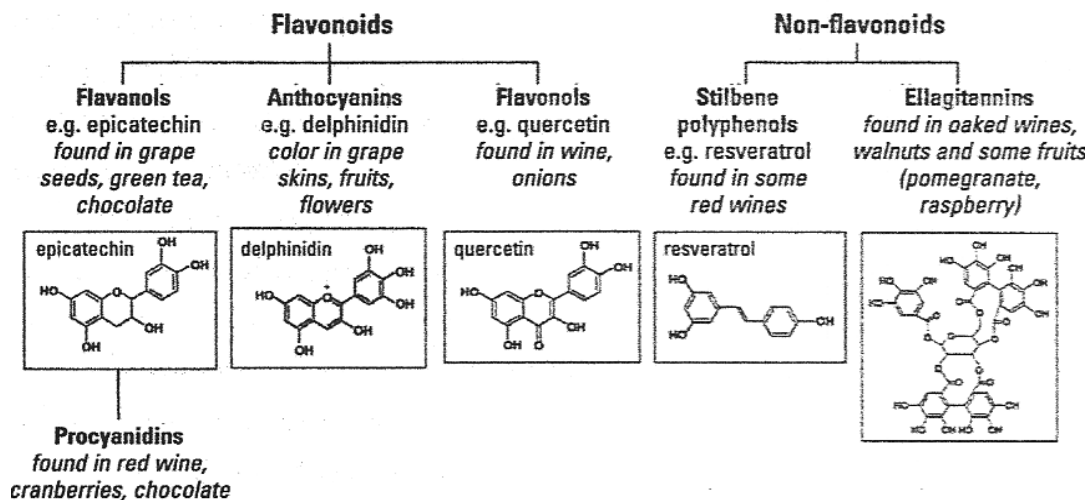
*How to keep blood vessels healthy*

The endothelium releases a host of compounds that are important in maintaining a healthy blood circulation. Changes in the endothelium can result in many problem related to the blood and its circulation.

*Which substances in red wine have a beneficial effect?*

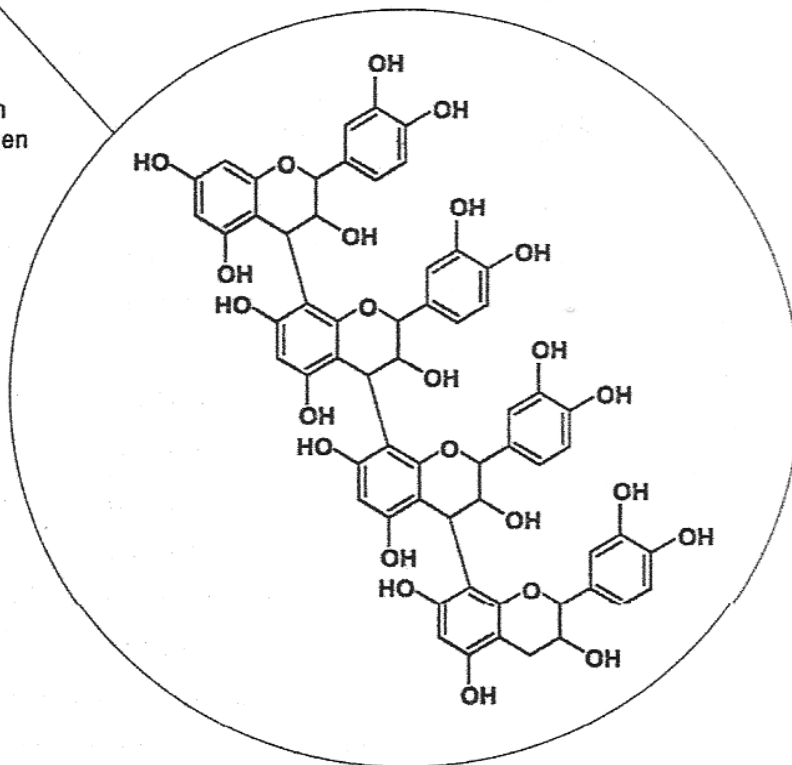
The simple answer is polyphenols...main contributors to color and taste. But there are many polyphenols with different properties. The polyphenols most commonly found in wine are called flavonoids. In red wines, the most abundant are flavonols and anthocyanins. (Quercetin and resveratrol are minor components.)

## POLYPHENOLS FOUND IN WINE



These examples show the molecular structure of just a few of the thousands of different polyphenols. The most common polyphenols in wine are classified as flavonoids. The most abundant flavonoids fall into two main groups: flavanols and anthocyanins. Of lesser importance are the flavonols (not the same as flavanols) and the non-flavonoids, such as resveratrol.

O = Oxygen  
H = Hydrogen



### A PROCYANIDIN MOLECULE

This procyanidin molecule, tetra-epicatechin, consists of four repeated units of epicatechin molecules (tetra means four in Greek).

Flavanols, such as catechin and epicatechin, are found mainly coating grape seeds. Grapes with smaller berries generally produce wines richer in these polyphenols. Grape seed flavanols are mainly present as procyanidins. When these polymers are composed of three to ten repeated units of smaller molecules (like catechin and epicatechin) they are called oligomeric procyanidins.

Procyanidins are the most abundant polyphenol in young red wines. Total polyphenols may be about 3 grams per liter in young reds and procyanidins may account for 1 to 2 grams per liter. Procyanidin molecules are not very soluble in grape juice. As fermentation proceeds the alcohol created will extract the procyanidins into the wine. These are the main cause of astringency. Over time, procyanidins combine with each other and form longer polymers called condensed tannins. As wines age the condensed tannins grow in length. They soon become less soluble and precipitate to your bottles bottom.

The colored pigments in red wine are anthocyanins. The anthocyanins in red wine are mainly extracted during fermentation from the grape skin. Rosé and white wines have almost no skin and seed polyphenols.

Polyphenols can also come from wood cooperage. Fresh oak has high levels of nonflavonoid polyphenols called gallotannins. These will dissolve into wine after about six months.

Polyphenols are very unstable molecules. During fermentation and aging, they react with one another and with other substances such as sugars. They also readily oxidize. Because of the myriad of reactions, it has been estimated every bottle of wine could contain several thousand possible compounds. This explains the evolution of a bottle aging wine. So, red wines are complex well mixed elixirs.

The two main areas studied vis-à-vis red wine polyphenols are on platelets and LDL-cholesterol. Platelets are tiny blood cells without a nucleus. Their main roll is to stop bleeding by plugging blood

vessels at the site of wounds and controlling blood coagulation. If they become too sticky, they can bind to the epithelium and form small blood clots. Some work has shown that people from red wine regions in France have lower blood clotting speeds than do people from non-wine regions like southwest Scotland. These studies are on going.

Cholesterol is a fatty substance produced by the body. Some is needed for good health. Too much production results in their accumulation on blood vessel walls. With time, these fatty deposits can oxidize and harden to form plaques-an early stage of atherosclerosis.

Arteriosclerosis refers to a hardening of medium and large arteries. Cholesterol travels in the blood stream mated with proteins. This combination of fat and protein is known as lipoproteins. Low-density lipoproteins (LDL-cholesterol) have a high proportion of fat to protein. It forms deposits on blood vessels and carries the tag " bad" . HDL-cholesterol is mostly protein. Not much fat. " Good" . The good guys mop up the bad guys in the blood and other tissue cells and cart them to the liver. The liver break them up and chuck them out. The HDL-cholesterol has many benefits and helps explain why low level of HDL-cholesterol is a risk factor for heart disease.

Experimentally, red wine polyphenols are more effective antioxidants than Vitamin C and E. Oxidized LDL is not readily eliminated. It can stimulate inflammation of the artery walls. This is a trigger to arteriosclerosis. If LDL-cholesterol is prevented from oxidizing, it is less likely to cause arteriosclerosis. However there has yet to be shown a correlation between antioxidant intake and heart attack incidences. So maybe the anti-oxidant properties in red wine or any food are not relevant.

*So, what' s going on?*

The endothelium function is very important in preventing arteriosclerosis. High blood pressure, raised LDL-cholesterol , diabetes, lack of exercise, age and smoking all reduces the protective property of the epithelium. After reduced protection, blood vessels in

the heart and other tissues have trouble resisting arteriosclerosis. It is known that red wine polyphenols protect the epithelium from raised LDL-cholesterol.

Some work in the 1990' s showed that red wine and grape extract caused endothelium-dependent vasodilation through nitric oxide releases. Healthy subjects were given 500-ml of red wine over a period of time. They produced endothelium-dependent vasodilation. A similar group was given vodka with no similar results. (Vasodilation is the widening of blood vessels resulting from relaxation of the muscular wall of the vessels. What widens is actually the diameter of the interior (the lumen) of the vessel. The opposite of vasoconstriction.)

In another study, patients with coronary heart disease were given 350-ml of Concord purple grape juice twice a day for two weeks. They showed an improvement in endothelium-dependent vasodilation. The susceptibility of LDL to oxidation was also decreased by this treatment.

Still, what is it in red wine and Concord purple grape juice that modifies vascular function and prevents arteriosclerosis? There are known vasoconstrictors. They narrow blood vessels and hence raise blood pressure. So if red wines can be shown to restrict vasoconstrictor synthesis, this could give protection from heart disease.

Studies have shown that all red wines suppressed vasoconstriction. Red grape juice has about 10% of the activity of average red wine and white and pink wine none. This led to the thoughts the benefits all started in the skin or seeds.

So, they honed in on the red polyphenols in seeds and skins. The most potent isolated were the procyanidins of various sizes and structures. Other work has shown procyanidins are best at preventing platelet aggregation.

Further work has shown that a wine's ability to control vascular problems is directly related to the procyanidin content of the wine. Many red wines have high procyanidin content, with amounts close to 1 gram per liter. For your information that's about 1,000 times greater than the normal levels of the once championed resveratrol.

### *Processing foods*

Polyphenols of all types tend to be rather astringent. So man has modified fruits and vegetables that may be too astringent or bitter to make them more palatable. Unfortunately, these processes generally strip the polyphenol benefits. Chocolate was originally made as a bitter drink. It is now a highly processed, sugared, fatted beverage with virtually no procyanidin.

### *The history of cocoa*

Cacao trees are native to parts of Central and South America. The Olmec grew the trees 3,500 years ago. The Maya and later the Aztecs did also. Naturally bitter, it was at times flavored with vanilla beans. It was never sweetened. The Aztecs called it *cacahuatl* or "bitter water". Columbus and then Cortés brought some back to Europe. The Europeans made it more palatable by adding sugar.

Cocoa beans are one of the richest sources of procyanidins, but chocolate manufacturing has evolved where the health-promoting compounds are gone from the final products.

Studies have shown controlled diets of non-manufactured cocoa have yielded lower blood pressure, faster blood vessel response and better vascular functions than control groups. It also seems to be more beneficial with population age.

If it's chocolate you want, the most beneficial from a health standpoint comes from Ecuador. It is particularly tannic. But approximately one ounce of good dark chocolate containing 70 to 86%

cocoa solids, or about three tablespoons of unsweetened cocoa powder, is equivalent to a 4-ounce glass of procyanidin-rich red wine. That's about 150 calories of chocolate. The main problem is chocolates on the market are loaded with sugar and fat.

### *Others foods*

**Apples** contain only moderate amounts of vitamin C, potassium, folic acid and fiber. Research has shown they are a good source of procyanidins. The average procyanidin content of a medium apple is equivalent to a 4-ounce glass of procyanidin-rich red wine. Eat them fresh.

**Cranberries** are a rich source of procyanidins. About 2 ounces of fresh or frozen berries or about 8-ounces of juice containing 25% cranberry is roughly equivalent to a 4-ounce glass of procyanidin-rich red wine. The juice phase can be too high in sugar.

**Raspberries** are loaded with polyphenols. Approximately 2 ounces of raspberries, or 4 ounces of blackberries, strawberries or red currants, contain are the same as a 4-ounce glass of procyanidin-rich red wine.

**Pomegranate** is high in procyanidins. One medium pomegranate will yield about 4 ounces of juice. This is equivalent to a 4-ounce glass of procyanidin-rich red wine.

**Walnuts** are very rich in polyphenols. They are not procyanidins but a mixture of antioxidant polyphenols. A serving of 1.5 ounces of walnuts provide the same benefit as a 4-ounce glass of procyanidin-rich red wine.

Beans, grains, cinnamon and other foods can be beneficial. The preparation is critical to not destroy the potency. Tea has very few large procyanidin molecules.

### *Will you live to be 100?*

Some societies feel this is reasonable and achievable. In Sardinia, the common greeting is "A kent' annos" - "to one hundred years". Sardinia's mountainous Nuoro province has the highest relative number of centenarians in Europe. Medical care in the province is basically

nonexistent. Life style is important. Smoking. Exercise. All important. The Nuoro residents are pretty much like most other parts of Europe in regard to these items.

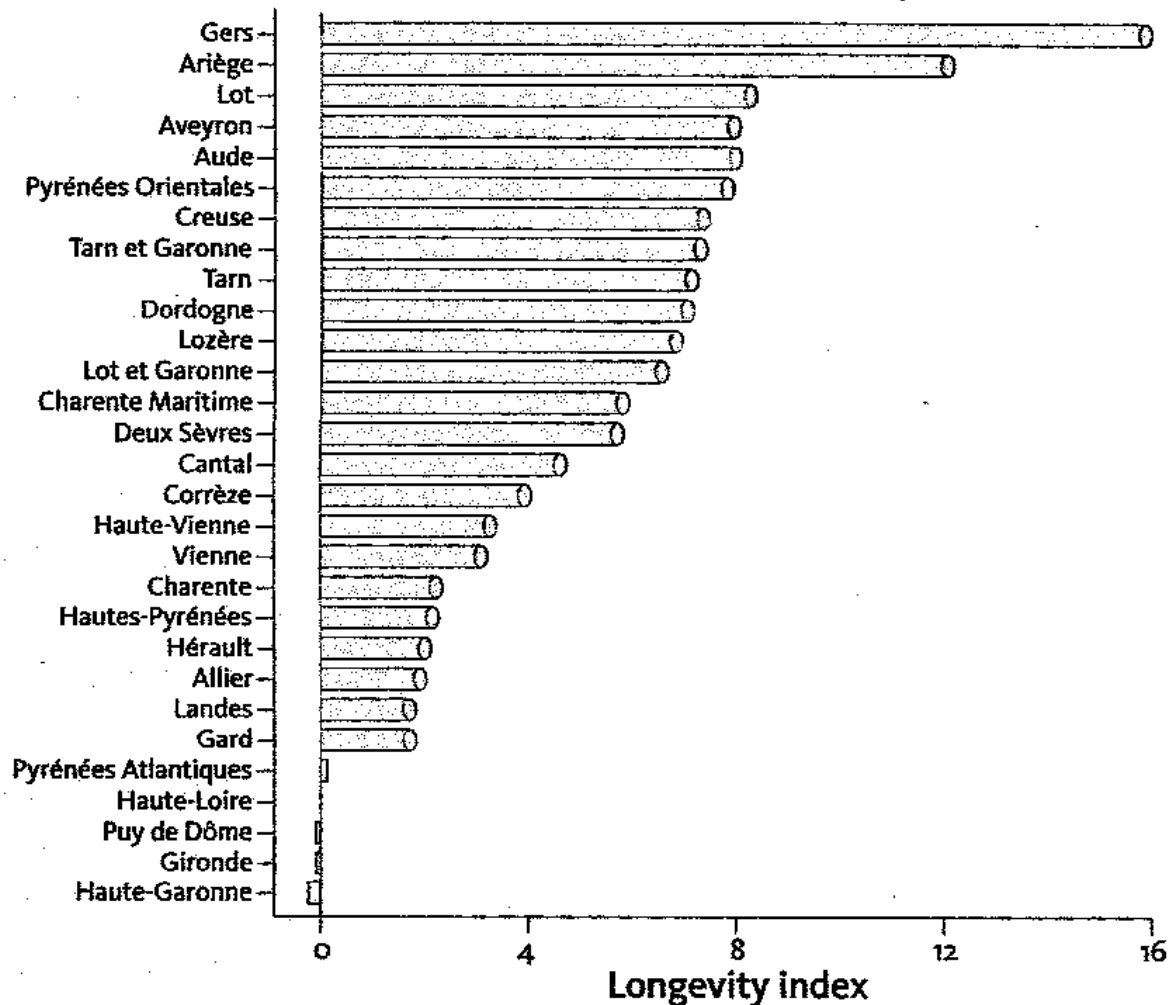
Diet wise, they eat a large proportion of roasted meat and cheese. The wines produced in that area are made mainly from Cannonau (same as Grenache), Barbera, Monica and Muristellu. Lab analysis of the wines from the province showed higher levels of procyanidins than wines from Sardinia' s coastal regions. Just to be noted. Not evidence.

Similar studies show other population centers with high percentage of centenarians also consume wines with high levels of procyanidins.

Everybody remembers the French Paradox of the 1980' s. Red wine consumption accounted for low occurrence of heart disease in France. It has been further studied if longevity differences exist in France. 1999 census data was used to analyze the regional distribution of men and women aged 75 years and more. The analysis showed six regions in southwest and central-southern France where relative numbers of men aged 75 or older was more than 25% higher than the national average. Further analysis showed that all over France, for every man in this older age range there are approximately two women (2.12 to be exact). The département of Ger had a ratio of men to women that was more than 20% of the national average. Gironde, which includes Bordeaux, was the same as the average. Ger also had double the national average of men aged 90 or more.

## LONGEVITY INDEX FOR MEN IN SOUTHWEST FRANCE

Relative Longevity—% difference from national average for men aged 75+



Is this an intra-French paradox? Ger is famous for its foie gras, cassoulet, saucisson, and many great cheeses. Analysis of the wines from the area, notably Madiran, indicated three to four times more procyanidin than Argentine Cabernet Sauvignons. These Cabs are known for high procyanidin levels. This means, one small glass of Madiran can provide greater benefit than two bottles of most California red wine. It seems probable these wines are linked to the high survival rate to the men of Ger.

Why are these wines special? The primary grape of the region is Tannat. The winemaking methods are centuries old. The wines can be

tannic and not suitable for drinking standing up. But when sipped with robust local foods, the high tannin of these wines is hardly noticeable. In fact, most other wines are dwarfed by the dishes and are poor matches. The winemakers in the area still harvest at fairly low sugars and do not yet practice hang time to get fruit forward characters and soft ripe tannins in their grapes.

### *Hunt for procyanidin wines*

Polyphenols are a large group of unstable compounds. Different tastes in wines can be attributed in large part to the variety of polyphenols wine contains. Polyphenols also interact with acids and create additional flavors. Young red wines are often astringent, and procyanidins are thought to be one of the causes in giving a wine astringency. This is mouthfeel and not taste. Astringency is sensed as a rough dry mouthfeel. It's puckering. It's caused by the interaction of saliva proteins and polyphenols. The interacted polyphenols then precipitate and become insoluble so the lubricating effect of saliva is briefly lost. Acid does the opposite. It makes the mouth salivate more. The astringency and acid must be in balance in a wine to be appreciated. Astringency declines as wines age.

### *Key factors in vineyards for making high procyanidin wines*

There are complex interactions playing into what harvested grapes are like. Some observations:

Infertile land

Well-drained soil

Long, slow ripening

High altitudes

Low yields

### *What can the winemaker do?*

Extended maceration is the process of leaving a red wine in contact with the skins after fermentation is complete. This technique is employed when a winemaker wishes to modify the amount, and types, of tannin present when pressing the wine to barrel. In red fermenters,

the peak in anthocyanin extraction occurs within the second day of fermentation and those of skin tannins and flavonoids (or total phenols) usually show complete extraction by the end of fermentation. So, extended maceration will result in the continued extraction from seeds only. It may seem counterintuitive but this extended amount of time in contact with the skins and seeds can actually soften the tannin structure of a wine that finishes fermentation with an elevated sharp tannin structure.

These are just suggestions.

### *Procyanidin Rich Wines*

A 4-ounce glass of red wine containing:		
Average	30 to 45 mg procyanidins.	♥
Shows Promise	45 to 60 mg procyanidins.	♥ ♥
Good	60 to 90 mg procyanidins.	♥ ♥ ♥
Very Good	90 to 120 mg procyanidins.	♥ ♥ ♥ ♥
Excellent	120 or more mg procyanidins.	♥ ♥ ♥ ♥ ♥

Searching for wines in the regions listed below may result in high procyanidin wines.

**Excellent**      **120 or more mg procyanidins.**      ♥ ♥ ♥ ♥ ♥

Southwest France

Languedoc-Roussillon

Pommard

Umbria

Sardinia

Washington

**Very Good**

**60 to 190 mg procyanidins.**



Argentina

Bordeaux

Rhone

Piedmont

Veneto

Chianti

Sicily

Douro

Rioja

Uruguay

Napa

**Good**

**60 to 90 mg procyanidins.**



Chile

Australia

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Proanthocyanidins.doc Education VWT 180 Folder

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