




## Wine: Better with Age

*The Benefits of Wine for the Aging Process*



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## Objectives

- ❖ 1. Define the French Paradox
- ❖ 2. Describe the biological components of wine
- ❖ 3. Explore the proposed health and anti-aging benefits of wine
- ❖ 4. Examine the future marketing of wine as a nutraceutical product

## Wine through Time

- ❖ Earliest evidence: pottery jars
  - ❖ 7,000 year old wine
  - ❖ Calcium salts of tartaric acid only present in grapes
- ❖ Used as a medicine for 5000 years
  - ❖ Hippocrates: Father of modern medicine
    - ❖ Diuretic
    - ❖ Antiseptic
    - ❖ Fever Reducer

De Lange DW. *Thrombosis Research* 2007; 119: 403-406  
Images from: <http://www.dnorie.info/images/hippocrates.jpg>  
<http://www.archaeology.org/9609/newsbriefs/wi>

## MONICA Project

- ❖ Multinational **MON**itoring of trends and determinants in **CA**rdiovascular disease
- ❖ Trends in CV risk factors and incidence rate over a ten year period
- ❖ 32 centers in 21 countries
- ❖ 10 million men and women
- ❖ Ages 25-64 years

WHO MONICA Project. *MONICA Manual*. (1998-1999). <http://www.kfi.fi/publications/monica/manual/index.htm>

## MONICA Project

	Annual CHD Mortality per 100,000 population		Mean Serum Cholesterol (mg/dL)	
	Male	Female	Male	Female
Japan	33	9	--	--
China (Beijing)	49	27	163	166
France (Toulouse)	78	11	230	224
USA (Stanford, CA)	182	48	209	205
UK (Belfast)	348	88	232	236
UK (Glasgow)	380	132	244	248

Adapted from: Renaud S, de Lorgeril M. *Lancet* 1992; 339: 1523-26

## The French Paradox: 1992

- ❖ UK, US, France share similar
  - ❖ Intake of saturated fats
  - ❖ Smoking habits
  - ❖ Lack of exercise
- ❖ France
  - ❖ ↓ CHD mortality rate
- ❖ Explained through Mediterranean diet of vegetables, fruits, olive oil and red wine
- ❖ Inverse association with moderate wine consumption and CHD
- ❖ Proposed mechanism: red wine inhibits platelet aggregation

Renaud S, de Lorgeril M. *Lancet* 1992; 339: 1023-26



## Biological Components: The Recipe

- ❖ Grape juice, skins, and seeds
  - ❖ 500 different types of antioxidants
  - ❖ Polyphenols
    - ❖ Flavonoids
    - ❖ Nonflavonoids
  - ❖ 8-15% Ethanol (by weight)
  - ❖ Combine and allow to ferment



German JB, Walzem RL. *Ann Rev Nutr.* 2000; 20: 561-93

## Polyphenols



- ❖ Responsible for bitterness and color
- ❖ **Antioxidant**
- ❖ **Found in grape skin, seeds and stems**
- ❖ **Red wine**
  - ❖ Skins and stems **left in contact** for prolonged periods
  - ❖ Contains 1.8 g/L polyphenols
- ❖ **White wine**
  - ❖ Skins and stems **rapidly separated** after juice extraction
  - ❖ Contains 0.2-0.3 g/L of polyphenols

German JB, Walzem RL. *Ann Rev Nutr.* 2000; 20: 561-93



## 1 Glass of Red Wine (150 mL)=

- 12 glasses white wine=
- 2 cups tea=
- 5 apples=
- 5 onions=
- 5.5 portions of eggplant=
- 3.5 glasses of black currant juice=
- 500 ml beer=
- 7 glasses orange juice=
- 20 glasses of apple juice=

## Units of Antioxidant Activity

German JB, Walzem RL. *Ann Rev Nutr.* 2000; 20: 561-93

## Polyphenols: Flavonoids

- ❖ Found in **grape seeds, skins, and stems**
- ❖ **Catechins**
  - ❖ Inhibits oxidation of LDL (Oxidized LDL → atherogenic)
- ❖ **Procyanidins**
  - ❖ Inhibits Angiotensin-Converting Enzyme (ACE) activity
- ❖ **Proanthocyanidins**
  - ❖ Strong antioxidant: scavenges free radicals
  - ❖ Decreases myocardial infarct size in rats
- ❖ **Quercetin**
  - ❖ Anti-inflammatory
  - ❖ Antioxidant

Bertelli AAA, Das DK. *J Cardiovasc Pharmacol.* 2009; 54(6): 468-76

## Polyphenols: Non-flavonoids

- ❖ **Resveratrol**
  - ❖ Trans-Resveratrol
  - ❖ Phytoestrogen
- ❖ Found in grape skins, peanuts, mulberries, rhubarb and 70 species of plants
  - ❖ More concentrated in red wines
- ❖ Naturally synthesized by grapes in response to a fungal attack
- ❖ Activates protein deacetylases of *Sir2* (*sirtuin*) enzymes

Oplie LH, Lecour S. *European Heart Journal* 2007; 28: 1683-93

## Resveratrol: Benefits

- ❖ **Inhibits**
  - ❖ LDL oxidation
  - ❖ Inflammatory response (cyclooxygenase inhibition)
- ❖ **Possesses**
  - ❖ Anti-platelet properties
  - ❖ Free-radical scavenging activity
  - ❖ Anti-cancer effects (↓ tumor growth, ↑ apoptosis)
  - ❖ Anti-stroke benefits (neuroprotective in ischemic injury)
- ❖ **Activates sirtuins**
  - ❖ Mimics caloric restriction
  - ❖ Increases lifespan/longevity in worms, flies, and mice
  - ❖ Decreases diet-induced obesity and insulin resistance in mice

Oplie LH, Lecour S. *European Heart Journal* 2007; 28: 1683-93

## Ethanol

- ❖ J-shaped curve
- ❖ Moderate ethanol consumption\* significantly reduces mortality relative to alcohol abstinence
- ❖ No intake or increased intake:
  - ❖ ↑ mortality



\*1-2 glasses per day

German JB, Walzem RL. Ann Rev Nutr. 2000; 20: 561-93

## Benefits of Moderate Ethanol Intake

- ❖ Decreases CHD incidence
- ❖ Reduces HDL degradation (↑HDL)
- ❖ Inhibits platelet aggregation
- ❖ Increases fibrinolysis
- ❖ Enhances insulin sensitivity / glucose utilization (up to 24 hours)
- ❖ Reduces inflammation
  - ❖ ↓ C-reactive protein

German JB, Walzem RL. Ann Rev Nutr. 2000; 20: 561-93

## Red or White?



- ❖ White wine
  - ❖ Lacks anthocyanin activity
  - ❖ Different protective benefits
  - ❖ Contains anti-inflammatory substances
    - ❖ May ↓ inflammatory reaction in atherosclerosis
- ❖ Short-term studies
  - ❖ Equal effects as red wine
    - ❖ Fibrinolysis
    - ❖ ↓ Platelet aggregation

Oplie LH, Lecour S. European Heart Journal 2007; 28: 1683-93

## Wine: A Panacea?

- ❖ Studies report wine *may* have a beneficial effect on:
  - ❖ Cancers
  - ❖ Diabetes
  - ❖ CV function
  - ❖ Alzheimer's
  - ❖ Parkinson's
  - ❖ Appetite loss
  - ❖ Renal function
  - ❖ Anxiety
  - ❖ Bone mass
  - ❖ Waist circumference
  - ❖ Macular degeneration
  - ❖ Bacteria/Viruses

## Cancer



- ❖ Moderate wine consumption *decreased* the risk of non-Hodgkin's lymphoma by 20-40%
- ❖ *Decreased lung cancer* risk when compared to beer and other spirits
- ❖ MOA: Wine *may* inhibit cell events associated with cancer development and progression

Stockley CS. Int J Wine Res. 2009; 1: 195-207

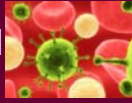
## Neurologic



- ❖ Multiple studies suggest that light to moderate wine or alcohol consumption improves cognitive function and memory
- ❖ MOA: Possible anti-atherosclerotic effect by preservation of brain vasculature or through stimulation of acetylcholine in hippocampus

Stockley CS. Int J Wine Res. 2009; 1: 195-207

## Antimicrobial



- ❖ **Red and white wines**
  - ❖ May reduce *Salmonella*, *Shigella*, and *E. coli*
  - ❖ Kill cavity-causing bacteria
- ❖ **Red wine**
  - ❖ May control *H. pylori* proliferation in the stomach (resveratrol)
- ❖ **Wine may protect against the incidence of the common cold virus**

Halpern GM. Inflammopharmacology 2008; 16: 240-44

## Resveratrol: The New Nutraceutical

- ❖ **Resveratrol-enhanced red wine**
  - ❖ White wine: 1-2 mg/L
  - ❖ Red wine: 3-6 mg/L
  - ❖ Enhanced: 155 mg/L
- ❖ **Sirtis Pharmaceuticals**
  - ❖ In the pipeline:
    - ❖ Drugs to mimic resveratrol
    - ❖ Strengthens body's resistance to diseases of aging
      - ❖ Cancer, Diabetes, Alzheimer's
- ❖ **Recommended dose: *unknown***
- ❖ **Bioavailability: low (due to rapid metabolism and elimination)**
- ❖ **Drug interactions: may inhibit CYP3A, CYP1A, and CYP2E1, increases bleeding risk with anticoagulant/antiplatelet drugs**



Norie PA. Int J Wine Res. 2009; 1: 167-68  
Sirtispharma.com

## U.S. Department of Health and Human Services

- ❖ **Healthy People 2010**
  - ❖ National health promotion and disease prevention initiative
  - ❖ Supports the promotion of moderate alcohol consumption
- ❖ **♀ : 1 drink per day\***
- ❖ **♂ : 2 drinks per day\***
- ❖ \* 5 fluid ounces per serving

**with meals**

US Department of Agriculture, US Department of Health and Human Services. Dietary Guidelines for Americans: 2005, 2010.  
Peregryn T. J Am Diet Assoc. 2005; 105 (7): 1053-1054

## Not So Fast!



- ❖ **Drinking alcohol linked to:**
  - ❖ **Cancers**
    - ❖ Breast, Colon, Mouth, Rectal, Throat, Larynx
  - ❖ **Heart failure**
    - ❖ Chronic, large amounts of alcohol → cardiomyopathy
  - ❖ **Hypertension**
    - ❖ 2+ drinks/day: 1.5-2x ↑ incidence hypertension vs nondrinkers
  - ❖ **Arrhythmias**
    - ❖ Binge, heavy chronic alcohol ↑ incidence A.fib
  - ❖ **Liver disease**
  - ❖ **Stroke**
    - ❖ 4+ drinks/day: ↑ risk all strokes

Tangney CC, Rosenson RS. In: UpToDate, Gersh BJ (Ed). UpToDate. Waltham, MA, 2009

## Conclusions

- ❖ **Benefits suggested when wine intake is only in moderation**
- ❖ **Studies unreliable**
  - ❖ Confounding factors: lifestyle or wine?
  - ❖ Observational studies = self reporting
- ❖ **Results conflicting**
  - ❖ Lack of human studies: in vitro, animal, ex vivo
- ❖ **Need randomized, blinded trials**
  - ❖ Difficult, unethical
- ❖ **Alcoholic beverages should not be recommended as a substitute to well-proven CV risk-reducing alternatives: low fat diet, exercise, pharmacotherapy**

## Questions



1. Evidence shows that the more red wine an individual consumes, the greater the cardioprotective and neuroprotective benefits achieved.
2. Resveratrol, naturally found in grapes, peanuts and mulberries, is synthesized in response to a fungal infestation of the plant.
3. The skin portion of the grape is the only source of antioxidants in the fruit.