



## Workshop

### Protective / preventive role of bioactive food components in human health

## Nutraceutical Bioactive compounds



Prof. Silvana Hrelia  
Department for Life Quality Studies  
Alma Mater Studiorum-University of  
Bologna (Italy)

Novi Sad, December 13-14, 2016

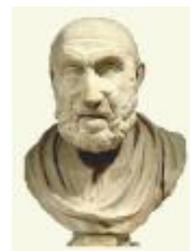
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IL PRESENTE MATERIALE È RISERVATO AL PERSONALE DELL'UNIVERSITÀ DI BOLOGNA E NON PUÒ ESSERE UTILIZZATO AI TERMINI DI LEGGE DA ALTRE PERSONE O PER FINI NON ISTITUZIONALI



## Nutrition to support well being

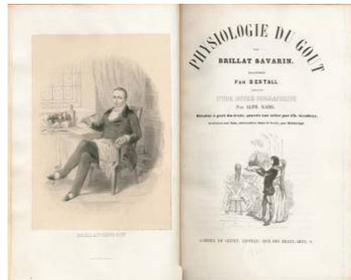
- Nutritional discoveries from the earliest days of history have had a positive effect on our health and well-being.
- 400 B.C. -- Hippocrates, the "Father of Medicine", said to his students, "**Let thy food be thy medicine and thy medicine be thy food**".  
He also said "A wise man should consider that health is the greatest of human blessings."



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## “YOU ARE WHAT YOU EAT” ?



"Dis-moi ce que tu manges, je te dirai ce que tu es."

Anthelme Brillat-Savarin, *Physiologie du Gout, ou Meditations de Gastronomie Transcendante*, 1826

He was simply stating that the food one eats has a bearing on what one's state of mind and health.



## What is Nutrition?

- The word **nutrition** itself means “The process of nourishing or being nourished, especially the process by which a living organism assimilates food and uses it for growth and replacement of tissues.”
- Today more than ever, obtaining nutritional knowledge can make a big difference in our lives



## Nutrition 1.0

### BALANCED DIET

...needs to have a *balance* of macronutrients / energy ( fats, proteins, and carbohydrates ) and micronutrients to meet the needs for :



- support the growth,
- maintain body weight,
- prevent the development of dietary deficiency diseases such as rickets, goiter, anemia, scurvy, etc

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## Nutrition 2.0

### OPTIMUM NUTRITION

...eating the right amounts of nutrients on a proper schedule to...

- achieve the best performance and the longest possible lifetime in good health,
- decrease the risk of chronic/degenerative diseases



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## The era of Functional food and Nutraceutical

- Consumers are increasingly interested in the **health benefits** of foods and have begun to look beyond the basic nutritional benefits of food to the **disease prevention** and **health enhancing compounds** contained in many foods.
- This combined with a more widespread understanding of **how diet affects disease**, health-care costs and an aging population have created a market for functional foods and natural health products

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## Functional Food

- a food can be regarded as “**functional**” if it is satisfactorily demonstrated to affect beneficially **one or more** target functions in the body, beyond adequate nutritional effects, in a way which is relevant to either the state of **well-being and health** or the **reduction of the risk of a disease**”.

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# What is a Functional Food?

Functional Foods



Natural food?

Fortified food?

Modified food?

Designer food?

## Working Definition:

*Foods that may provide a health benefit beyond basic nutrition.*

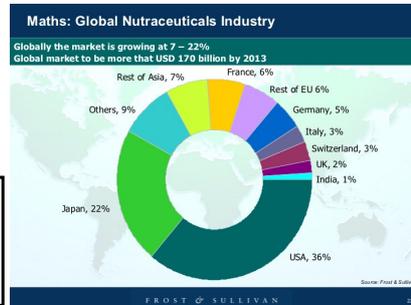
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Health care costs  
Life span increase  
Life style changes  
Chronic/degenerative diseases

Scientific research  
New technologies

Functional food

Health  
Life quality  
Ageing





# FOSHU “Food for Specified Health Use”



The concept of functional foods was established in Japan in 1991  
FOSHU must be approved by the Minister of Health and Welfare after the submission of comprehensive science-based evidence



## European Commission Concerted Action on Functional Food Science in Europe - FUFOSE coordinated by the International Life Science Institute (ILSI) Europe (1995-1998)



### Scientific Concepts of Functional Food in Europe: Consensus Document

A.T. Diplock, P.J. Aggett, M. Ashwell, F. Bornet, E.B. Fern & M.B. Roberfroid.

*Brit. J. Nutr.* (1999) Vol. 81, S1-S27

- Introduction
- Scientific basis
- Target functions
- Technological aspects
- Communication of health benefits (Health Claims)



## European consensus document

The unique features of functional foods are:

- Conventional or every day food;
- Consumed as part of a normal diet;
- Composed of naturally occurring components;
- Having a positive effect on physiological function beyond nutritive value (basic nutrition);
- Having authorized and scientifically substantiated health claims

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## Scientific proof

Biological Level	Main Type of Evidence
Molecular Sub-Cellular Cellular Tissue Organ	<i>Biochemical &amp; Physiological Mechanism</i> <i>in vitro</i> <i>ex vivo</i> <i>in vivo</i> <i>in situ</i>
Whole Body Sub-Populations Populations	'Practical " Effect Intervention Trials Epidemiological Meta-analyses
Nutrigenomics	'Individual " Effect 'Analytical'

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## Health Claims

- The EU Concerted Action supports the development of two types of health claims relevant to functional foods, which must always be valid in the context of the whole diet and must relate to the amounts of foods normally consumed.



## Health Claims

- **TYPE A: "Enhanced function"** claims that refer to specific physiological, psychological functions and biological activities beyond their established role in growth, development and other normal functions of the body. This type of claim makes no reference to a disease or a pathological state
- **TYPE B "Reduction of disease-risk"** claims that relate to the consumption of a food or food component that might help reduce the risk of a specific disease (e.g. folate can reduce a woman's risk of having a child with neural tube defects, and sufficient calcium intake may help to reduce the risk of osteoporosis in later life).



## Nutraceuticals

- **Nutraceutical**, a term combining the words “**nutrition**” and “**pharmaceutical**”, is a **food constituent** that provides health and medical benefits, including the prevention and treatment of disease
- The term nutraceutical was originally defined by Dr. Stephen L. DeFelice, founder and chairman of the Foundation of Innovation Medicine (FIM), Crawford, New Jersey (USA)

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## Nutraceuticals

- These food constituents are chemical components mainly present in plant food or of microbial sources, and provide medicinal benefits valuable to long-term health. Examples of these nutraceutical chemicals include **probiotics, antioxidants and phytochemicals**



*The regular fruit and vegetable consumption is associated to a reduced risk of chronic/degenerative diseases.*



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## Nutraceutical diet

*Institutions like FAO and WHO recommend a daily intake of at least 400 grams of fruits and vegetables a day, if possible in 5 different servings*

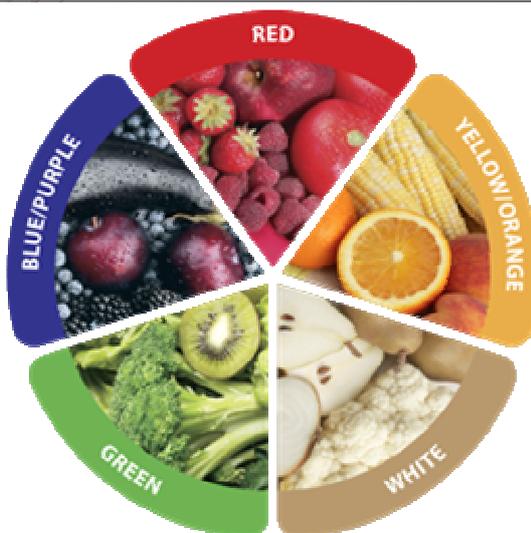


World Health Organization

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## Eat the colours of life



To get the most benefits out of eating fruits and vegetable, you should eat at least one daily serving from each of the five color groups:  
blue/purple,  
green,  
white,  
yellow/orange  
red  
as the "Color Way" campaign suggests. This campaign is also known as "The Five Color Diet" or the "5 A Day" diet.

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## 5 Colors of Phytonutrients

8/10 Americans Don't Eat Enough Color...

<p><b>74% Don't Eat Enough Red</b></p> <p>Phytonutrients: lycopene, ellagic acid, quercetin, hesperidin, anthocyanidins</p>	<p><b>Red Benefits</b></p> <p>Supports prostate, urinary tract and DNA health. Protects against cancer &amp; heart disease.</p>
<p><b>76% Don't Eat Enough Purple/Blue</b></p> <p>Phytonutrients: resveratrol, anthocyanidins, phenolics, flavonoids</p>	<p><b>Purple Benefits</b></p> <p>Good for heart, brain, bone, arteries, &amp; cognitive health. Fights cancer &amp; supports healthy aging.</p>
<p><b>69% Don't Eat Enough Green</b></p> <p>Phytonutrients: lutein/zeaxanthin, isoflavones, EGCG, indoles, isothiocyanates, sulphoraphane</p>	<p><b>Green Benefits</b></p> <p>Supports eye health, arterial function, lung health, liver function, &amp; cell health. Helps wound healing &amp; gum health.</p>
<p><b>83% Don't Eat Enough White</b></p> <p>Phytonutrients: EGCG, allicin, quercetin, indoles, glucosinolates</p>	<p><b>White Benefits</b></p> <p>Supports healthy bones, circulatory system, &amp; arterial function. Fights heart disease &amp; cancer.</p>
<p><b>80% Don't Eat Enough Yellow/Orange</b></p> <p>Phytonutrients: alpha-carotene, beta-carotene, beta cryptoxanthin, lutein/zeaxanthin, hesperidin</p>	<p><b>Yellow Benefits</b></p> <p>Good for eye health, healthy immune function, &amp; healthy growth &amp; development.</p>

**Goal: Eat two foods from each color group daily**

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By eating fruits and vegetables of a variety of different colors, one can get the best all-around health benefits. Each different color fruit and vegetables contains unique health components that are essential to our health.

## Non nutrient components: Phytochemicals

<p><b>Turmeric</b></p> <p>Curcumin</p>	<p><b>Grapes</b></p> <p>Resveratrol</p>
<p><b>Chili peppers</b></p> <p>Capsaicin</p>	<p><b>Honey</b></p> <p>Caffeic acid phenethyl ester</p>
<p><b>Ginger</b></p> <p>[6]-Gingerol</p>	<p><b>Garlic</b></p> <p>Diallyl sulphite</p>
<p><b>Green tea</b></p> <p>Epigallocatechin-3-gallate</p>	<p><b>Cabbage</b></p> <p>Indole-3-carbinol</p>
<p><b>Soybeans</b></p> <p>Genistein</p>	<p><b>Broccoli</b></p> <p>Sulphoraphane</p>
<p><b>Tomatoes</b></p> <p>Lycopene</p>	

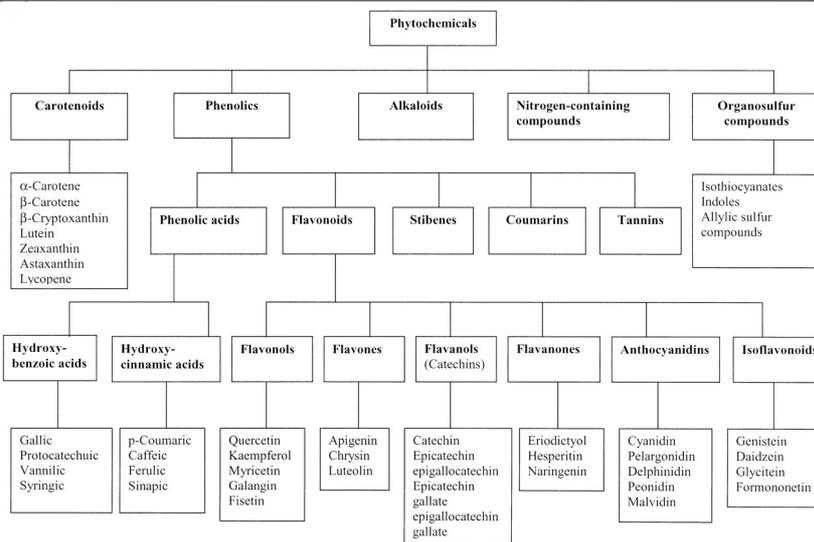
Phytochemicals are non-nutritive plant chemicals that have protective or disease preventive properties.

They are **non-essential nutrients**, meaning that they are not required by the human body for sustaining life.

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## Classification of dietary phytochemicals



Rui RH. *J Nutr* 134: 3479S-3485S (2004)

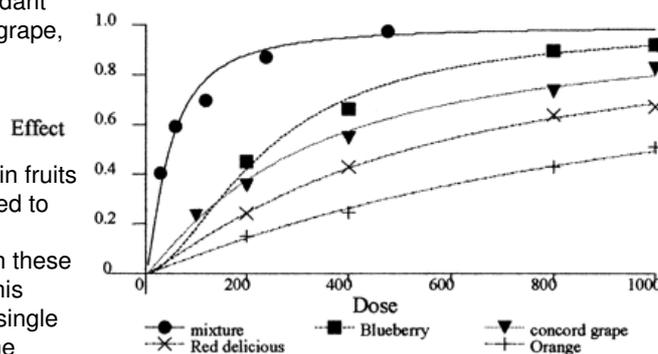
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## Sinergy of dietary phytochemicals

Dose-response of antioxidant activity of orange, apple, grape, blueberry and 4-way combination.

The benefit of a diet rich in fruits and vegetables is attributed to the complex mixture of phytochemicals present in these and other whole foods. This partially explains why no single antioxidant can replace the combination of natural phytochemicals in fruits and vegetables in achieving the observed health benefits.



Rui RH. *J Nutr* 134: 3479S-3485S (2004)

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## Pharmacological vs physiological dose

It is important to differentiate the **pharmacological dose** from the **physiological (or nutritional) dose**.

Pharmacological doses are used clinically to treat specific diseases in certain situations and require a doctor's prescription;

physiological (or nutritional) doses are used to improve or maintain optimal health, such as in foods.

The pharmacological dose is not equal to the physiological (or nutritional) dose and, in some cases, **can be toxic** for long-term use.

Currently, there are no recommended dietary allowances for phytochemicals. Therefore, **it is not wise to take megadoses of purified phytochemicals as dietary supplements before the appearance of strong supporting scientific evidence**.



### ORIGINAL ARTICLE

## Increased consumption of fruit and vegetables is related to a reduced risk of coronary heart disease: meta-analysis of cohort studies

FJ He<sup>1</sup>, CA Nowson<sup>2</sup>, M Lucas<sup>2</sup> and GA MacGregor<sup>1</sup>

<sup>1</sup>Blood Pressure Unit, Cardiac and Vascular Sciences, St George's University of London, London, UK and

<sup>2</sup>Centre for Physical Activity and Nutrition Research, School of Exercise and Nutrition Sciences, Deakin University, Australia

**The analysis of data collected in 12 different studies, which enrolled 280000 subjects revealed that people consuming 3-5 or more than 5 servings/day had a risk reduction for coronary heart disease of 7% and 17%, respectively when compared with subjects who consumed less than 3 servings/day.**





## Phytochemicals In the Spotlight

- Phytochemicals have been discovered within the past two decades.
- They are in the “Nutrition Spotlight” and are the “New Nutritional Frontier.”
- Research present in both in the private and public sectors.



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## So What are Phytochemicals?

- Phytochemicals are “plant chemicals.”
- They are naturally occurring compounds.
- However, most of their functions/roles in most plants are unknown.
- They provide healthier benefits and treat/prevent diseases.
- There are tens of thousands in the foods we eat (especially fruits, vegetables, and grains).

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## Phytochemicals: main actions

- **Detoxifiers**
  - helps body recognize and destroy toxins
- **Antioxidants**
  - removes cell-damaging molecules (free radicals)
- **Cell Regulators**
  - helps control growth of tumor cells
- **Hormone Modulators**
  - mimic hormones or prevent production

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## Allylic Sulfides

- **Garlic, onions, leeks, shallots, chives**



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## Allylic Sulfides (nutraceutical value)

- Stimulate enzymes that inhibit bacterial growth
- Lower blood pressure and cholesterol levels
- Strengthen immune and cardiovascular system
- Anti-growth activities for fungi and parasites
- Cancer preventive properties



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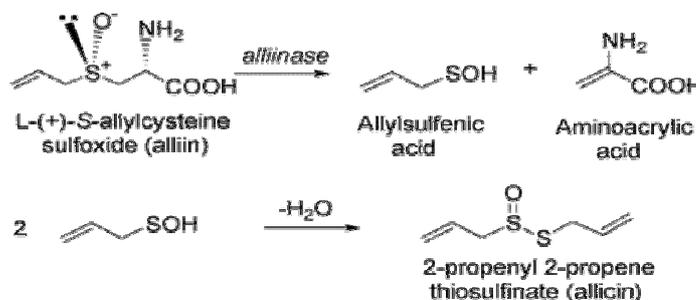


## Allylic Sulfides

The most abundant allylic sulphide in garlic is **allicin** which represent 70% of all the allylic sulphides in garlic, possessing antibacterial properties.

The immediate precursor of allicin is **alliin**, (+)-S-allyl-L-cysteine S-oxide.

Allicin is formed by action of the C-S lyase enzyme **alliinase** (released by cutting or crushing garlic cloves) on the stable precursor alliin in 10 s at room temperature!

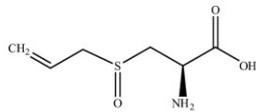


Martins N et al. Food Chem 211:41-50 (2016)

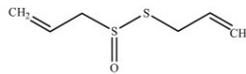
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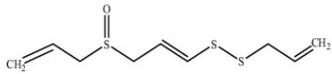
## Allylic Sulfides



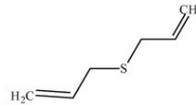
Alliin



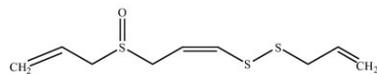
Allicin



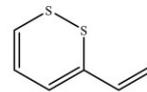
(E)-ajoene



Allyl sulfide



(Z)-ajoene



1,2-vinyldithiin

Stereochemical structure of the most representative bioactive constituents from *Allium sativum* L



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## Garlic and blood pressure

High blood pressure is an important risk factor for cardiovascular disease and is attributed to an estimated 70% of heart attacks, strokes, and chronic heart failure .

Garlic supplements have shown promise in lowering blood pressure in several meta-analyses .

Garlic contains a number of active sulfur compounds that modulate **endothelium-relaxing and -constricting factors**, leading to blood pressure reduction. Specifically, garlic has been shown to stimulate the **production of NO** and hydrogen sulphide (H<sub>2</sub>S), both gasotransmitters leading to vasorelaxation. In addition, garlic reduces the production of the vasoconstricting factors **endothelin 1 and angiotensin II**.

Moreover, garlic regulates slightly elevated cholesterol concentrations, and stimulates the immune system by increasing macrophage activity, natural killer cells, and the production of T and B cells



Ried K. J Nutr 146:389S-396S (2016)

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# Flavonoids

- Flavonoids (and bioflavonoids) are a class of plant secondary metabolites. The name is coming from the Latin word *flavus* (yellow)
- Most fruits and vegetables, some intensely colored (blue to red colors in fruits, flowers, leaves)
- **black and green tea, onions, red wine, and apples**

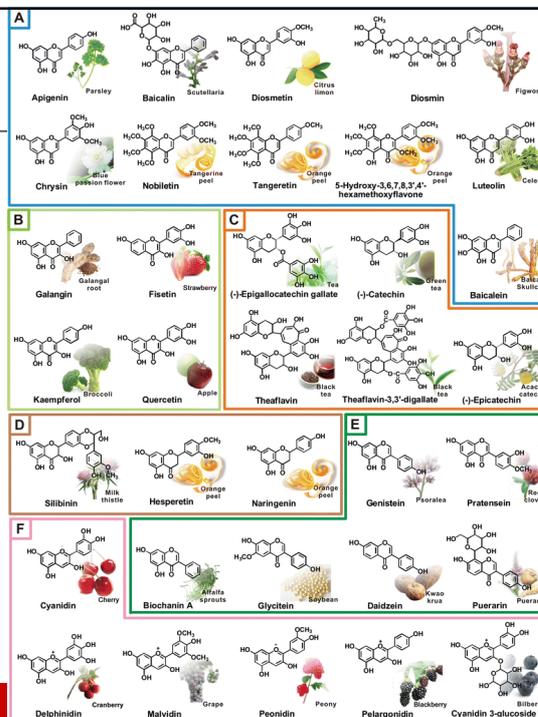


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Representative natural flavonoids and their dietary sources

- (A) flavones,
- (B) flavonols,
- (C) flavanols,
- (D) flavanones,
- (E) isoflavones,
- (F) anthocyanidins.



Pan MH et al. Food Funct 1:15-31 (2010)



## Flavonoids (nutraceutical value)

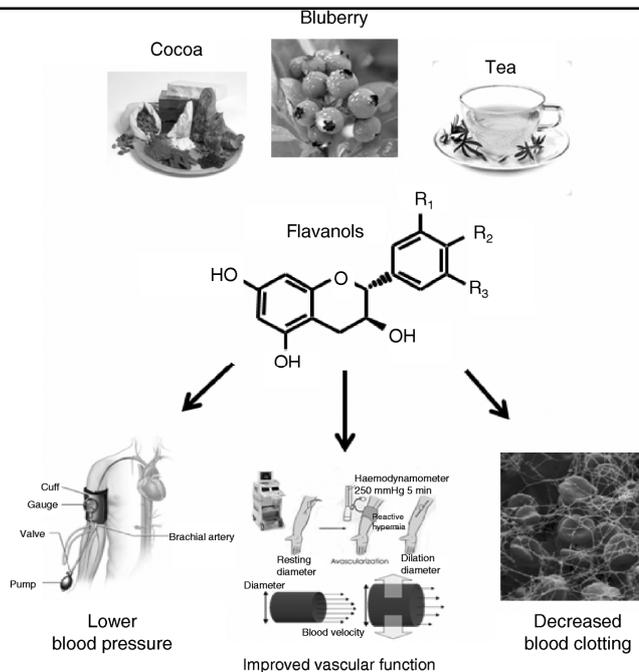
- black and green tea, onions, red wine, and apples protect against cholesterol damage
- More than 3 cups of (green) tea a day protects against heart disease
- lower the death rate from heart disease
- help block carcinogenic effects of UVB radiation
- reduces risks of cancers



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### Peripheral vascular and cardiovascular effects of flavonoid rich foods

- Vasodilation
- Blood pressure
- Insuline resistance
- Glucose tolerance
- Platelet reactivity
- Immune response



Spencer JPE. Proc. Nutr. Soc. 69:244 (2010)

Reduced risk of CVD



## Anthocyanins

- Grapes, raspberries, blueberries, cherries, onions, blackberries, strawberries
- Red to purple pigments found in plants

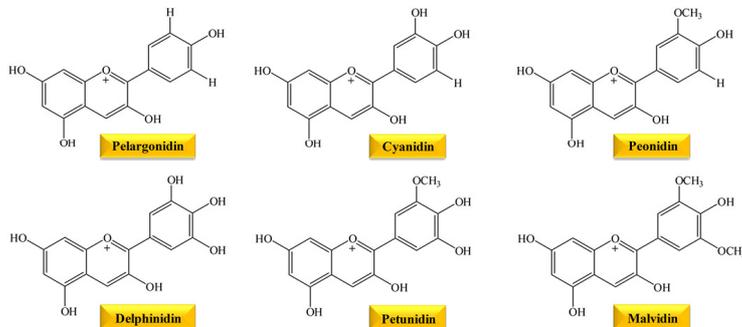


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## Anthocyanins

Anthocyanins (from Greek *άνθος* (*anthos*) = flower and *κυανός* (*kyanos*) = blue) constitute the largest and probably the most important group of water-soluble plant pigments. They belong to the widespread flavonoid group of polyphenols, which are responsible for the blue, purple and red colour of many plant tissues. They are commonly glycosides at C3 position (esose and pentose)



Smeriglio A. *Phytoterapy Res* 30:1265-1286 (2016)

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# Anthocyanins

Anthocyanins are rapidly absorbed in the stomach and small intestine and appear in the bloodstream within a few minutes (6 to 20 min).

Anthocyanins appear to have a **high organotropism** as can readily cross the blood–brain barrier. Anthocyanin accumulation has been demonstrated in the eyes, suggesting that these compounds also readily cross the blood–retinal barrier, which could justify the potential health effects of these substances to these areas .

Numerous *in vitro* and *in vivo* studies suggest that anthocyanins may be positively implicated in human health.

They exert different biological effects, and it seems that the consumption of foods such as juices or other formulations rich in these compounds may be correlated with antidiabetic and anti-obesity effects. These compounds may also be useful as neuroprotective agents, in reducing inflammation and exerting cardiovascular protection as well as in preventing and inhibiting cancer growth.

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## Anthocyanis (nutraceutical value)

- Also known as flavonols
- Provide bridges that connect and strengthen intertwined strands of collagen protein
  - soft tissue, tendons, ligaments, bone matrix
  - most abundant protein in the body
- Scavengers for free radicals



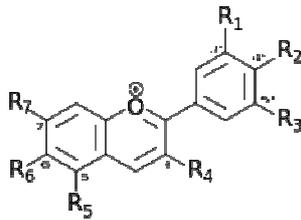
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## Blonde or Red?



Red oranges include three particular cultivars of oranges (Moro, Tarocco, Sanguinello) grown only in Sicily and the island of Malta

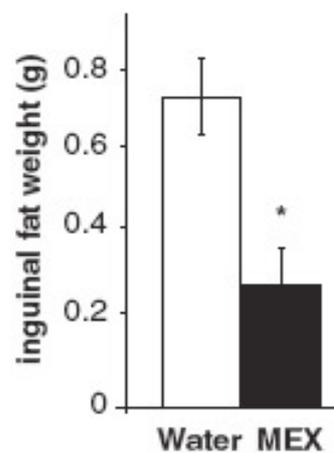
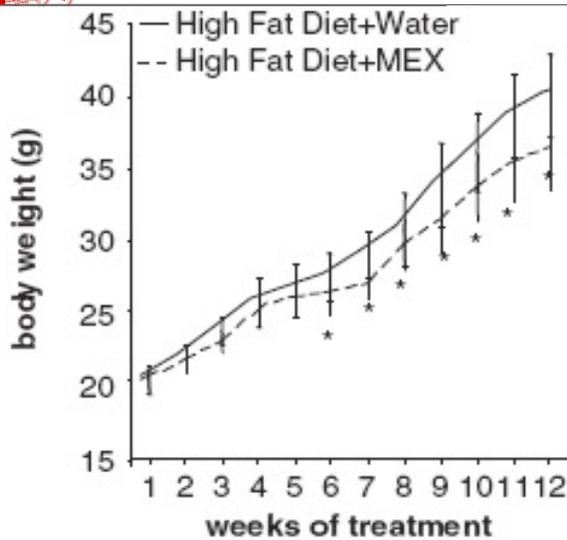


With similar Vitamin C content with blond oranges, their nutraceutical value depends on the presence of anthocyanins, which are absent in other cultivars

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## Blonde or Red?



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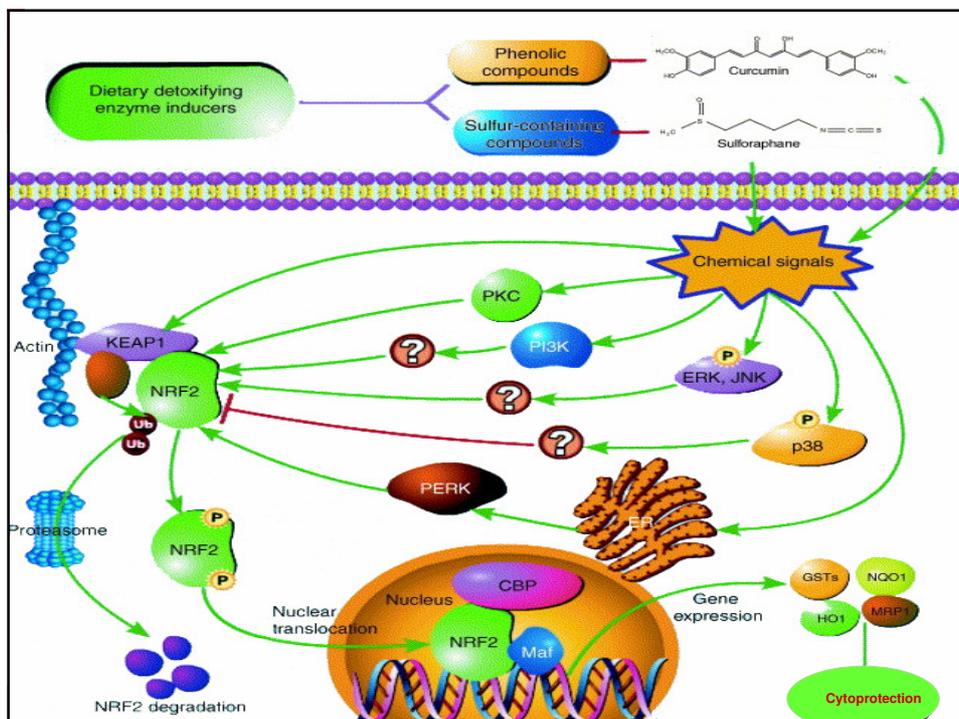


## Isothiocyanates (nutraceutical value)

- Activate liver detoxifying enzymes
- Block enzymes that promote tumor growth (liver, colon, lung, breast, stomach, esophagus)
- Increase enzyme activity involved in detoxifying carcinogens and other harmful substances
- Inhibit DNA damage that triggers cancer



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## “Eat Your Vegetables”

- Mother was right when she told you to “Eat your vegetables.”
- When phytochemicals are added to the diet, the capacity of human genes to protect and restore optimal health is far greater than previously recognized.



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## Your Diet Is Important

- People who consume little fat and eat plant -rich, high-fiber diets have a lower incidence of certain diseases, such as cancer, heart disease, and diabetes.
- 70% of preventable cancers and 33% of cancer deaths are attributed to dietary factors.



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## Diet Recommendations

### Fresh Facts



- The mediterranean food pyramid recommends at least 3-5 servings of vegetables a day and 2-4 servings of fruit a day.
- Eat around 5 different colored fruits and vegetables a day.
- Also, increase the amount of fiber you are getting.



## Are There Alternatives?

- People who know they should eat more fruits and veggies, but have trouble doing so, question **whether veggie pills and other supplements are beneficial.**
- Are they none toxic?
  - So far, **evidence for supplements is far less convincing than fresh fruits and vegetables.**



## Supplements, Less Than The Best

- Pills and powders try to mimic the components of food, but are far less successful.
  - Can never get all the known and unknown phytochemicals in a supplement.
  - Some nutrients and fibers can be lost when concentrated into pill form
  - Are more expensive.



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## Why Fruits and Veggies Win Over

- Nutraceuticals in fruits and vegetables overlap each other and possibly have interactive and synergic effects.
- Fruits and vegetables help best to activate the body's own disease-fighting resources.



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You have to take a lot of medicine if you want to become as big as your father

Can I hope for another alternative if I take less?

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***“If I’d known I was going to live this long, I would have taken better care of myself.”***

Eubie Blake  
American ragtime musician

**The day of his 100 birthday**



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Silvana Hrelia  
Department for Life Quality  
[silvana.hrelia@unibo.it](mailto:silvana.hrelia@unibo.it)

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