Nutraceuticals: a new paradigm of proactive medicine.

Antonello Santini

Department of Pharmacy, University of Napoli Federico II
e-mail: asantini@unina.it

3rd International Conference and Exhibition on Probiotics, Functional and Baby Foods September 23-25, 2014 - Napoli, Italy
Àha¬rasambhavam vastu roga¬s'
câ-ha¬rasambhava¬h,
Hita¬hitavis' esa¬s' ca vis' esah sukhaduhkhkhayoh

Caraka Samhita Sutrastrhana (1, 28:45)
“The physical body is the product of diet and sensory input (lifestyle). Similarly, all diseases are the result of non correct diet and lifestyle. Diet and lifestyle wholesome and unwholesome are the foundations of health and illness”

Caraka Samhita Sutrasthana (1, 28:45)
The definition of health status.

“Health is a state of complete well-being, physical, mental and social, and not merely the absence of disease”

(World Health Organization, 1947)
The main focus.

“Do not be worried on how to add days to our life, but on how to give more life to our days”

(Dame Cicely Mary Saunders)
i. The **wholeistic medical approach**.

ii. The **static approach**: the patient, often unaware of a potential health risk, waits till the clear signs of the onset of a disease appear (watchful waiting or active surveillance medicine) and then obtain a diagnosis and starts using prescription drugs.

iii. The **nutraceutical dynamic approach** also known as “**initiative medicine or proactive medicine**”: taking preventive action before the onset of a disease instead of waiting for the disease to become evident.
The available tools.

Primary prevention  
Secondary prevention

• Lifestyle – behaviour – dietary habits

Possible approaches:

• Drugs (waitchful waiting medicine)
• Nutraceuticals (pro active medicine)
The possible approaches.

**Health Food**
- Conventional Food
- Nutraceuticals: a preventive approach
- Consumer demand
  - Food required for well-being and nice-being.
  - Proactive medical approach.

**Over the Counter Medicines**
- Prescription Medicines
- Professional demand
  - Pharmaceuticals for health conditions.
  - Watchful waiting medicine.
Nutraceuticals: TORs.

- 1989 Stephen DeFelice, President of the Foundation for Innovation in Medicine (Cranford), NJ, USA.

Nutraceutical: food or part of food that provides medical or health benefits, including the prevention and/or treatment of a disease.

(Merriam-Webster, 2013)
The term **nutraceutical** refers to products for oral use containing high concentrations of active principles derived from food, and provide health benefits from a preventive and/or therapeutic point of view.

They are not considered drugs, there is lack of controlled studies stating their real efficacy.

There is lack of a shared regulation assessment.
Nutraceuticals: TORs.
Nutraceuticals can be classified based on:

- Natural source
- Pharmacological conditions
- Chemical constitution
### Classification based on the chemical groups

<table>
<thead>
<tr>
<th>s.no</th>
<th>Class</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Inorganic mineral supplements</td>
<td>Minerals</td>
</tr>
<tr>
<td>2</td>
<td>Probiotics</td>
<td>Helpful bacteria</td>
</tr>
<tr>
<td>3</td>
<td>Prebiotics</td>
<td>Digestive enzymes</td>
</tr>
<tr>
<td>4</td>
<td>Dietary fibres</td>
<td>Fibres</td>
</tr>
<tr>
<td>5</td>
<td>Antioxidants</td>
<td>Natural antioxidants</td>
</tr>
<tr>
<td>6</td>
<td>Phytochemicals</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fatty acids</td>
<td>Omega 3 fatty acids</td>
</tr>
<tr>
<td></td>
<td>Phenolics</td>
<td>Tea polyphenols</td>
</tr>
<tr>
<td></td>
<td>Isoprenoids</td>
<td>Carotenoids</td>
</tr>
<tr>
<td></td>
<td>Lipids</td>
<td>Sphingolipids</td>
</tr>
<tr>
<td></td>
<td>Proteins</td>
<td>Soyaproteins</td>
</tr>
<tr>
<td>7</td>
<td>Herbs as functional food</td>
<td></td>
</tr>
</tbody>
</table>
## Nutraceuticals: classification.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Nutraceuticals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergy relief</td>
<td>Ginkgo biloba</td>
</tr>
<tr>
<td>Arthritis support</td>
<td>Glucosamine</td>
</tr>
<tr>
<td>Cancer prevention</td>
<td>Flax seeds, green tea</td>
</tr>
<tr>
<td>Cholesterol lowering</td>
<td>Garlic</td>
</tr>
<tr>
<td>Digestive support</td>
<td>Digestive enzymes</td>
</tr>
<tr>
<td>Diabetic support</td>
<td>Garlic, monordica</td>
</tr>
<tr>
<td>Female hormone support</td>
<td>Black cohosh</td>
</tr>
<tr>
<td>Immunomodulator</td>
<td>Ginseng</td>
</tr>
<tr>
<td>Prostate support</td>
<td>Tomato lycopenes</td>
</tr>
</tbody>
</table>
**QUESTION** placed at the European Commission E-000065/2011 (dr. Christian Muscardin) about the presence on the market of products, called "nutraceuticals", which, unlike normal dietary supplements, have the effects of preventing or reducing the risk of disease, especially degenerative of a particular structure or function of the organism.

• **ANSWER** given by Commissioner John Dalli on behalf of the European Commission, February 21, 2011:

  • The term "nutraceutical" is not currently defined in Community legislation.

  • These products, under the current legislation, should be classified as dietary supplements or following authorization for marketing as drugs.
Nutraceuticals: food or drugs?

Court of Justice of the European Union: medicine/drug food.

- if it is presented as having properties for treating or preventing disease in human beings (definition of "presentation");

- if it is to be administered to human beings with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions (definition "by function").

Plant-based products marketed in the form of dietary supplements (vegetable origin similar to nutraceuticals) must comply with Directive 2002/46/EC on food supplements and Regulation (EC) n. 1924/2006 on the claims about the effects of nutrition and health foods.

If a product, taking into account all its characteristics, may fall within the definition of a medicinal product and the definition of a product covered by other Community legislation, apply the Directive 2001/83/EC revised by Directive 2004/27/EC (food and drugs nutraceuticals).
Nutraceuticals: where can be found.

An approximate number of about 30,000 phyto components have been identified in plants.

- Approximately 5,000-10,000 are present in plant foods of common use/consumption.

- Assuming 5 daily servings of fruits and vegetables, you ensure the intake of about 1.5 g / day of nutraceuticals phytocomponents.
## Nutraceuticals: where can be found.

<table>
<thead>
<tr>
<th>Food</th>
<th>Phytochemical(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allium vegetables (garlic, onions, chives, leeks)</td>
<td>Allyl sulfides</td>
</tr>
<tr>
<td>Cruciferous vegetables (broccoli, cauliflower, cabbage, Brussels sprouts, kale, turnips, bok choy, kohlrabi)</td>
<td>Indoles/glucosinolates, Sulfaforaphane, Isothiocyanates/thiocyanates, Thiols</td>
</tr>
<tr>
<td>Solanaceous vegetables (tomatoes, peppers)</td>
<td>Lycopene</td>
</tr>
<tr>
<td>Umbelliferous vegetables (carrots, celery, cilantro, parsley, parsnips)</td>
<td>Carotenoids, Phthalides, Polyacetylenes</td>
</tr>
<tr>
<td>Compositae plants (artichoke)</td>
<td>Silymarin</td>
</tr>
</tbody>
</table>
Nutraceuticals: where can be found.

<table>
<thead>
<tr>
<th>Citrus fruits (oranges, lemons, grapefruit) Glucarates</th>
<th>Monoterpenes (limonene) Carotenoids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other fruits (grapes, berries, cherries, apples, cantaloupe, watermelon, pomegranate)</td>
<td>Ellagic acid Phenols Flavonoids (quercetin)</td>
</tr>
<tr>
<td>Beans, grains, seeds (soybeans, oats, barley, brown rice, whole wheat, flax seed) Protease inhibitors</td>
<td>Flavonoids (isoflavones) Phytic acid Saponins</td>
</tr>
<tr>
<td>Herbs, spices (ginger, mint, rosemary, thyme, oregano, sage, basil, turmeric, caraway, fennel)</td>
<td>Gingerols Flavonoids Monoterpenes (limonene)</td>
</tr>
<tr>
<td>Licorice root Green tea Polyphenols</td>
<td>Glycyrrhizin Catechins</td>
</tr>
</tbody>
</table>
Nutraceuticals: where can be found.

### Most Commonly Studied Phytochemicals

<table>
<thead>
<tr>
<th>Food</th>
<th>Phytochemical(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allium vegetables (garlic, onions, chives, leeks)</td>
<td>Allyl sulfides</td>
</tr>
<tr>
<td>Cruciferous vegetables (broccoli, cauliflower, cabbage, Brussels sprouts, kale, turnips, bok choy, kohlrabi)</td>
<td>indoies/glucosinoiotes Sulfatoraphane Isothiocyanates/thiocyanates Thiols</td>
</tr>
<tr>
<td>Solanaceous vegetables (tomatoes, peppers)</td>
<td>Lycopene</td>
</tr>
<tr>
<td>Umbelliferous vegetables (carrots, celery, cilantro, parsley, parsnips)</td>
<td>Carotenoids Phthalides Polyacetylenes</td>
</tr>
<tr>
<td>Compositae plants (artichoke)</td>
<td>Silymarin</td>
</tr>
</tbody>
</table>
## Nutraceuticals: where can be found.

<table>
<thead>
<tr>
<th>Food</th>
<th>Phytochemical(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citrus fruits (oranges, lemons, grapefruit)</td>
<td>Monoterpenes (limonene) Carotenoids</td>
</tr>
<tr>
<td>Glucarates</td>
<td></td>
</tr>
<tr>
<td>Other fruits (grapes, berries, cherries, apples, cantaloupe, watermelon, pomegranate)</td>
<td>Ellagic acid Phenols Flavonoids (quercetin)</td>
</tr>
<tr>
<td>Beans, grains, seeds (soybeans, oats, barley, brown rice, whole wheat, flax seed) Protease inhibitors</td>
<td>Flavonoids (isoflavones) Phytic acid Saponins</td>
</tr>
<tr>
<td>Herbs, spices (ginger, mint, rosemary, thyme, oregano, sage, basil, turmeric, caraway, fennel)</td>
<td>Gingerols Flavonoids Monoterpenes (limonene)</td>
</tr>
<tr>
<td>Licorice root Green tea Polyphenols</td>
<td>Glycyrrhizin Catechins</td>
</tr>
</tbody>
</table>
Nutraceuticals: therapeutic uses.

Prevention/Therapy using nutraceuticals.

- Hypercholesterolemia
- Hypertension
- Type II diabetes
- Hypertryglyceridemia
- .......... 

Metabolic syndrome

A nutraceutical pro active approach is possible?
Metabolic syndrome (SM): some data.

50% of people from Europe are overweight
30% suffer from obesity
23-24% of USA suffer from SM

WHO estimated an about 2.5 millions of people dead worldwide due to overweight and to cardiovascular diseases

SM: ICD-9-CM code = 277.7

Metabolic syndrome “cluster” of risk factors.

- Abdominal obesity
- Glucose intolerant/Insulin resistency
- Hypertension
- Aterogen dislipidemia
- Proinflammatory state/
- Protrombotic

*National Cholesterol Educational Program (NCEP), Adult Treatment Panel (ATP) III; 2001*
Metabolic syndrome.

**Central obesity** (European and North American population).

i. Waist circumference $\geq 94$ cm (male) and $\geq 80$ (female)

   **Together** with at least **TWO** of the following:

ii. TG $> 150$ mg/dL or specific treatment

iii. CHDL $< 40$ mg/dL (male) e $< 50$ mg/dL (female) or specific treatment

iv. SBP $\geq 130$ mmHg e/o DBP $\geq 85$ mmHg or anti hypertension treatment

v. Glycemic index $\geq 100$ mg/dL or a DM2 diagnosis
Therapeutic approach.

- Metabolic Syndrome
  - Yes
    - Organ Damage Presence
      - Yes
        - Pharmacologic Therapy
      - No
        - Lifestyle Change
  - No
    - Nutraceuticals
Monomeric and oligomeric phenols.
Catecolic derivatives.

- Hydroxytyrosol
- Oleuropein
- Curcumin
- Alkylresorcinols
- Carnosol
Resorcinic derivatives.

Amorpha fruticosa

Liquorice

Resveratrol

Tomatoes, grapes, cauliflower
Oligomeric polyphenols – Tannins.

Apple

Dates

Raspberry

Pomegranate
Nutraceuticals: possible uses.

An example.
The *artichoke* (*Cynara scolymus*) extract polyphenols: the main components are chlorogenic acid, caffeic acid and cynarin. In year 1900 scientific research has focused on the properties hepatostimulants, hepatoprotective, choleretic and hypocholesterolemic associated to extracts of *Cynara* leaves, as advocated by medicine doctors already in year 1700.
Nutraceuticals: possible uses.

Artichoke: bioactive substances.

Chlorogenic acids

- 5-O-caffeilchinic acid
- 1,5-dicaffeilchinic acid
- Caffeic acid

Cynara extracts

Flavanoids

- Luteoline
- Cinaroside
- Scoliminoside
## Nutraceuticals: possible uses.

<table>
<thead>
<tr>
<th>Artichoke variety</th>
<th>mg chlorogenic acid/100g</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Romolo stem</strong></td>
<td>27,826</td>
</tr>
<tr>
<td><strong>Romolo head</strong></td>
<td>6,276</td>
</tr>
<tr>
<td><strong>Romolo leaves</strong></td>
<td>0,5</td>
</tr>
</tbody>
</table>

### Anti oxidant activity:

<table>
<thead>
<tr>
<th>Artichoke variety</th>
<th>Total phenolic content mg AGE/100g</th>
<th>DPPH μmol TE/100g</th>
<th>FRAP μmol TE/100g</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Romolo stem</strong></td>
<td>21,35</td>
<td>78,61</td>
<td>104,46</td>
</tr>
<tr>
<td><strong>Romolo head</strong></td>
<td>4,53</td>
<td>38,95</td>
<td>24</td>
</tr>
<tr>
<td><strong>Romolo leaves</strong></td>
<td>26,44</td>
<td>124,47</td>
<td>64,54</td>
</tr>
</tbody>
</table>
Nutraceuticals: recovery/uses.

Sustainable use of industrial wastes.

Bioactive molecules rich sources
Nutraceuticals: possible uses.

**Cholesterol-lowering** action of artichoke extracts.

1. increased choleresis and then increased excretion of salts and bile acids rich in cholesterol;
2. inhibition of cholesterol biosynthesis.

- Cholesterol is synthesized in the liver from acetyl-CoA and released in plasma.
- The extent of hepatic biosynthesis is controlled by the intracellular concentration of cholesterol.
Nutraceuticals: possible uses.

Green tea: functional food/nutraceutical

Obtained from a plant: *Camellia sinensis* (L.).

The freshly harvested leaves are immediately processed to inactivate the enzymatic oxidation process.

- Green tea has the highest concentration of polyphenols than other types of tea.
- Green tea has hypoglycemic properties.

<table>
<thead>
<tr>
<th>catechine</th>
<th>R₁</th>
<th>R₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGCG</td>
<td>Gallato</td>
<td>OH</td>
</tr>
<tr>
<td>ECG</td>
<td>Gallato</td>
<td>H</td>
</tr>
<tr>
<td>EGC</td>
<td>H</td>
<td>OH</td>
</tr>
<tr>
<td>EC</td>
<td>H</td>
<td>H</td>
</tr>
</tbody>
</table>
Nutraceuticals: possible uses.
Nutraceuticals: possible uses.

Catechins neuro protective role.
Nutraceuticals: possible uses.

Polyphenols presence in different tea varieties

- **C** = (-)-Catechina
- **EC** = (-)-Epicatechina
- **ECG** = (-)-Epicatechingallato
- **EGC** = (-)-Epigallocatechina
- **EGCG** = (-)-Epigallocatechingallato
- **GC** = (-)-Gallocatechina
- **CG** = (-)-Catechingallato

![Graph showing the presence of polyphenols in different tea varieties](image-url)
Nutraceuticals: possible uses.

Cholesterol uptake inhibition

Main responsible metabolites

ECG = (-)-Epicatechingallato
EGCG = (-)-Epigallocatechingallato
CG = (-)-Catechingallato
Nutraceuticals: possible uses.

Triglycerides uptake inhibition

Main responsible metabolites

C = (-)-Catechina  
ECG = (-)-Epicatechingallato  
EGCG = (-)-Epigallocatechingallato
Nutraceuticals: possible uses.

Catechins: antioxidant action.

Proprietà Antiossidanti Classiche:

Potenti scavengers di ROS e RNS
• Ruolo chemiopreventivo
• Ruolo cardioprotettivo
• Ruolo neuroprotettivo
Nutraceuticals: possible uses.

**Catechins**: cardio protective role.

Nei confronti del danno da ipossia riossigenazione indotto nella cellula cardiaca

Nutraceuticals: possible uses.

Apple: an *in se* functional food?

I. Significant source of phytocompounds (flavonoids) among which quercetin (5 - 15 mg / 100 g) is the main one.

II. Contains antioxidant polyphenols with proven efficacy.

III. Apple extracts inhibit the cholesterol uptake.

IV. The effect on the organism is similar to statins.
Nutraceuticals: possible uses.

Nutraceutical potential of polyphenolic fractions from Annurca apple (M. pumila Miller cv Annurca)

Gian Carlo Tenore a,*, Pietro Campiglia b, Paola Stiuso c, Alberto Ritieni a, Ettore Novellino a

a Department of Medicinal Chemistry, Università di Napoli Federico II, Via D. Montesano 49, 80131 Napoli, Italy
b Department of Pharmaceutical and Biomedical Sciences, University of Salerno, Via Ponte Don Melillo, 1, 84084 Salerno, Italy

Cholesterol uptake inhibition.
Nutraceuticals: possible uses.

Hypoglicemic metabolite/agent

Florizine

Bucce
Polpa
Nutraceuticals: possible uses.

Annurca  Red Delicious  Pink Lady  Fuji  Golden Delicious

Hypocholesterolemic metabolites

Oligomeric procyanidins

Bucce
Polpa
Nutraceuticals and metabolic syndrome.

Apple variety “annurca”
Lipidic profile in patients treated with atorvastatin v/s nutraceutical (NUT)

Apple variety “annurca”

![Graph showing lipid profile comparison between Atorvastatin and NUT](image)
Nutraceutical potential of grape polyphenols.

Flavonols
Antocianins

Pro-antocyanidins

“Antioxidant protection of the cardiovascular system”

Shao et al. (2006). *Grape seed proanthocyanidin extract attenuates oxidant injury in cardiomyocytes.* *Pharmacological Research*

*Poliphenols content:* juice > wine > grape/fruits
Main active molecules.

**Antocianins**

Malvidin-3-O-glucoside
114 mg/100 mL
35% anthocyanins

**Flavonols**

Myricetin-3-O-glucoside
93 mg/100 mL
27% flavonols

Quercetin-3-O-glucoside
80 mg/100 mL
23% flavonols

Quercetin-3-O-glucuronide
76 mg/100 mL
22% flavonols
### Main active molecules.

#### Polyphenolic profile

<table>
<thead>
<tr>
<th>Peak</th>
<th>Compound</th>
<th>mg ME/100 mL*</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Delphinidin-3-O-glucoside</td>
<td>34.78 ± 1.1</td>
<td>34.87 ± 1.3</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Cyanidin-3-O-glucoside</td>
<td>21.63 ± 1.2</td>
<td>21.63 ± 1.1</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Petunidin-3-O-glucoside</td>
<td>25.63 ± 1.4</td>
<td>25.68 ± 1.0</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Peonidin-3-O-glucoside</td>
<td>31.24 ± 1.0</td>
<td>31.15 ± 0.9</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Malvidin-3-O-glucoside</td>
<td>114.63 ± 1.9</td>
<td>114.50 ± 1.7</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Delphinidin-3-O-acetylglucoside</td>
<td>10.38 ± 1.5</td>
<td>10.40 ± 0.3</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Cyanidin-3-O-acetylglucoside</td>
<td>5.08 ± 0.9</td>
<td>5.01 ± 0.4</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Malvidin-3-(6-O-coumaroyl)glucoside (cis isomer)</td>
<td>12.38 ± 0.8</td>
<td>12.21 ± 0.4</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Malvidin-3-(6-O-caffeoyl)glucoside</td>
<td>52.99 ± 1.2</td>
<td>53.00 ± 0.6</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Peonidin-3-(6-O-coumaroyl)glucoside (trans isomer)</td>
<td>4.32 ± 1.0</td>
<td>4.32 ± 0.2</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Malvidin-3-(6-O-coumaroyl)glucoside (trans isomer)</td>
<td>14.66 ± 0.8</td>
<td>14.35 ± 0.1</td>
<td></td>
</tr>
</tbody>
</table>

#### Flavonols

<table>
<thead>
<tr>
<th>Peak</th>
<th>Compound</th>
<th>mg QE/100 mL*</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Myricetin-3-O-glucoside</td>
<td>93.1 ± 0.3</td>
<td>91.7 ± 0.2</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Quercetin-3-O-glucuronide</td>
<td>75.6 ± 0.2</td>
<td>73.5 ± 0.3</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Quercetin-3-O-glucoside</td>
<td>79.8 ± 0.07</td>
<td>78.4 ± 0.08</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Laricitrin-3-O-galactoside</td>
<td>13.3 ± 0.08</td>
<td>11.9 ± 0.06</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Kaempferol-3-O-glucoside</td>
<td>5.6 ± 0.02</td>
<td>5.6 ± 0.01</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Laricitrin-3-O-rhamnose-7-acid</td>
<td>18.2 ± 0.1</td>
<td>16.8 ± 0.2</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Kaempferol-3-O-caffeoylate</td>
<td>16.8 ± 0.02</td>
<td>16.8 ± 0.02</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Isorhamnetin-3-O-glucoside</td>
<td>24.5 ± 0.03</td>
<td>23.1 ± 0.04</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Syringetin-3-O-galactoside</td>
<td>19.6 ± 0.05</td>
<td>20.3 ± 0.03</td>
<td></td>
</tr>
</tbody>
</table>

### Antocianins
Red grape juice polyphenolic content before (RGJ) and after lyophilization (lioRGJ).
Antioxidant activity of red grape juice before (RGJ) and after lyophilization (lioRGJ)

FRAP = Antiradical indirect power
DPPH = Antiradical direct power
Nutraceutical potential of grape polyphenols.

“Antioxidant profile and in vitro cardiac radical-scavenging vs pro-oxidant effects of commercial red grape juices (Vitis vinifera L. cv. Aglianico N.)”
Gian Carlo Tenore, Michele Manfra, Paola Stiuso, Luigi Coppola, Mariateresa Russo, Isabel Maria Gomez Monterrey, Pietro Campiglia
Journal of Agricultural and Food Chemistry, 2012
Grape juice: "Functional food → Nutraceutical potential"

Possible use as *nutraceutical*:

*Support for the treatment of neoplastic diseases.*

(Jones et al., Int. J. Cancer Res., 10(1), 46-53, 2014)
Hyperglycemia: a new therapeutic approach.

PPARγ (proliferator-activated receptor gamma) a nuclear receptor has a primary role in lipid and carbohydrates metabolism.

**Problem:** PPARγ-targeting drugs are characterized by unwanted side effects.

Natural products from edible biomaterials are a structurally different resource to easy the complex side effects of common use drugs. It can be adopted a nutritional tailored approach to easy side unwanted effects.

**Amorfrutins,** extracted from the edible part of two legumes, namely *Glycyrrhiza foetida* and *Amorpha fruticosa,* are new and potent anti diabetes agents.

They selectively bond to the PPARγ receptor and activate it.
Hyperglycemia.
Pro active nutraceuticalical approach: when and where?

“Beyond diet, before drugs” (E. Novellino, 2012)

Pro active nutraceutical approach: when and where?

“Beyond diet, before drugs”
(E. Novellino, 2012)

Antonello Santini and Ettore Novellino
Current Bioactive Compounds, 2014, 10(1), 1-12.