Phytonutrients:

Polyphenols, Phytosterols and Other Antioxidants

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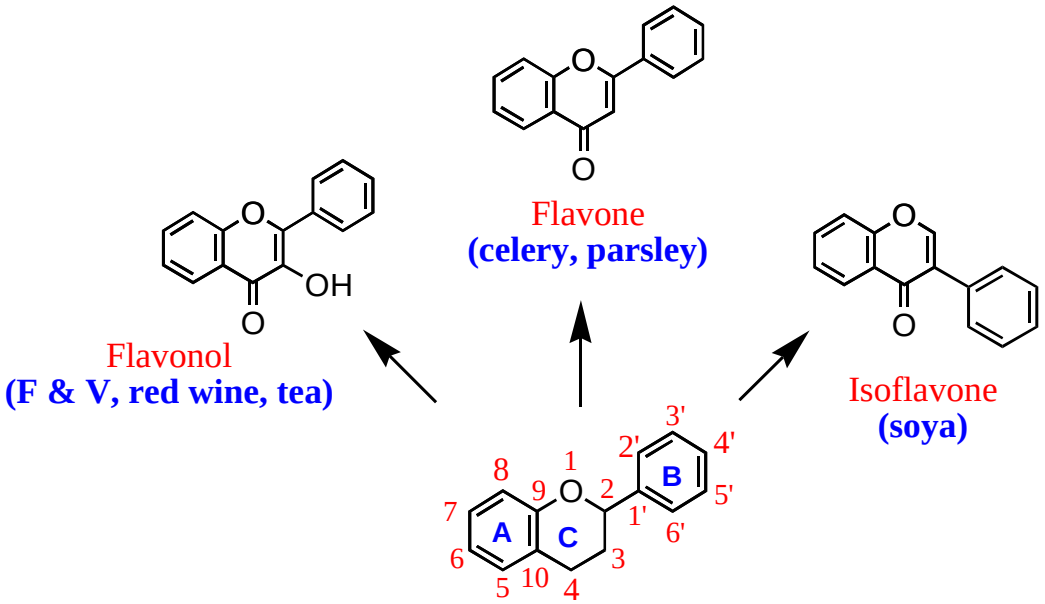
Polyphenolics: Flavonoid Group

Common C_6-C_3-C_6 Flavonoid Structures



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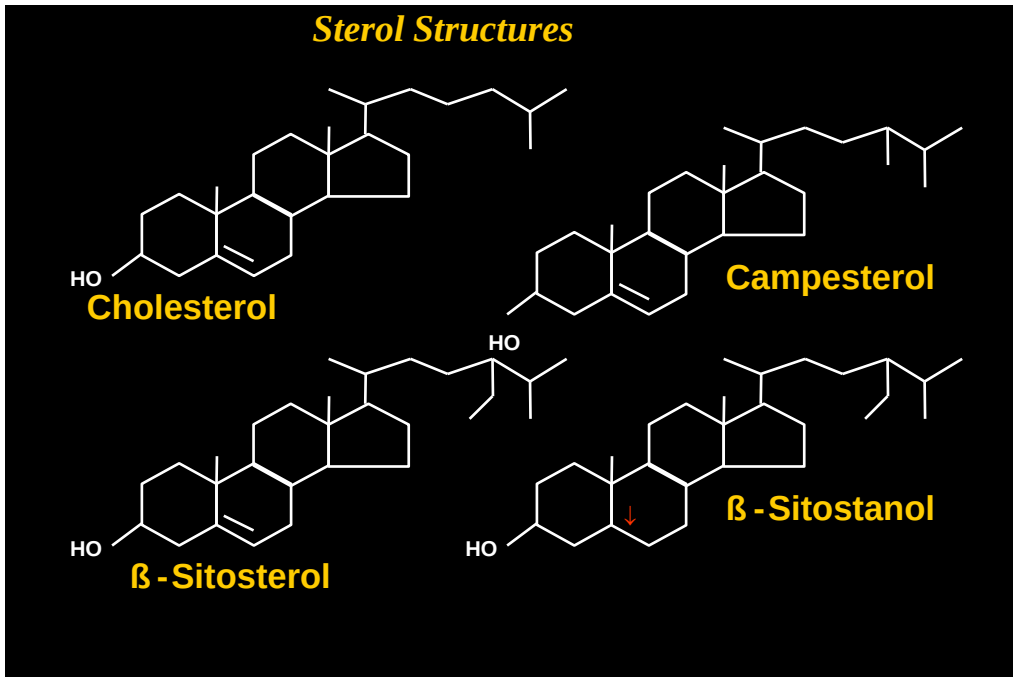
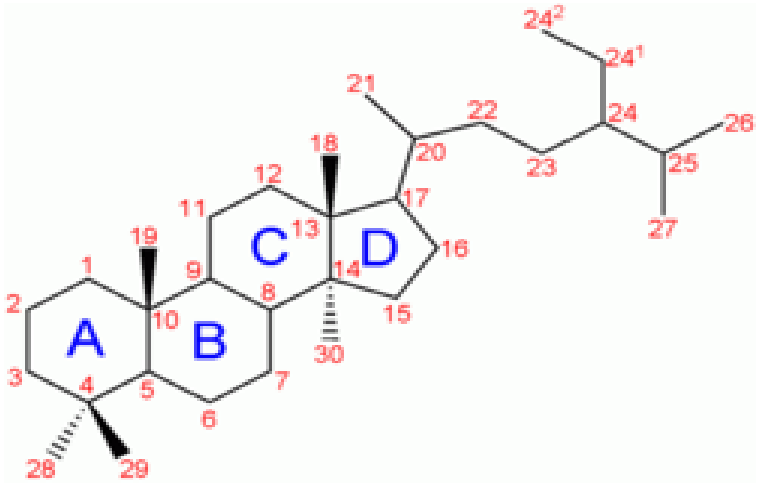
PHYTOSTEROLS

Plant Sterols





Nomenclature for steroid skeleton

- Present in diet (200 - 400 mg / d) in small amounts in vegetable oils, nuts, seeds, legumes.
- Need 1.5-2g for efficacy.
- 2500 tonnes oil needed for 1 tonne plant sterols

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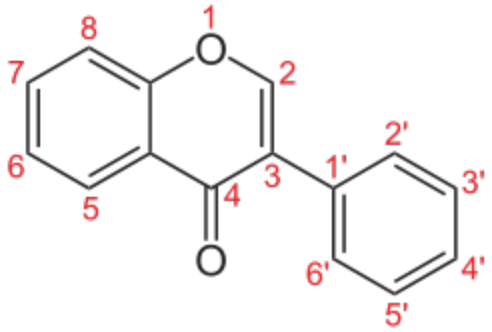
PHYTOHORMONES:

Plant Estrogens

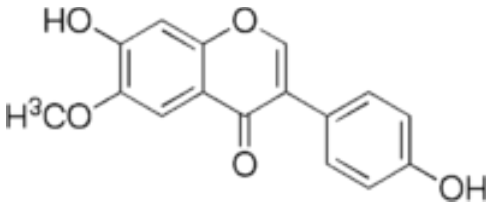


Isoflavones

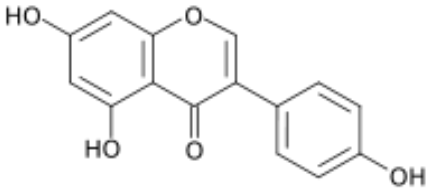
1. most concentrated in soy beans (genistein, glycitein and daidzein)

2. soy bean has 2-4 milligrams isoflavone/gram

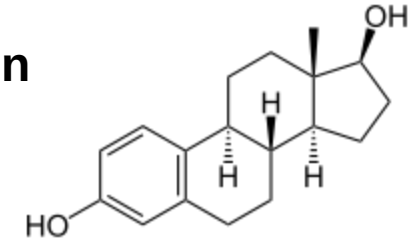
3. predominantly genistein found in legumes and pomegranate seeds



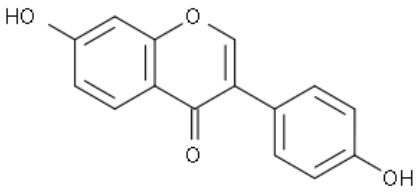
Glycitein



Genistein



17β-estradiol



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CHOLESTEROL FACTS

synthesized from acetyl CoA and eliminated as bile acids

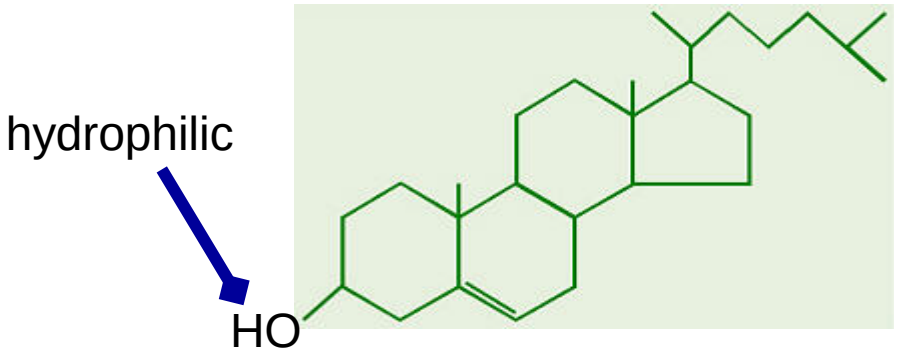
precursor of all other steroids in the body

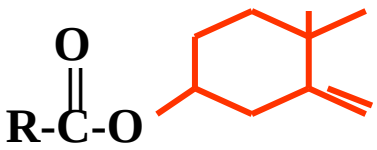
product of animal metabolism - in foods of animal origin

amphipathic lipid (hydrophobic and hydrophilic portions)

storage form is cholesterol ester found in most tissues.

essential structural component of membranes transported in the circulation in lipoproteins





Cholesterol ester (1st ring only)
R = fatty acid hydrocarbon chain

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OTHER ANTIOXIDANTS

- **1. Phenolic Acids**

  Ellagic acid, Chlorogenic acid, P-Coumaric acid
  Cinnamic acid, Ferulic acid, Vanillin, Phytic acid
  Hydroxycinnamic acid

- **2. Other Non-Flavonoid Phenolics**

  Curcumin, Resveratrol, Lignans

- **3. Glucosinolates**

  Phenylethyl Isothyocynate, Benzyl isothyocynate,
  Sulforaphane

- **4. Indoles**

  Indole-3-Carbinol (I3C)

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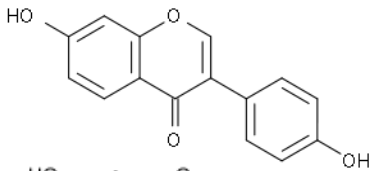
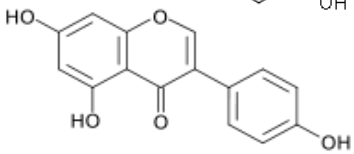
Examples of Phytonutrients

Class/Components	Source	Potential Benefit
FLAVONOIDS		
Anthocyanidins	berries, cherries, red grapes	bolster cellular antioxidant defenses; may contribute to maintenance of brain function
Flavanols, Catechins, Epicatechins, Procyanidins	tea, cocoa, chocolate, apple and grapes	may contribute to maintenance of heart health
Flavanones	citrus fruits	neutralize free radicals which may damage cells; bolster cellular antioxidant defenses
Flavonols	onion, apple, tea, broccoli	neutralize free radicals which may damage cells; bolster cellular antioxidant defenses
Proanthocyanidins	cranberries, cocoa, apple, strawberries, grapes, wine,	may contribute to maintenance of urinary tract

Plant Stanols/Sterols

Free Stanols/Sterols	corn, soy, wheat, wood oils, fortified foods and beverages	may reduce risk of CHD
Stanol/Sterol esters	fortified table spreads, stanol ester dietary supplements	may reduce risk of CHD

Phytoestrogens

Isoflavones: **Daidzein**  **Genistein** 	soybeans and soy-based foods	may contribute to maintenance of bone health, healthy brain and immune function; for women, maintenance of menopausal health

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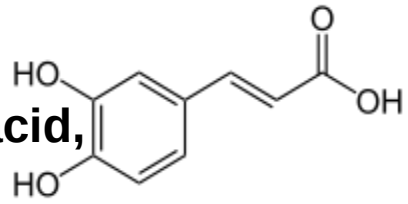
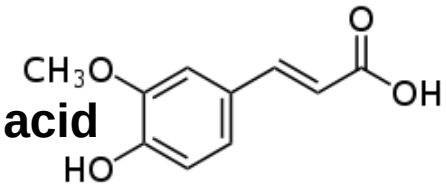
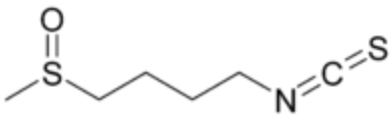
Phenolic acids

Caffeic acid,  **Ferulic acid** 	apple, pear, citrus fruits and some vegetables	may bolster cellular antioxidant defenses; may contribute to maintenance of healthy vision and heart health

Isothiocyanates

Sulforaphane 	cauliflower, broccoli, broccoli sprouts, cabbage, kale, horseradish	may enhance detoxification of undesirable compounds and bolster cellular antioxidant defenses

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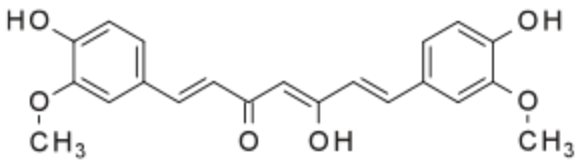
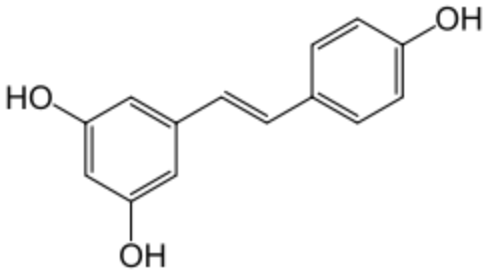
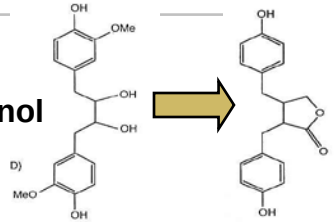
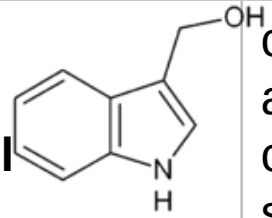
Other Non-Flavonoid Phenolics

Curcumin		Turmeric	curcumin may have antiarthritic, antiamyloid, anti-ischemic and anti-inflammatory properties
Resveratrol		skin of red grapes and in other fruits	anti-cancer, anti-inflammatory, blood-sugar-lowering and other beneficial cardiovascular effects.
Lignans	**Secoisolariciresinol**  **Enterodiol**	flax, rye, some vegetables	may contribute to maintenance of heart health and healthy immune function

Indoles (Indole-3-Carbinol)

Indole-3-carbinol		cruciferous vegetables such as broccoli, cabbage, cauliflower, brussels sprouts, collard greens and kale.	Anticarcinogenic, antioxidant and anti-atherogenic effects.

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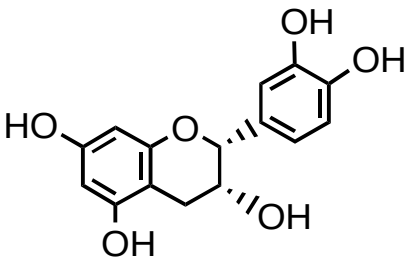
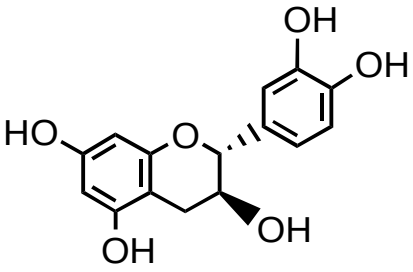
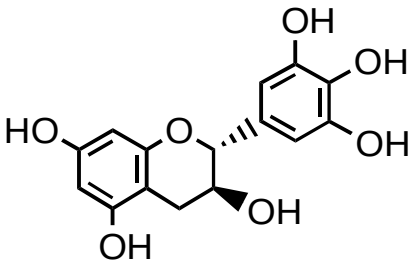
Green Tea Flavan-3-ol Structures



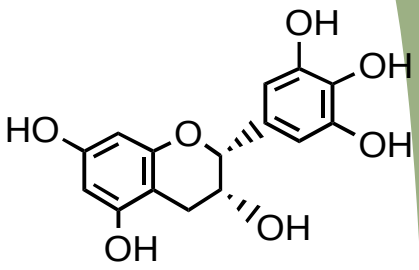
(-)-Epicatechin



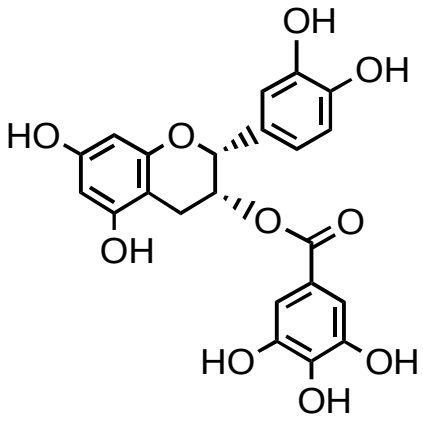
(+)-Catechin



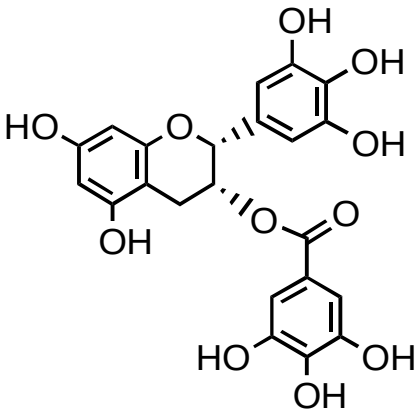
(+)-Gallocatechin



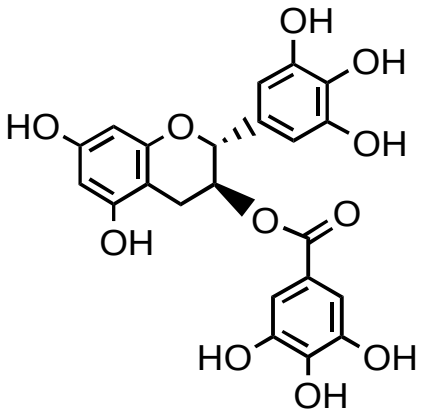
(-)-Epigallocatechin



(-)-Epicatechin gallate



(-)-Epigallocatechin gallate



(+)-Gallocatechin gallate

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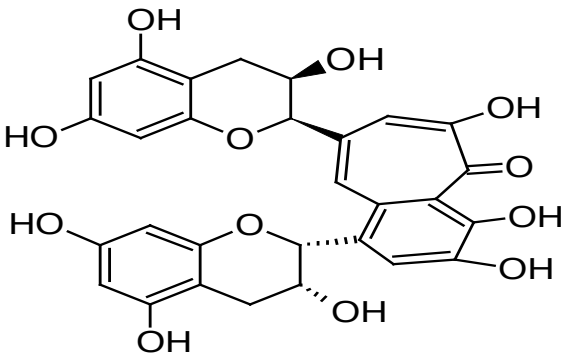
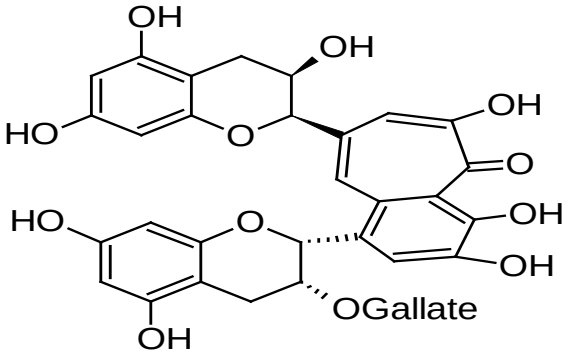
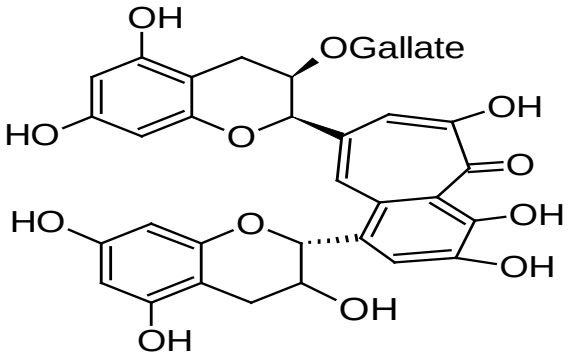
Principle phenolics in black tea



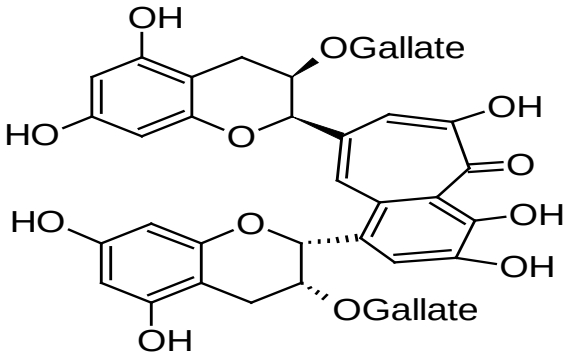
Theaflavin



Theaflavin-3-gallate



Theaflavin-3'-gallate



Theaflavin-3,3'-digallate

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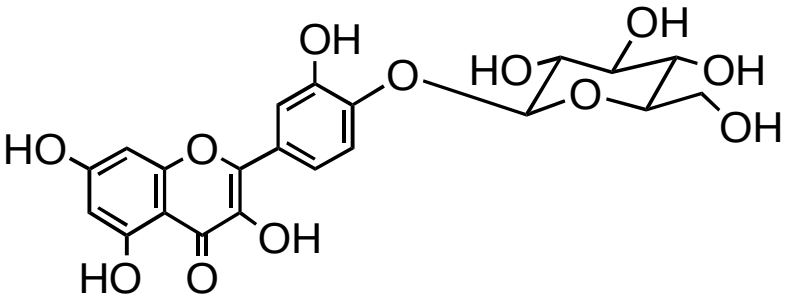
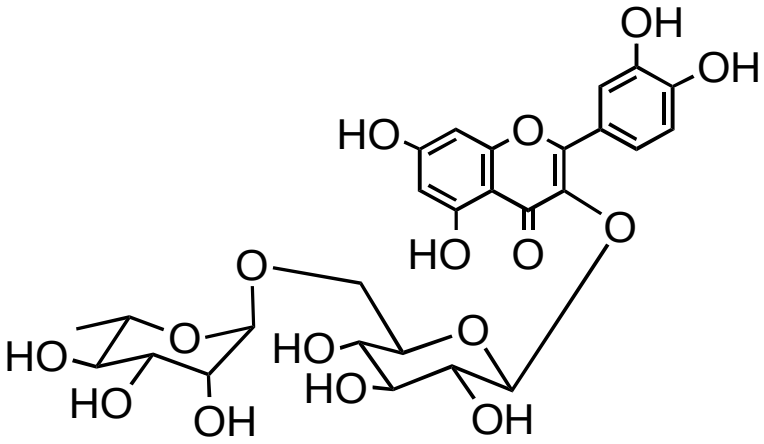
Flavonol Glycosides



Quercetin-4'-glucoside



Quercetin-3-rutinoside

200 g fried onion - 257 μmoles

300 mL tomato juice- 176 μmoles

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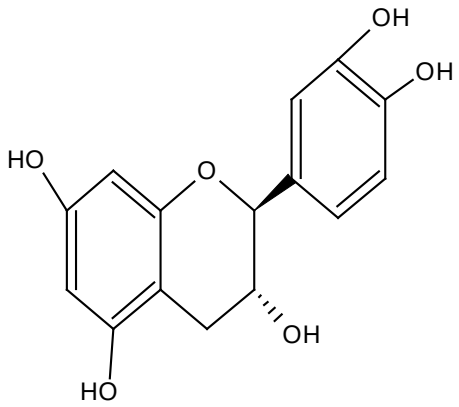
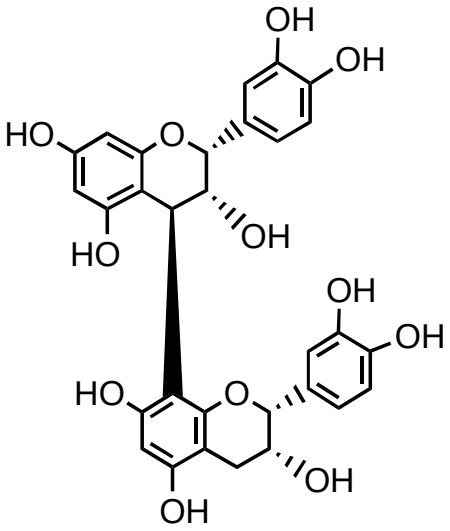
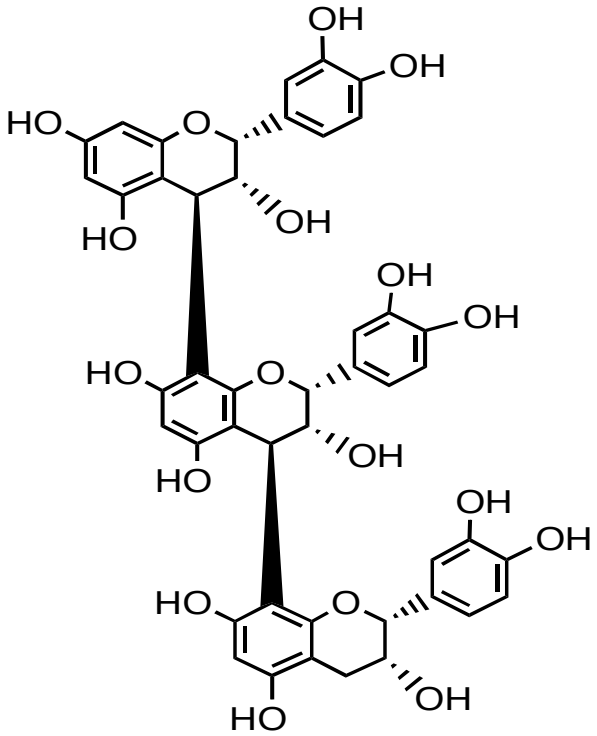
Cocoa and chocolate contain monomeric and polymeric flavan-3-ols



(-)-Epicatechin



Proanthocyanidin B_2 dimer



Proanthocyanidin C_1 trimer

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Types of Free Radicals

- Oxygen-centered radicals
  - Singlet oxygen, superoxide, hydroxyl radicals

Sulfur-centered radicals

  - Thiyl radical (RS•)
- Carbon-centered radicals
  - •CCl3, CH2•CHOH
- Nitrogen-centered radicals
  - NO•, R2NO•

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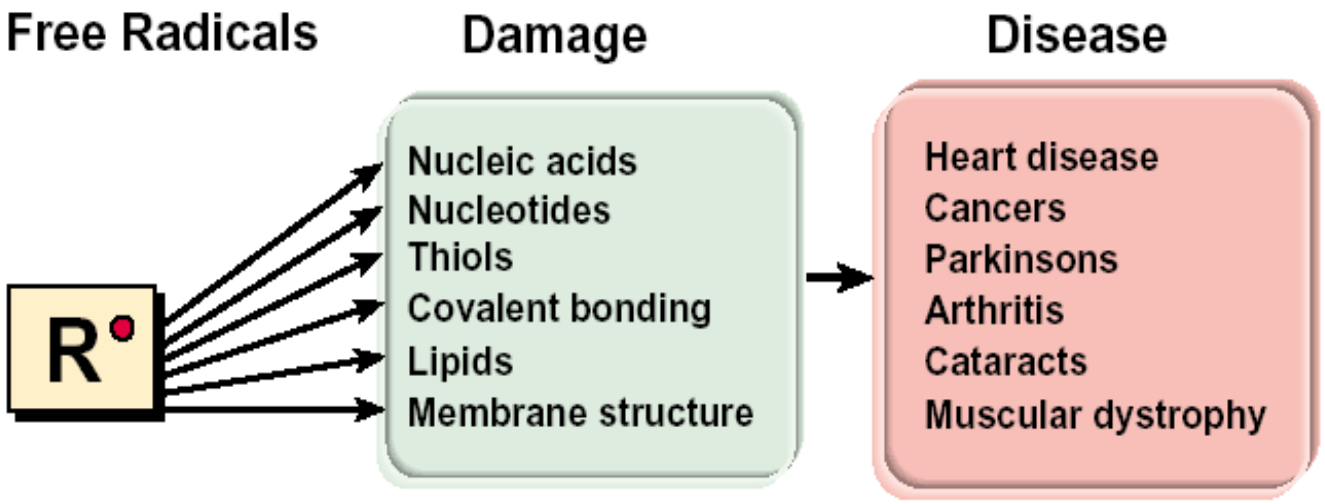
FREE RADICAL DAMAGE AND DISEASE



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MODE OF ACTION

REACTIVE OXYGEN SPECIES (ROS)

- **Reactive Species**

- **Includes:**
  - **hydroxyl radicals (.OH)**
  - **superoxide anions ($O^{\cdot}_2$-)**
  - **singlet oxygen($^1O_2$)**
  - **hydrogen peroxides (H_2O_2)**
  - **organic peroxides (R-OOH)**
  - **nitric oxide**
- **peroxynitrite**

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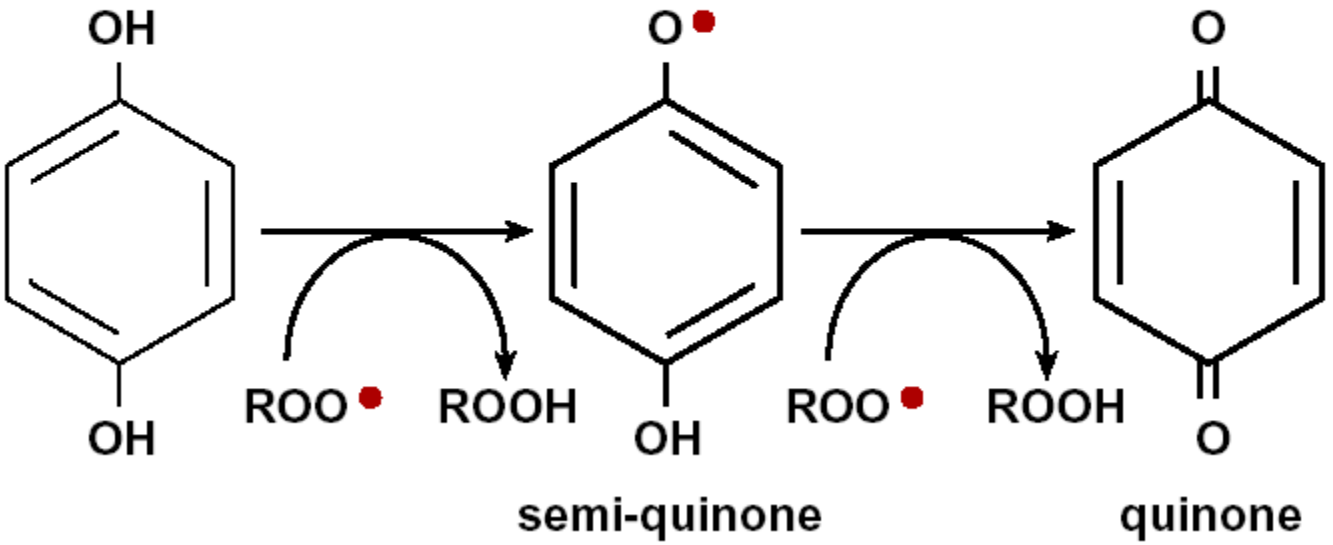
OXIDATIVE STRESS

Oxidant	Description
•O_2-, superoxide anion	One-electron reduction state of O_2, formed in many autoxidation reactions and by the electron transport chain. Rather unreactive but can release Fe^{2+} from iron-sulfur proteins and ferritin. Undergoes dismutation to form H_2O_2 spontaneously or by enzymatic catalysis and is a precursor for metal-catalyzed •OH formation.
H_2O_2, hydrogen peroxide	Two-electron reduction state, formed by dismutation of •O_2- or by direct reduction of O_2. Lipid soluble and thus able to diffuse across membranes.
•OH, hydroxyl radical	Three-electron reduction state, formed by Fenton reaction and decomposition of peroxynitrite. Extremely reactive, will attack most cellular components
ROOH, organic hydroperoxide	Formed by radical reactions with cellular components such as lipids and nucleobases
RO•, alkoxy and ROO•, peroxy radicals	Oxygen centred organic radicals. Lipid forms participate in lipid peroxidation reactions. Produced in the presence of oxygen by radical addition to double bonds or hydrogen abstraction.
HOCl, hypochlorous acid	Formed from H_2O_2 by myeloperoxidase. Lipid soluble and highly reactive. Will readily oxidize protein constituents, including thiol groups, amino groups and methionine
ONOO-, peroxynitrite	Formed in a rapid reaction between •O_2- and NO•. Lipid soluble and similar in reactivity to hypochlorous acid. Protonation forms peroxynitrous acid which can undergo homolytic cleavage to form hydroxyl radical and nitrogen dioxide.

PHENOLICS as ANTIOXIDANT

Phenolic antioxidant mechanism



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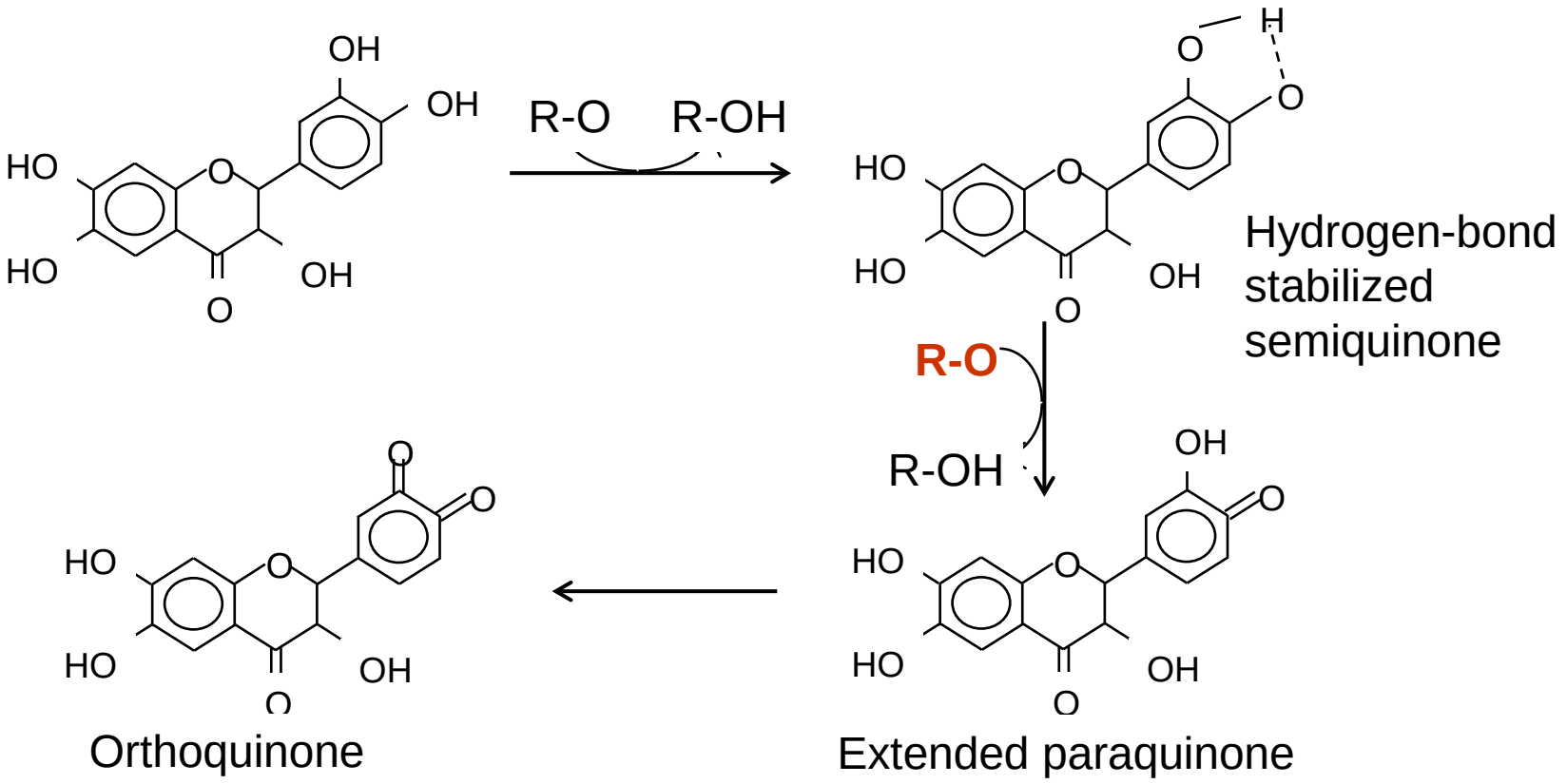
Two-Stage Oxidation of Quercetin



(J. Agric. Food Chem. 2003;51:1684-90)

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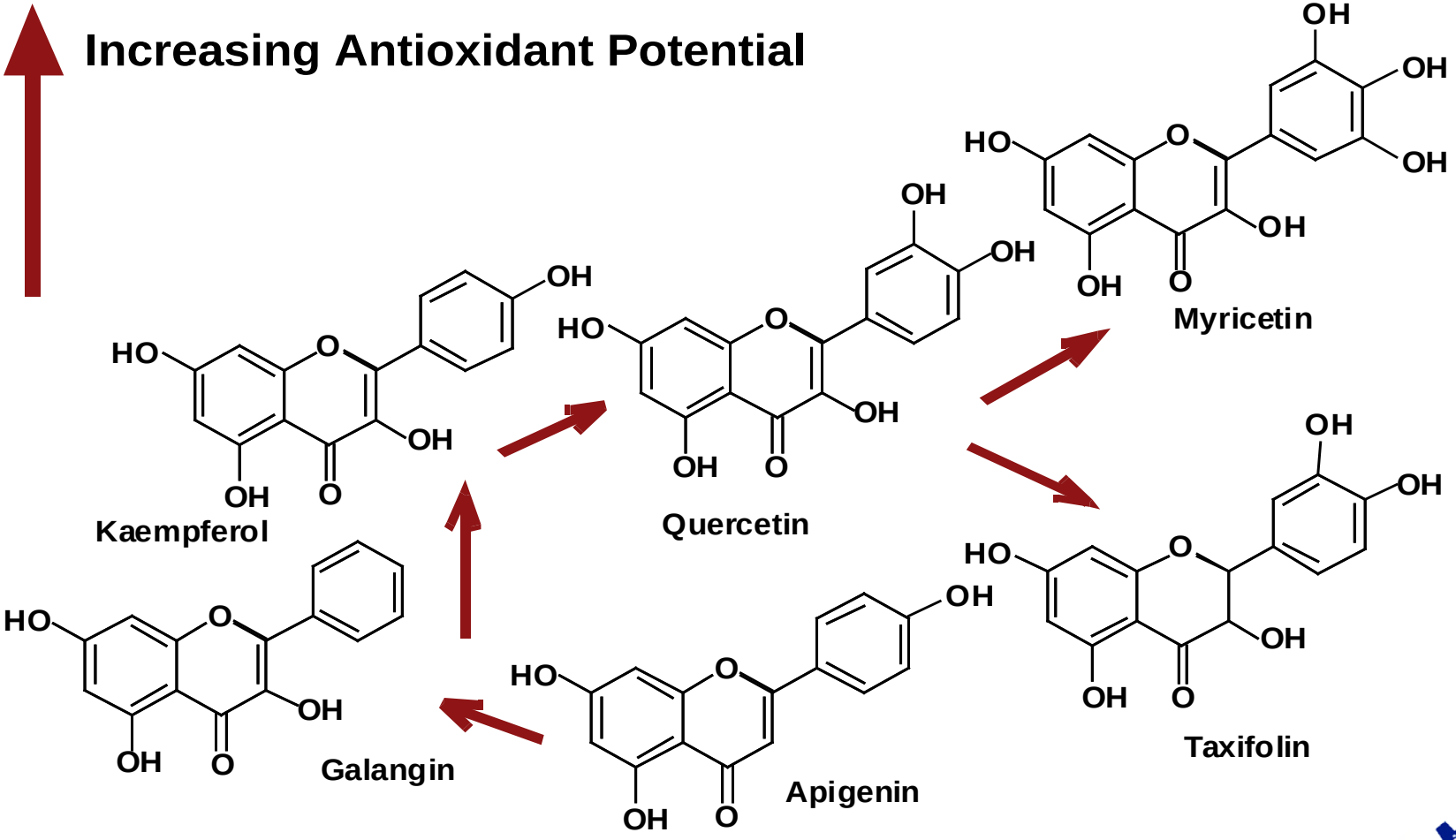
Structure – activity relationships



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ANTIOXIDANT MEASURE

Item	Antioxidant Capacity (μ mol Trolox/g DM)
Black Tea	927
Green Tea	814 30
Spinach	129 6
Beet	81 25
Leaf Letuce	49 7
Cauliflower	46 11
Garlic	46
Onion	40 2
Cabbage	32 2
Carrot	26 8
Corn	22 4
Potato	15 5
Cucumber	15 2
Sweet potato	14 2

J. Agric. Food Chem. **1996,** 44, 3426-3431

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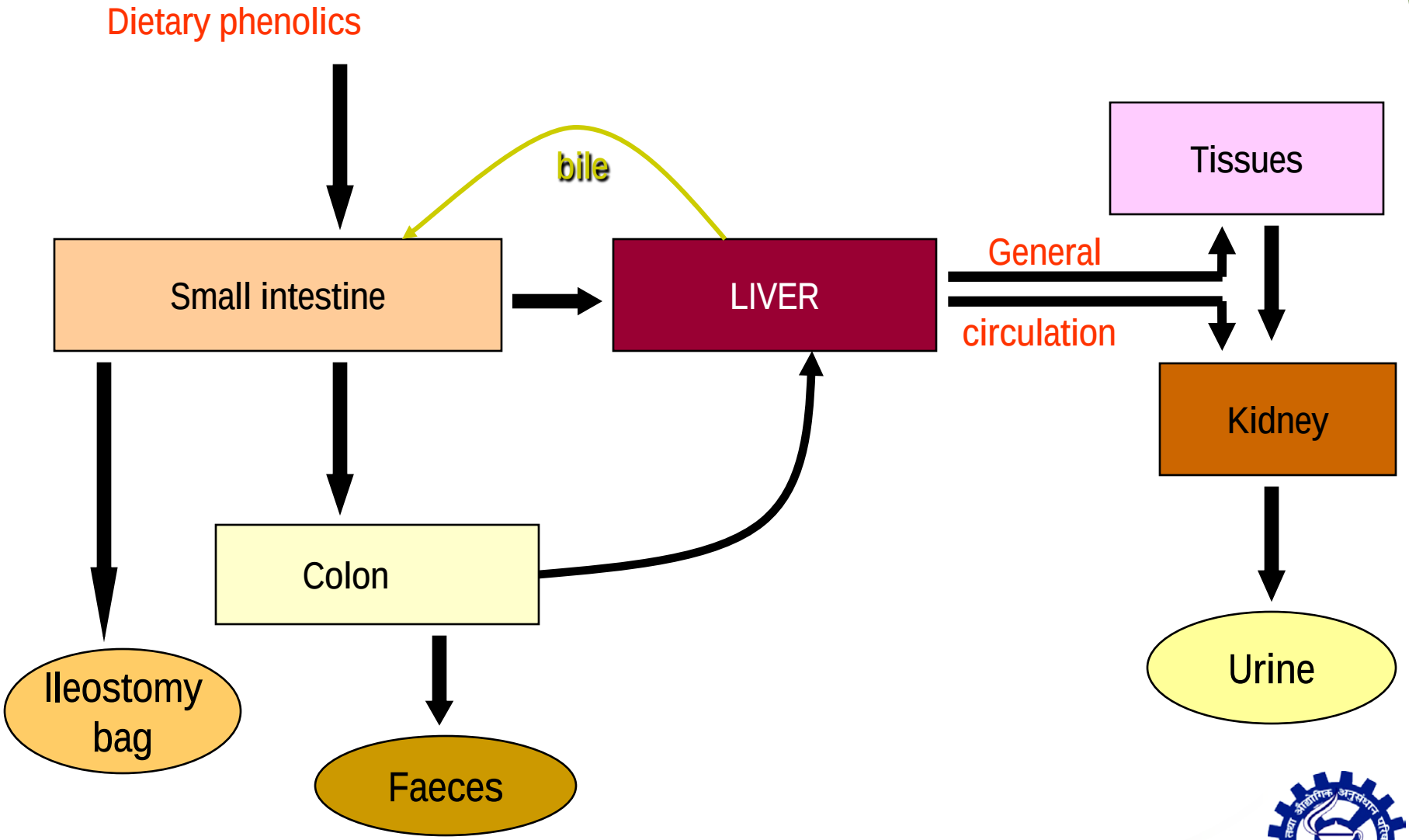
Consumed Dietary Phenolics Metabolism in Humans



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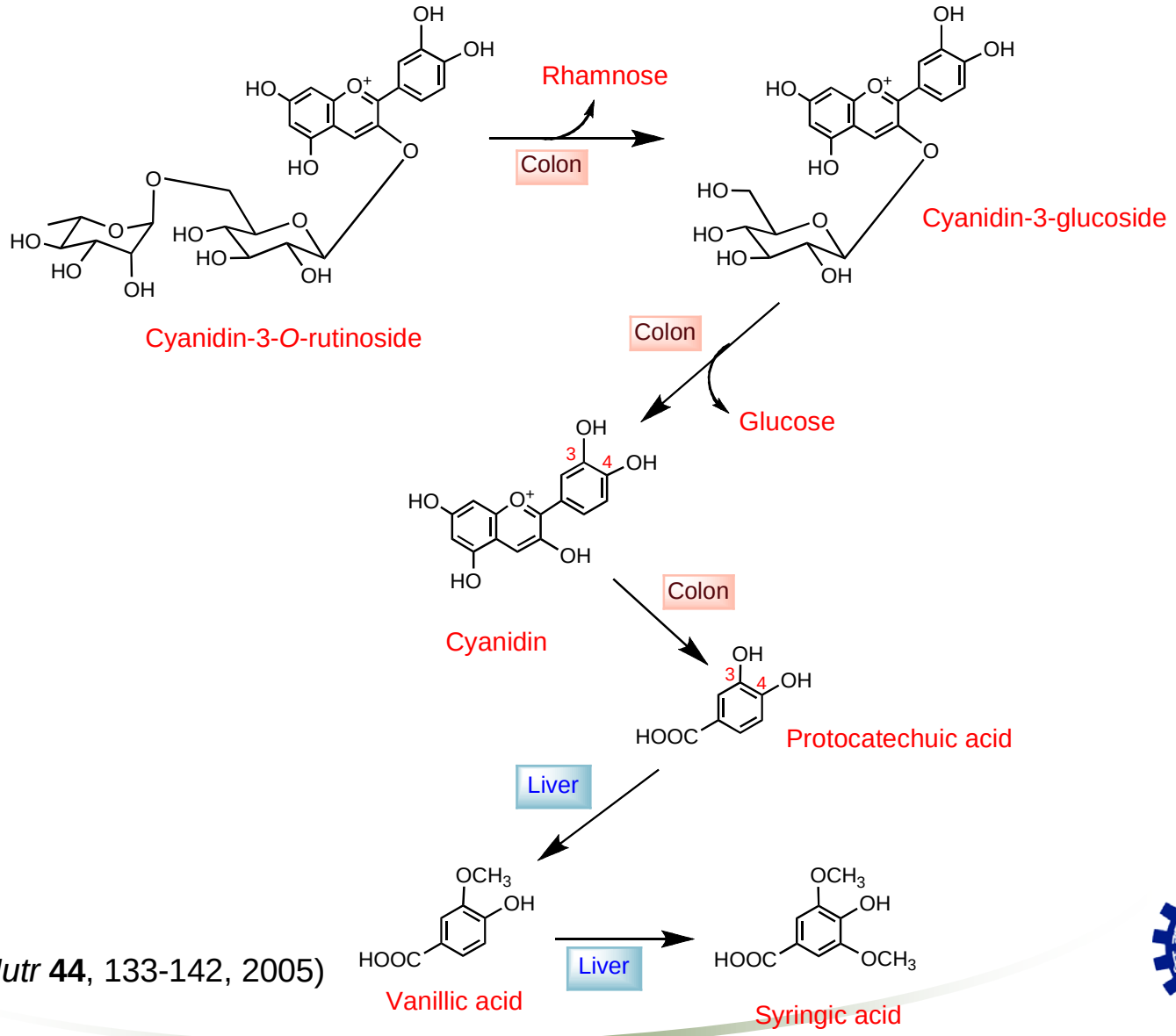
Colonic degradation of anthocyanins



(Aura et al., *Eur J Nutr* **44**, 133-142, 2005)

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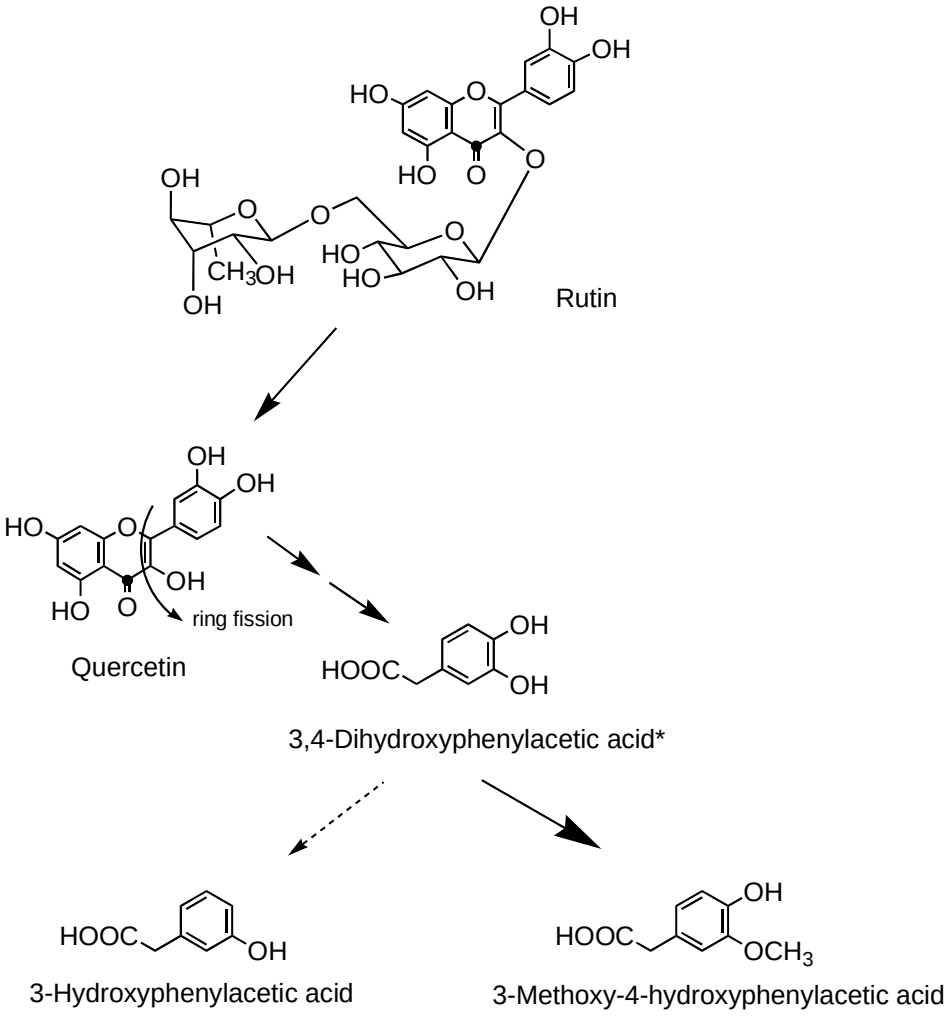
Fate of Rutin In The Large Intestine



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BIOAVAILABILITY

1.The maximum plasma concentrations attained after a polyphenol-rich meal, which are in the range of 0.1–10 µmol/L.

2. Catabolism of polyphenols in humans usually occurs only as a result of microbial activity in the (large) intestine.

3. Human tissues are exposed to polyphenols via the blood,which is the only route through which dietary polyphenols can reach tissues and their cells, except for the cells lining the intestinal tract.

4. Phenolic acids account for about one third of the total intake and flavonoids account for the remaining two thirds. The most abundant flavonoids in the diet are flavanols (catechins plus proanthocyanidins), anthocyanins and their oxidation products. The main polyphenol dietary sources are fruit and beverages (fruit juice, wine, tea, coffee, chocolate and beer) and, to a lesser extent vegetables, dry legumes and cereals.

J. Nutr. 130: 2073S—2085S, 2000.

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5. Endogenous plasma antioxidants, especially ascorbate, are required for disposal of the resultant phenoxyl radicals .

6. Over 95% of the intake passes to the colon and is fermented by the gut microflora. A fraction of the resulting microbial metabolites is absorbed and appears in the plasma primarily as mammalian conjugates.

7. **More than 2 d are needed for the phytoestrogen metabolites to reach the baseline concentrations in plasma and urine after the consumption of soy milk and flaxseed, respectively.**

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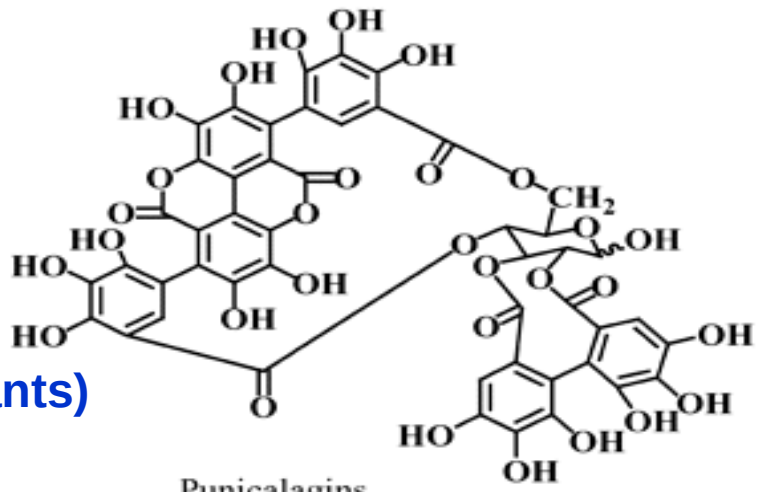
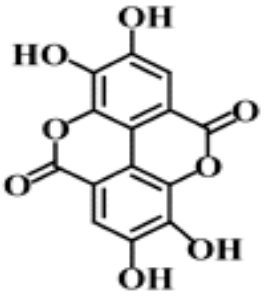
METABOLISM IN GI

- **Ellagitannins (antioxidants) are not absorbed**
- **Metabolized *in vivo* to bioavailable urolithins**
- **Urolithins are weakly antioxidant**
- **Large inter-individual variability**

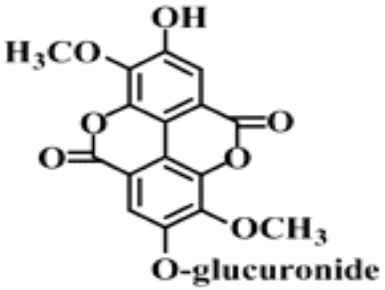


Punicalagins

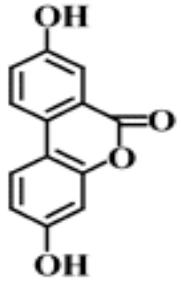
ET



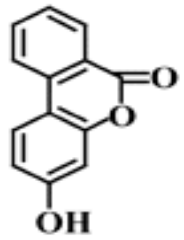
Ellagic acid (EA)



Dimethylellagic acid glucuronide (DMEAG)



Urolithin A



Urolithin B

IHBT

TISSUE DISTRIBUTION

Non-detected-in

- –Liver**, kydney**, muscle, adipose, heart, lung, brain.

Plasma concentrations

- –Below 1μM

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Thank You .....!

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