Phytochemicals: Plant-derived nutrients to fight aging in pets

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We eat protein (and fats a little) to build tissue
Carbohydrates (and fats a little) to provide energy,
BUT
Why eat fruit and vegetables ?

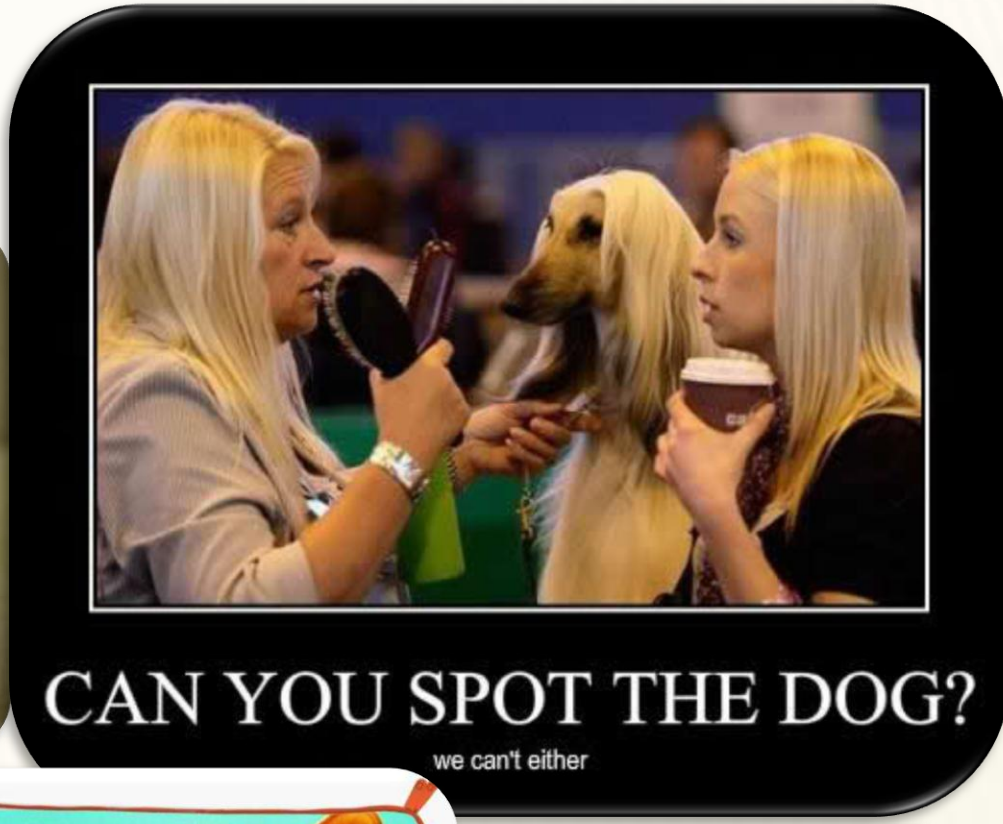
The role of plants in the diet is to provide vitamins, minerals and….

Phytochemicals, to slow the onset of diseases of aging


dreamstime.com

	Pet Food Company	A	B	C	D
Meat, (fat)	Chicken	✓	✓		✓
	Chicken Meal	✓		✓	✓
	Salmon Meal				
	Lamb Meal				
Fruits & Veggies	Wholesome Egg				✓
	Farm-Grown Spinach		✓		✓
	Farm-Grown Carrots	✓	✓		✓
	Vine-Ripened Tomatoes	✓	✓	✓	
	Farm-Grown Pumpkin				✓
	Sun-Ripened Blueberries	✓	✓		✓
	Sun-Ripened Cranberries	✓		✓	✓
	Sun-Ripened Pomegranate				
Carbs, fiber	Rolled Oats	✓	✓		
	Whole Brown Rice	✓	✓	✓	
	Whole Flaxseed	✓	✓	✓	
	Pure Sunflower Oil	✓		✓	

But please remember that , at least diet-wise, dogs and cats are not people



Bad food choices for pets

Chocolate: Chocolate/ cocoa beans contains methyxanthines (theobromine/caffeine), toxic to cats, dogs, horses. (**Cocoa Mulch also).**

Grapes and Raisins: In some dogs, causes kidney problems, even renal failure.

Fatty foods: Fatty foods can lead to possibly fatal pancreatitis in dogs.

Nuts: Macadamia nuts cause increased body temperature, weakness, depression and other neurological signs in dogs.

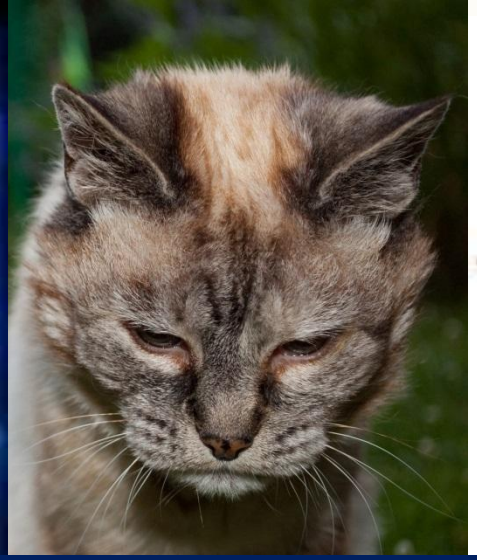
Onions & Garlic: Onions trigger hemolytic anemia in dogs and cats.

Nightshade family: Potatoes/Tomatoes/ Chilies/ Eggplant The toxin, solanadine, is in green tomatoes and green potato skins.

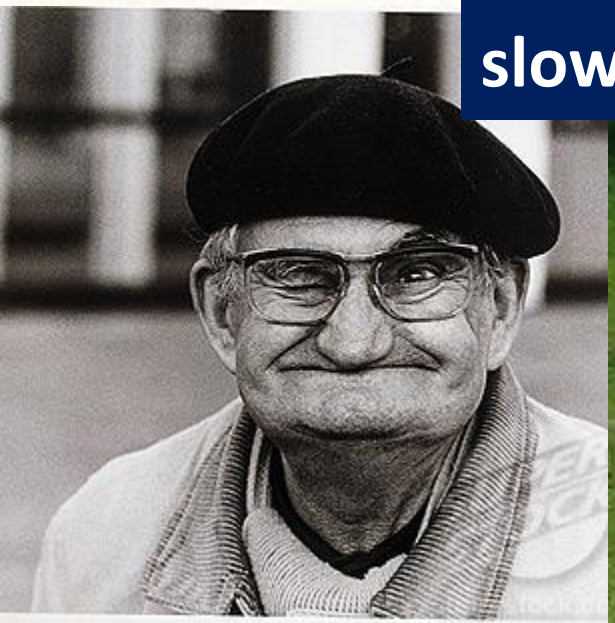
Artificial Sweeteners: Xylitol , in sugar-free gum etc., may cause a sudden drop in blood sugar in dogs, with depression, loss of coordination, and seizures.

Hops: Spent or raw hops cause an extreme, often fatal, increase in body temperature in dogs.

Avocardos: most dogs and cats are OK, but birds, horses, cows poisoned.



Like us, our companion animals grow old.
Can phytochemicals help slow age-related diseases?



Maybe phytochemicals cannot make them (or us) young again

But phytochemicals may improve quality of life?

What do phytochemicals do for your pet ?

Many different Phytochemicals → **Improve Detoxification Enzymes**

Antioxidants/

Polyphenolics

ω–3 Fatty Acids

→ **Enhance immune system Prevent CVD & cognitive decline**

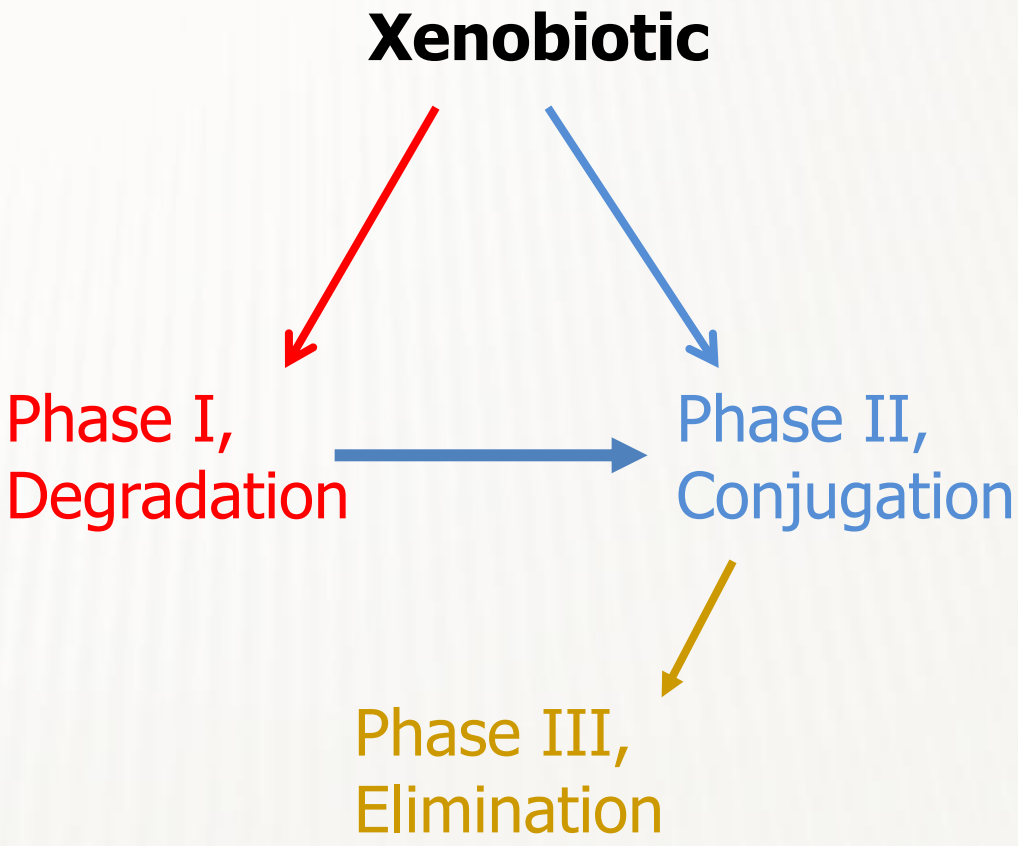
Glucosinolates → **Prevent Cancer**

broccoli's glucosinolate metabolites decrease cancer risk

Detoxification Enzymes

- Metabolize and secrete foreign compounds

- **Drugs**
- **Carcinogens**
- **Environmental contaminants**
- **Toxic chemicals**



Detoxification Enzymes

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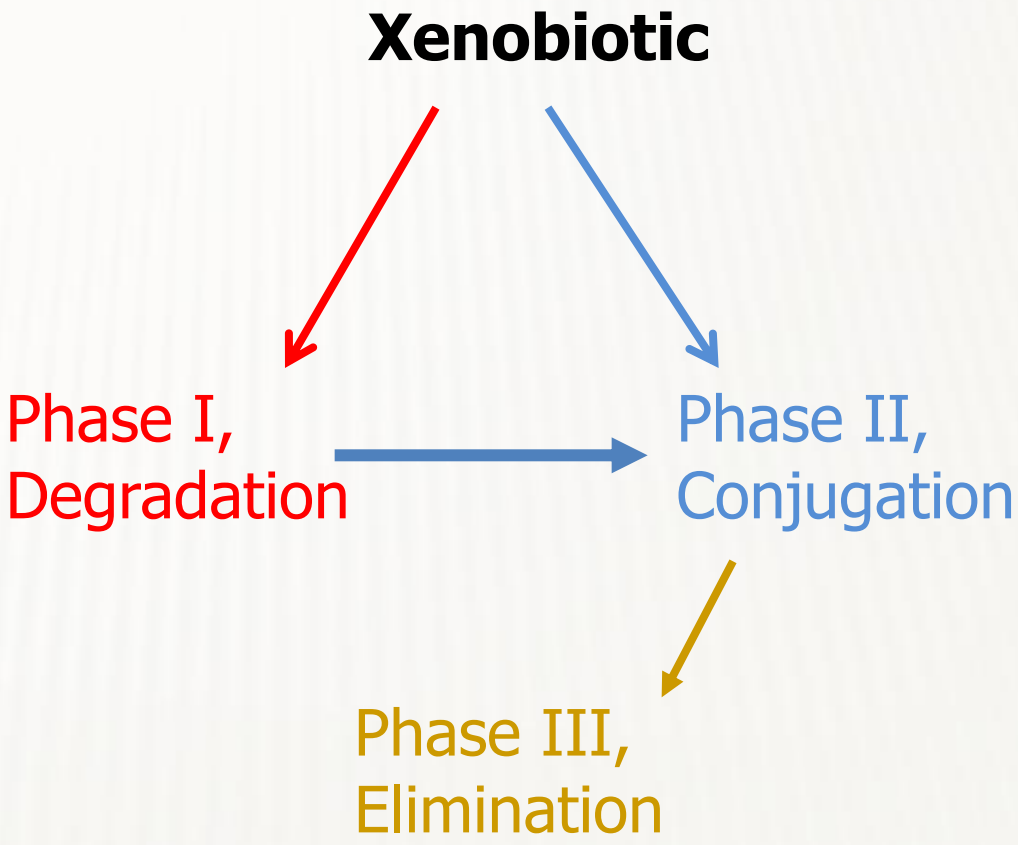
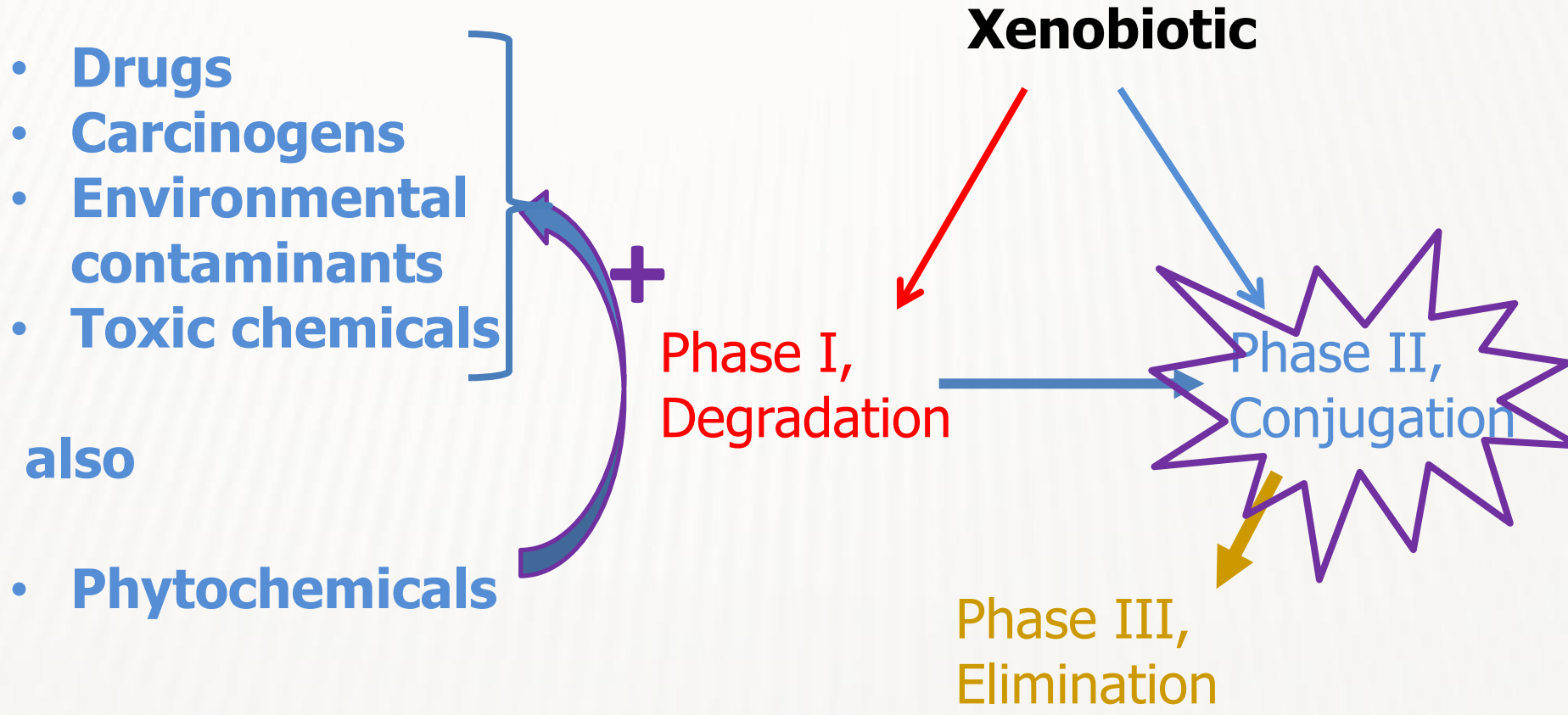
also

- **Phytochemicals**

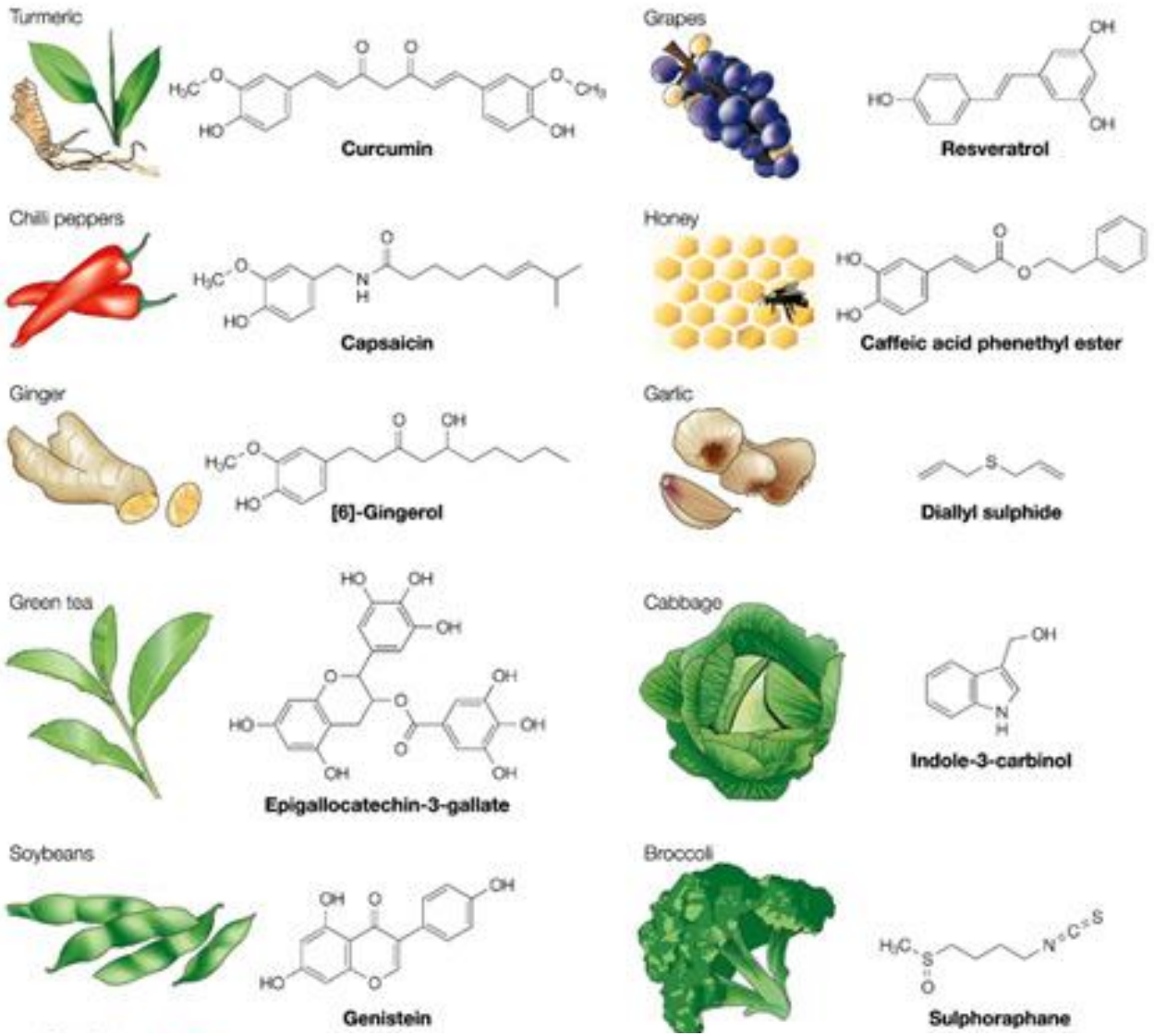


Many Phytochemicals Upregulate Phase II Detoxification Enzymes

- Metabolize and secrete foreign compounds



Bioactive Food Components

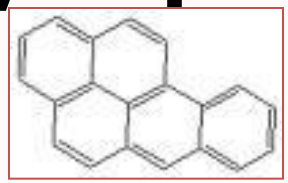


Dietary Anticarcinogens: Compounds that increase phase II enzymes can improve clearance of other toxic compounds

Surh Y-J, (2003) Nature Reviews Cancer **3**, 768-780

Many carcinogens are activated through Phase I enzymes: dietary anticarcinogens can rebalance detoxification by improving phase II

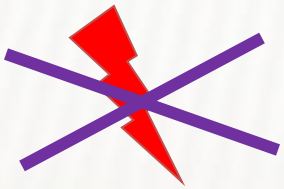
Benzpyrene from cigarettes



Dietary anticarcinogen enhances phase II

Reactive products bind to DNA

Phase II enzymes are sufficient to clear the benzypyrene metabolites



LUNG CANCER

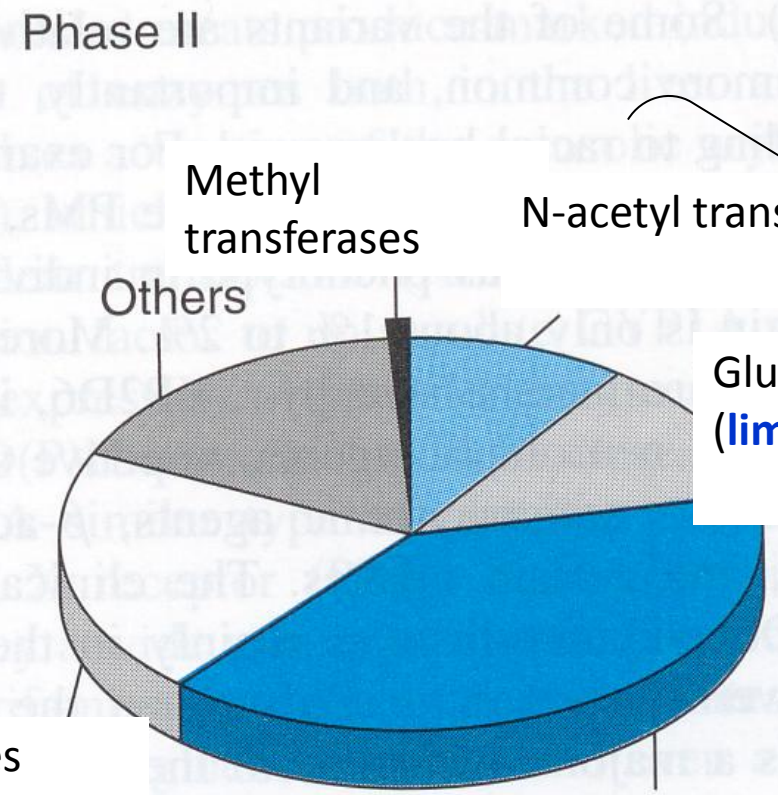
Excretion

Crucifers Lower Risk for Lung Cancer More Effectively in those at high risk

	Relative risk
Crucifers/ non-smokers	0.70 (ns)
Crucifers/smokers	0.31 ($p<0.05$)

Zhao et al, 2001, Cancer Epi Bio Prev 10:1063-7

Phase II conjugation



Problem for cats: missing a key Phase II glucuronosyl transferase enzyme, so cannot metabolize tylenol or aspirin.

Fruits, Vegetables & Cancer Prevention

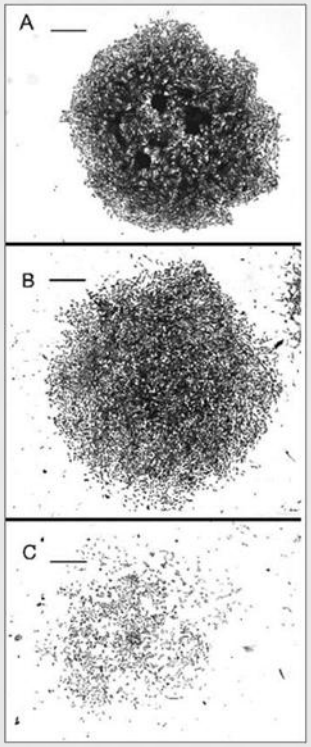
Variety or Category	% Positive
Vegetables	80% (59/74)
Fruits	64% (36/56)
Raw vegetables	87% (40/46)
Cruciferous Vegetables	69% (38/55)
Allium Vegetables	77% (27/35)
Green vegetables	77% (68/88)
Carrots	81% (59/73)
Tomatoes	71% (36/51)
Citrus Fruit	66% (27/41)

The 1997 World Cancer Research Fund and the American Institute for Cancer Research (WCRF/AICR) report: Food, Nutrition and the Prevention of Cancer: a global perspective, p442. by John D Potter and other panel members

Dog is a comparative tumor model

Chand Khanna (with Gracie, a lymphoma patient) is heading up NCI's Comparative Oncology Program, which will take advantage of the similarities between canine and human cancers to test cancer drugs in clinical trials of dogs.

Rapamycin-osteosarcoma study on canine cells:



0 (control)

0.3 nM Rapa

10 nM Rapa

New work on compounds from potato family may treat man and dogs.

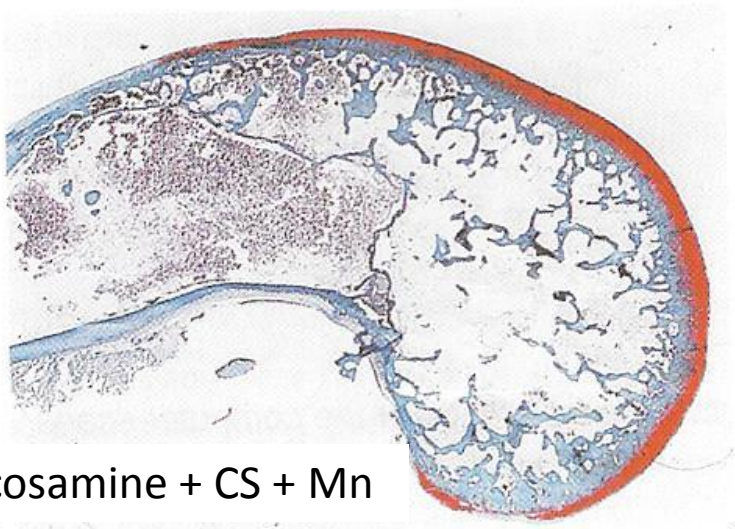
Glucosamine / Chondroitin sulfate

Randomised double-blind, positive-controlled trial to assess the efficacy ofglucosamine/chondroitin sulfate for the treatment of dogs with osteoarthritis
Dogs treated with Glu/CS showed statistically significant improvements in scores for pain, weight-bearing and severity of the condition by day 70 ($P < 0.001$). Onset of significant response was slower for Glu/CS than for carprofen-treated dogs. The results show that Glu/CS has a positive clinical effect in dogs with osteoarthritis

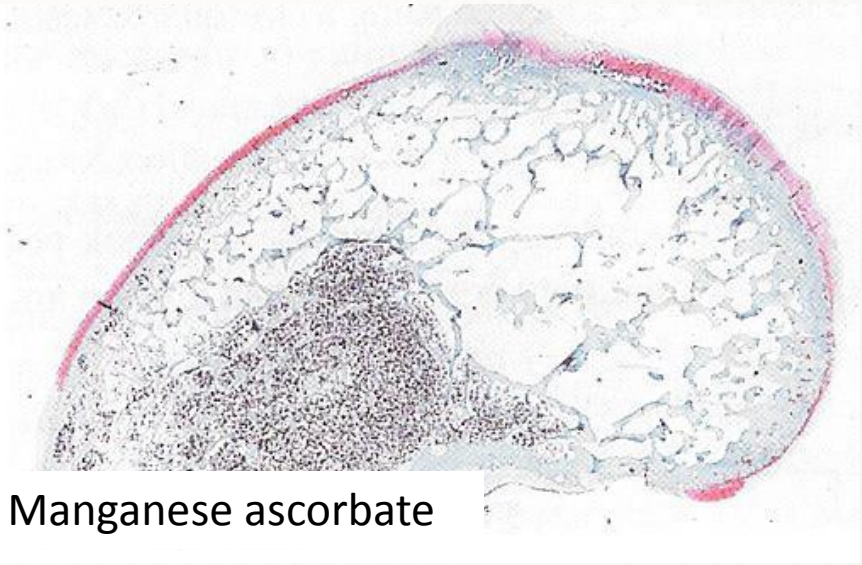
Parameter	Carprofen median (mean)	Glu/CS median (mean)	95% CI of difference in medians	*P*-value
Lameness	1.0 (1.1)	0.5 (0.6)	0, 1	0.0775
Joint mobility	1.0 (1.0)	0.5 (0.5)	0, 1	0.0907
Pain	1.0 (0.8)	1.0 (0.9)	−1, 1	>0.5
Weight bearing	1.0 (1.4)	1.0 (1.1)	0, 1	0.2380
Overall condition	1.0 (1.4)	1.0 (1.0)	0, 1	0.0587

McCarthy et al, (2007) Veterinary Journal, 174 , pp. 54-61.

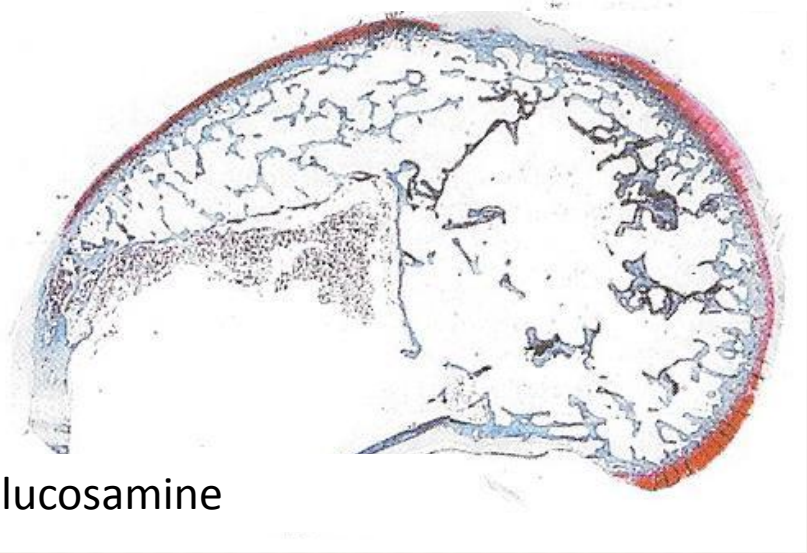
Effect of Glucosamine + Chondroitin sulfate and manganese on induced osteoarthritis in Rabbit median temporal condyle



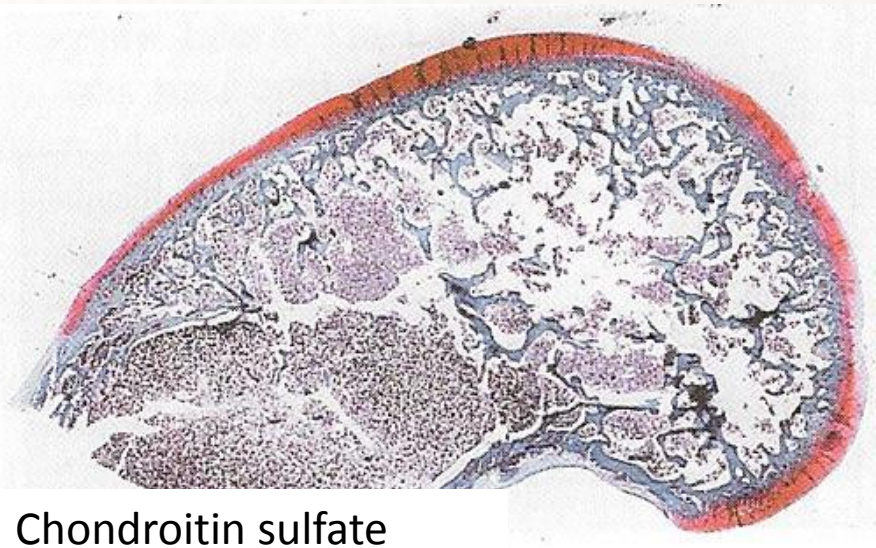
Glucosamine + CS + Mn



Manganese ascorbate



Glucosamine



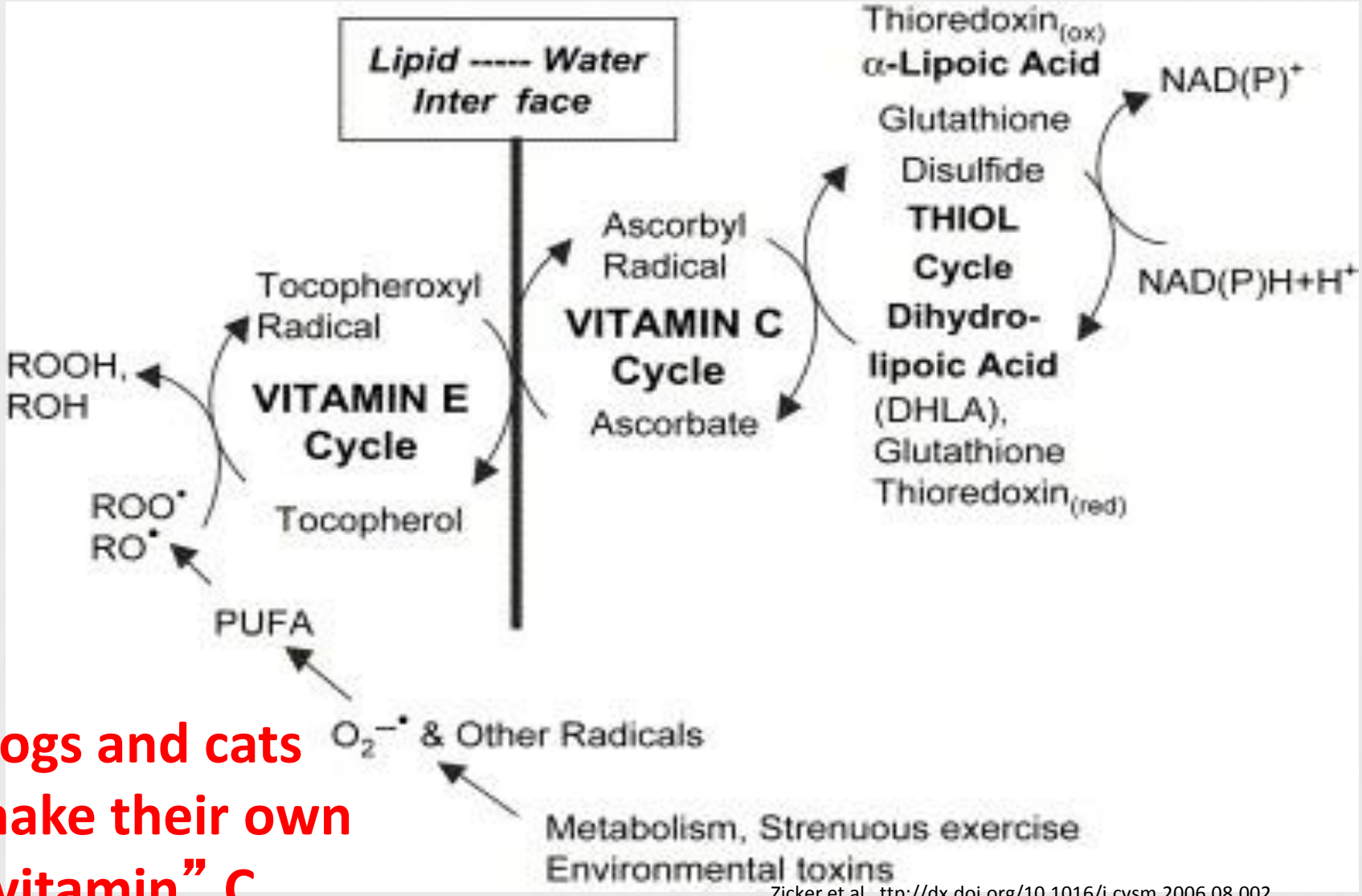
Chondroitin sulfate

Lippiello et al, clinical osteopedics 381: 229-239; 2000:

Berries: Foods rich in Antioxidants

What does this mean ?

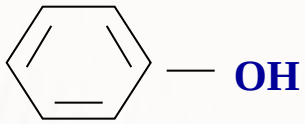
Vitamins E and C make excellent antioxidants because they cycle in the body, being reduced again after becoming oxidized



Dogs and cats make their own "vitamin" C

Zicker et al, ttp://dx.doi.org/10.1016/j.cvsm.2006.08.002

Antioxidants: Polyphenolics from fruits and vegetables, including flavonoids, that can donate reducing power and improve shelf-life

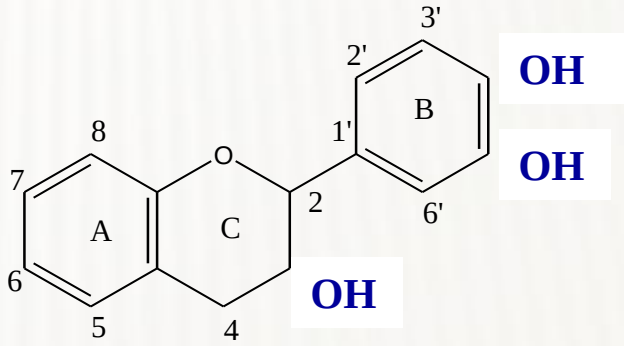


Monophenolics:

Ferrulic acid,
Caffeic acid etc.

Polyphenolics, flavonoids :

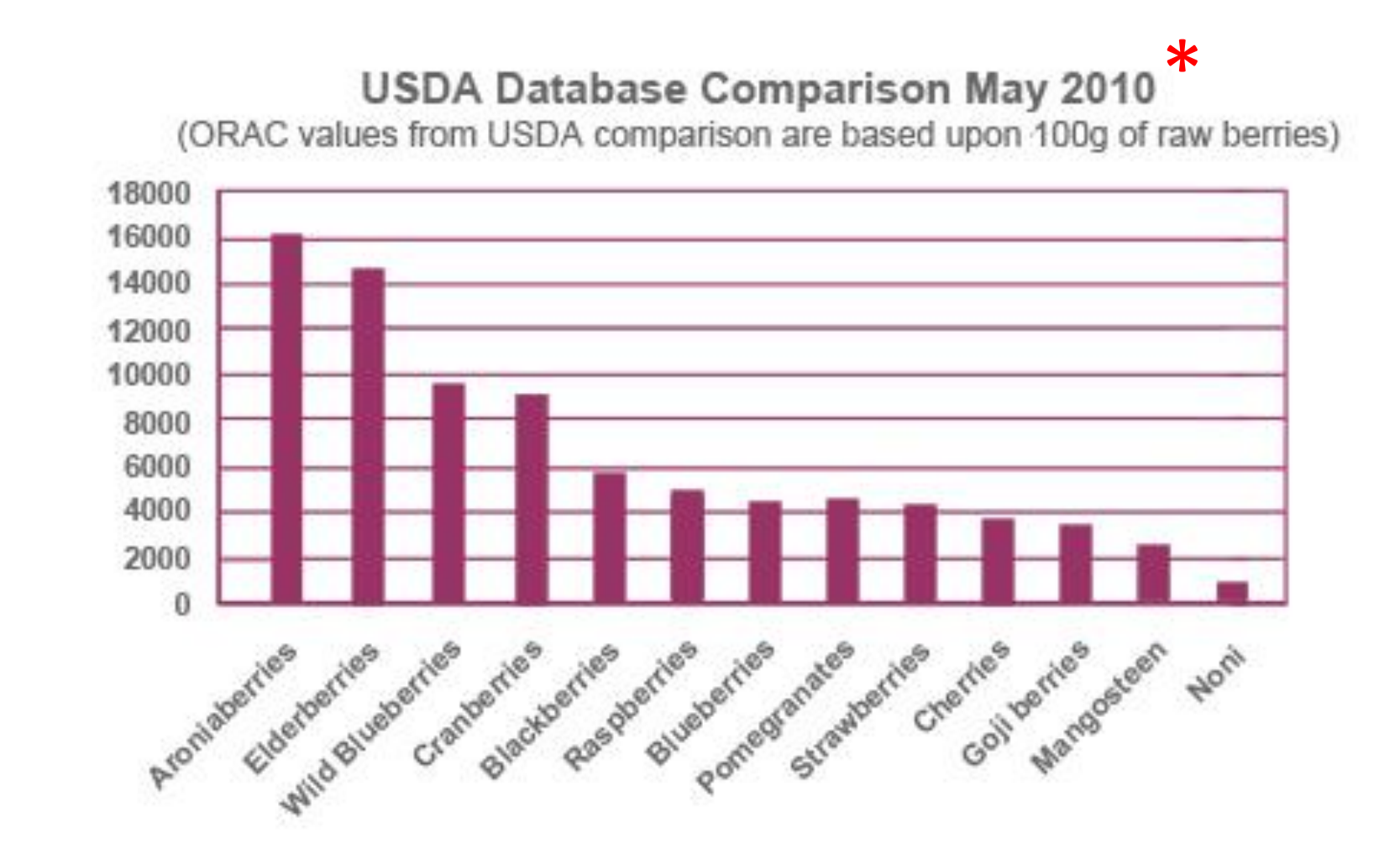
Quercetin, Kaempferol, Genistein, EGCG (epicatechogallocatechin)



Donating reducing power can improve shelf life/ freshness of foods.

http://www.ars.usda.gov/Services/docs.htm?docid=6231

Cranberries, like many other berries, are a rich source of polyphenolic antioxidants



* Note, USDA ha now removed ORAC values because of misinterpretation, see http://www.ars.usda.gov/services/docs.htm?docid=15866&pf=1

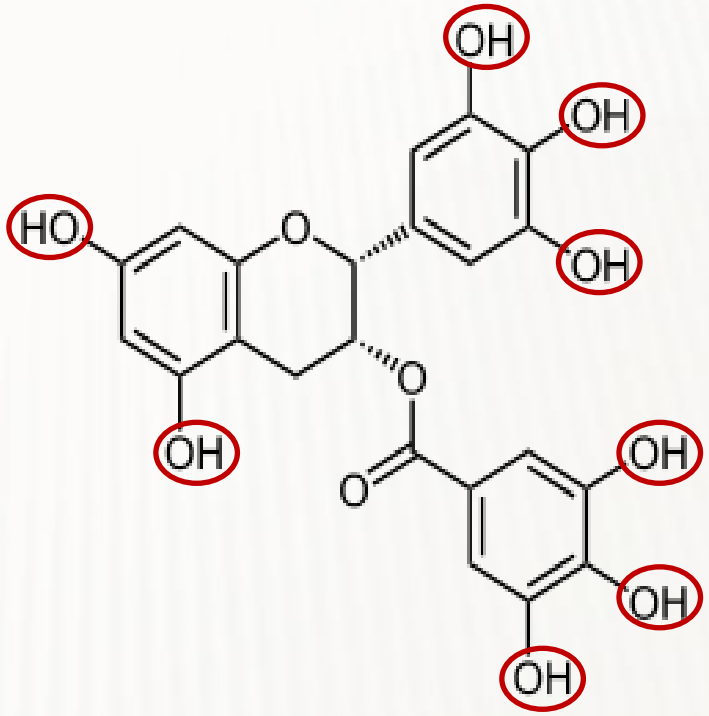
Polyphenolics are more than just antioxidants:

- Inhibit inflammation
- Increase detoxification enzymes that remove foreign compounds
- Estrogenic/ Antiestrogenic (esp. isoflavones)
- Often cause cell-specific cell death that lets cancer cells be killed, but not normal, healthy cells

Epigallocatechin 3-gallate (EGCG from green tea)

Slows or prevents chronic diseases including
Cancers
CVD
Diabetes
Possibly osteoarthritis

? **Mostly as an anti-inflammatory**?

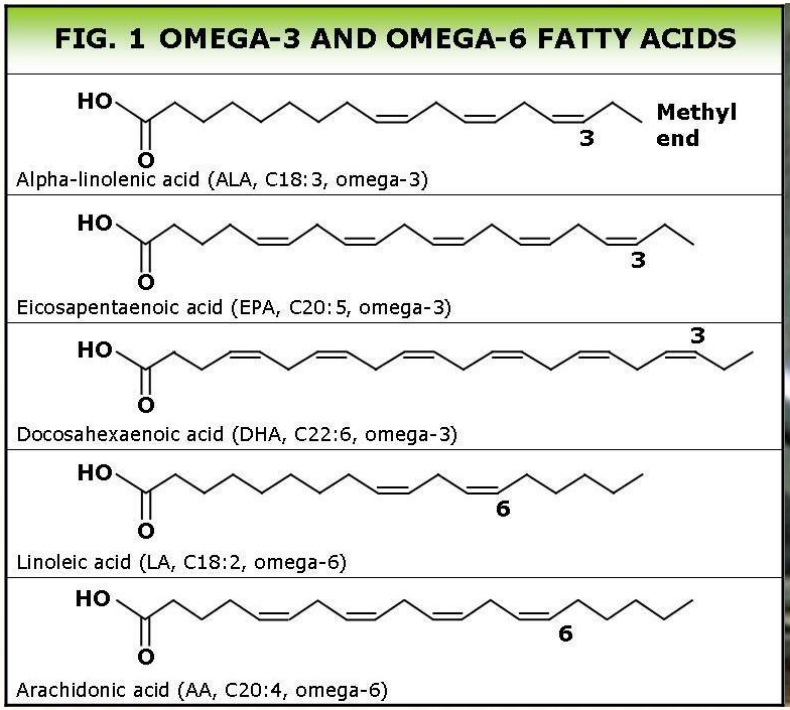


Caffeine and methylxanthines in tea can be toxic to dogs! Use purified EGCG

? Dose ?

OMEGA-3 FATTY ACIDS, DHA AND EPA

Salmon,
Herring,
Tuna,
Trout...



Fatty fish prevent cardiovascular disease, enhance immune function, fight inflammation

OMEGA-3 FATTY ACIDS DHA AND EPA

Salmon,
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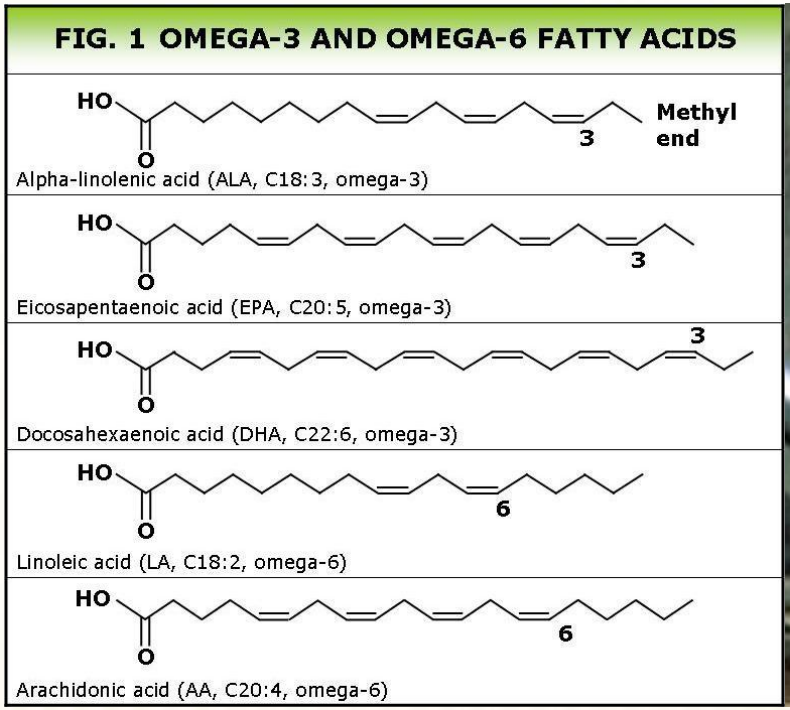
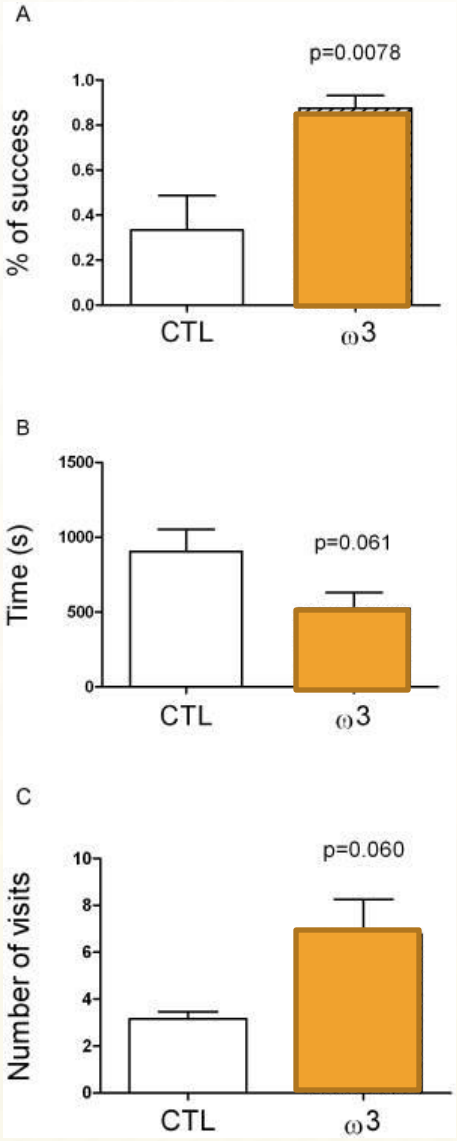
Trout...



Fatty fish prevent cardiovascular disease, enhance immune function, fight inflammation and fight cognitive impairment.....cats are wise !

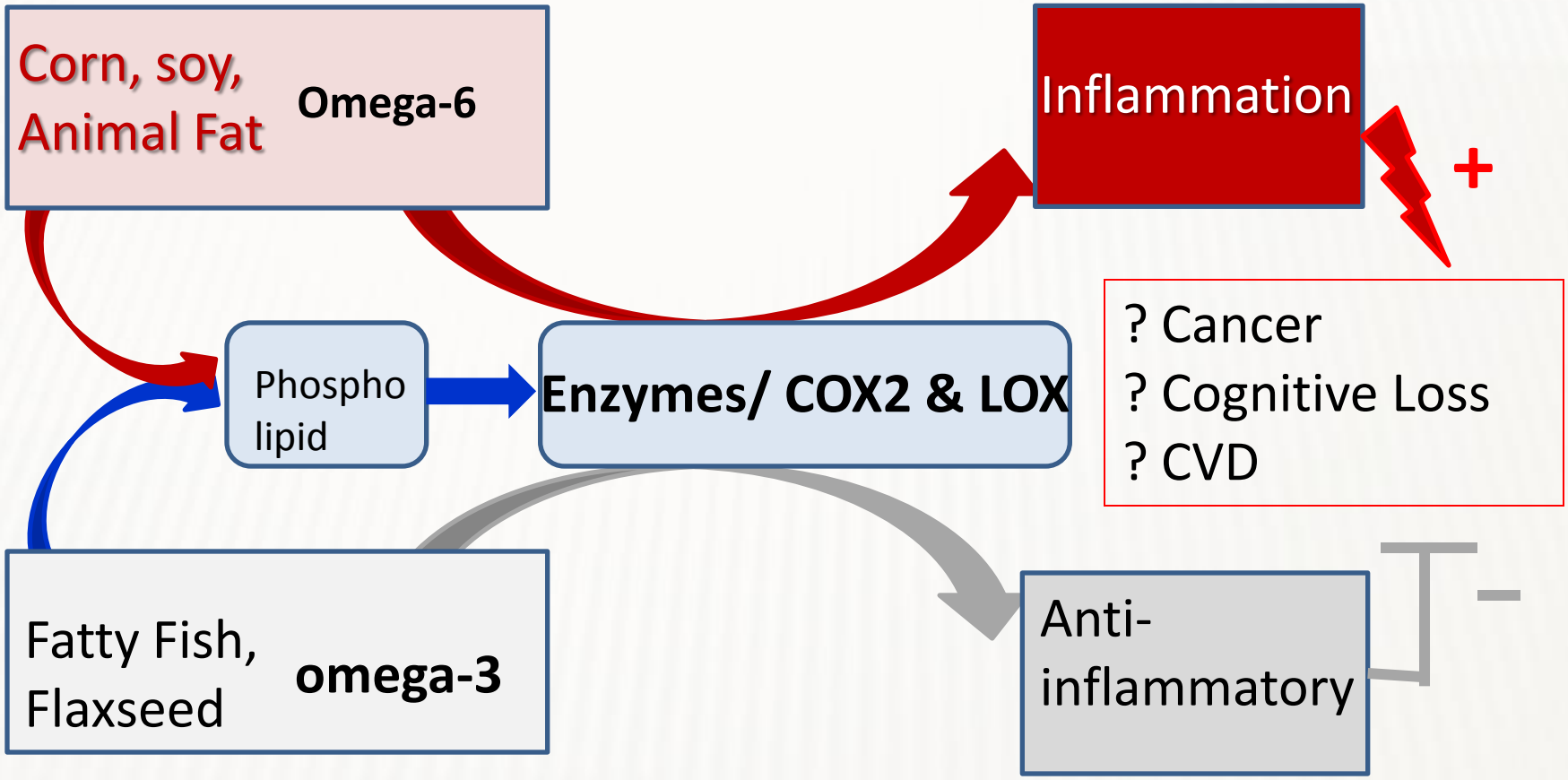
TUNA OIL HELPED PRIMATES IN COGNITION TASKS



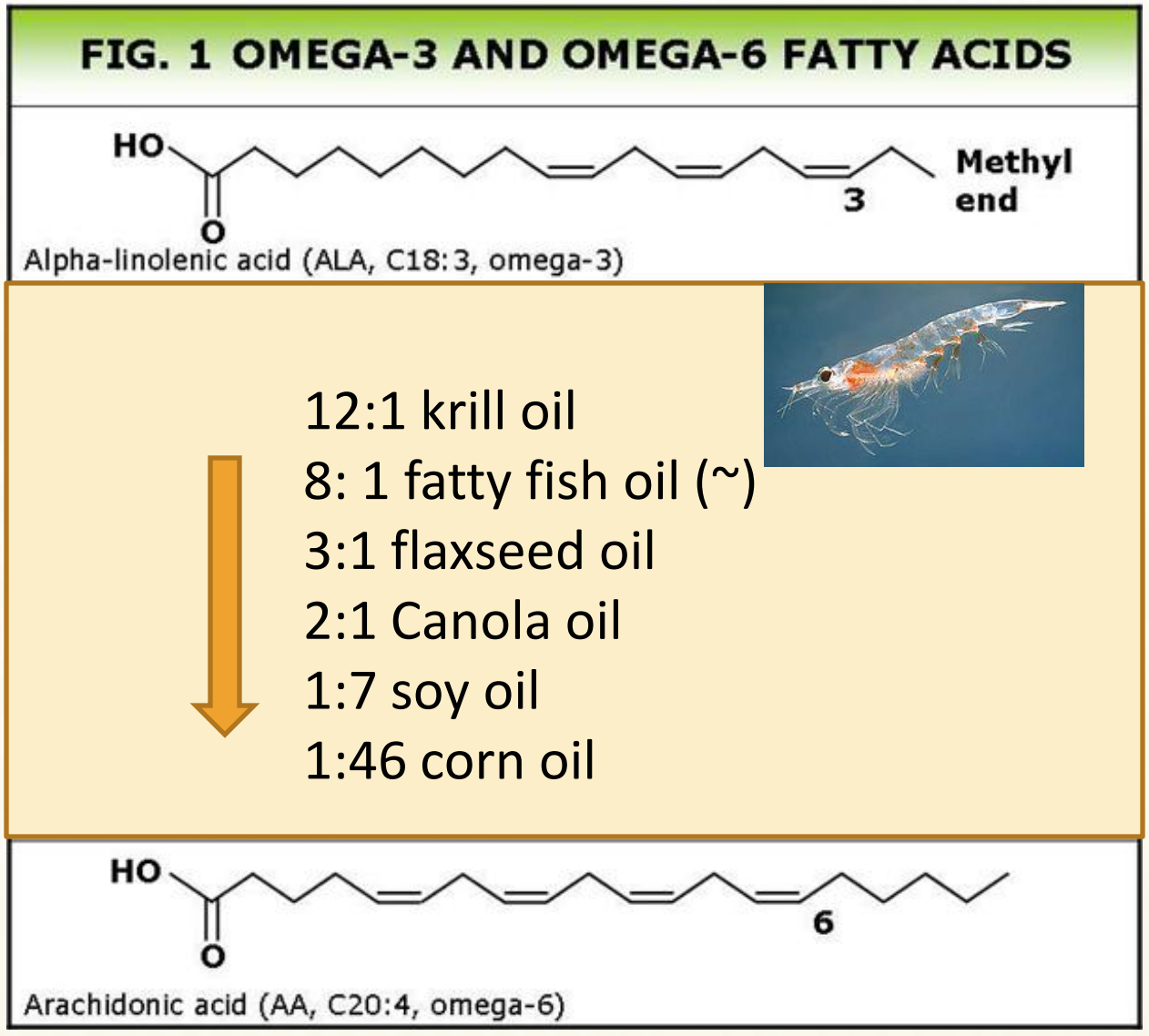
- A: Primates (Lemurs) in the tuna oil group (0.36% diet; 3 months) exhibited **87.5±5.0%** of success in this task compared to **33.3±15.4%** for animals of the control group (p=0.0078, t=3.313, df=10).
- B: They tended to spend less time to exit from the maze compared to controls (**524±106 s vs 906±145** s; p=0.060, t=1.706, df=10).
- C: Their exploratory activity (total number of visits) was increased (**6.8±1.5 vs 3.2±0.3**; p=0.061, t=2.117, df=10).

Vinot et al, 2011

The ratio of omega 6 and omega 3 is very high in the Western diet, promoting diseases of aging



The omega-3 : omega 6 ratio is very low in the Western diet, promoting diseases of aging



OMEGA-3 FATTY ACIDS IMPROVE CARDIOVASCULAR HEALTH

Cardiac disease affects 11% of all dogs and up to 20% of some feline populations.

Nutritional goals for animals with cardiac disease are not only to maintain optimal body condition, avoiding nutritional deficiencies and excesses, but provide a positive benefit from certain nutrients, such as Omega-3 fatty acids.

A dog with severe heart failure and cardiac cachexia and inflammation.

Detection of cachexia at an earlier and more subtle stage, allows greater possibility that intervention with omega-3 fatty acids will be beneficial.

Journal of Small Animal Practice 51: 462-470, 2010

Journal of Small Animal Practice 51: 462-470, 2010

Broccoli also provides cardiovascular disease prevention

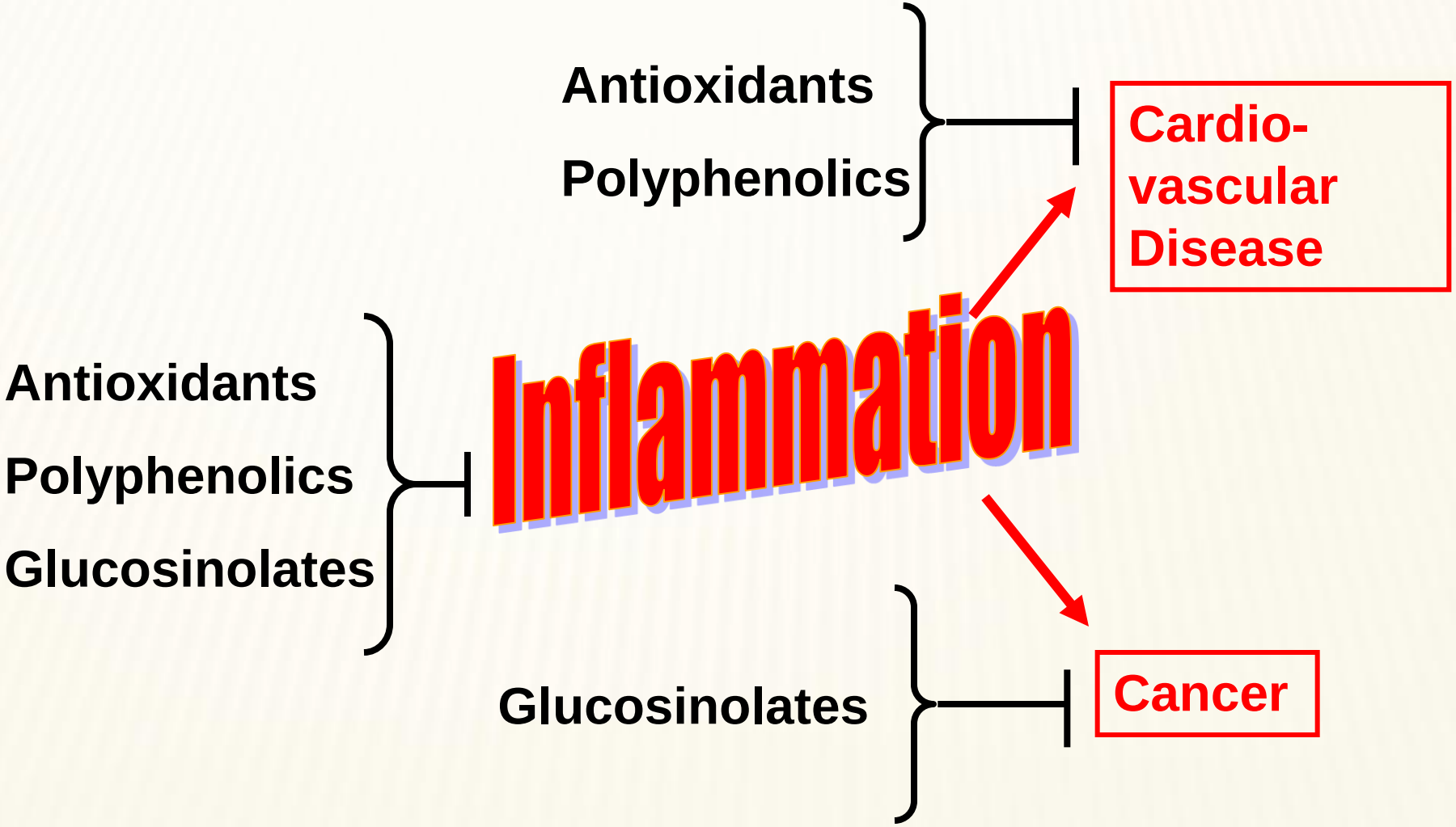
Risk is lower for myocardial infarct (MI) in those eating ~5 servings of broccoli a week

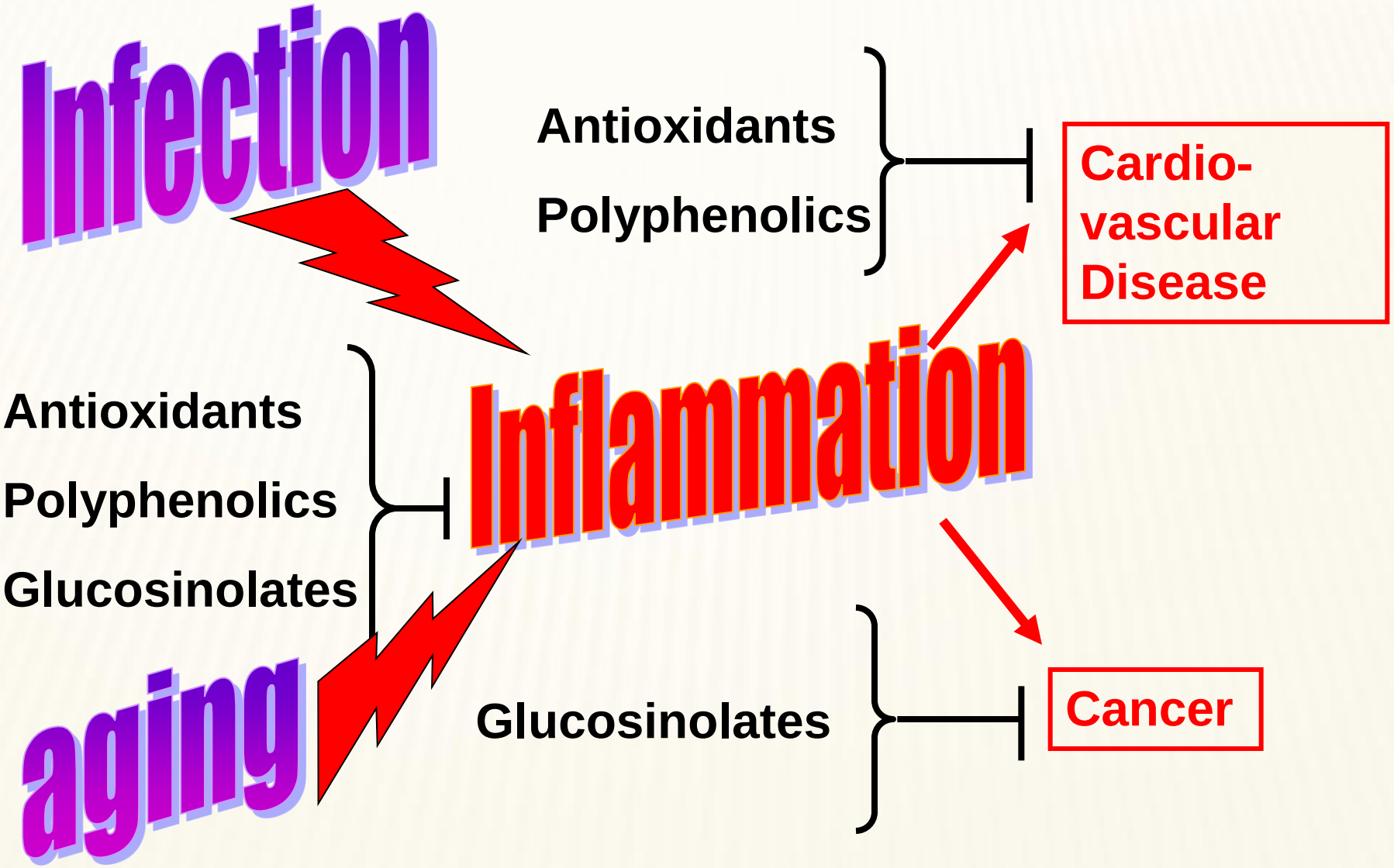
	Low Intake	Mid Intake	High Intake
Servings/ day	**0.08**	**0.43**	**0.86**
Risk for MI (OR)	1.00	0.88	0.63

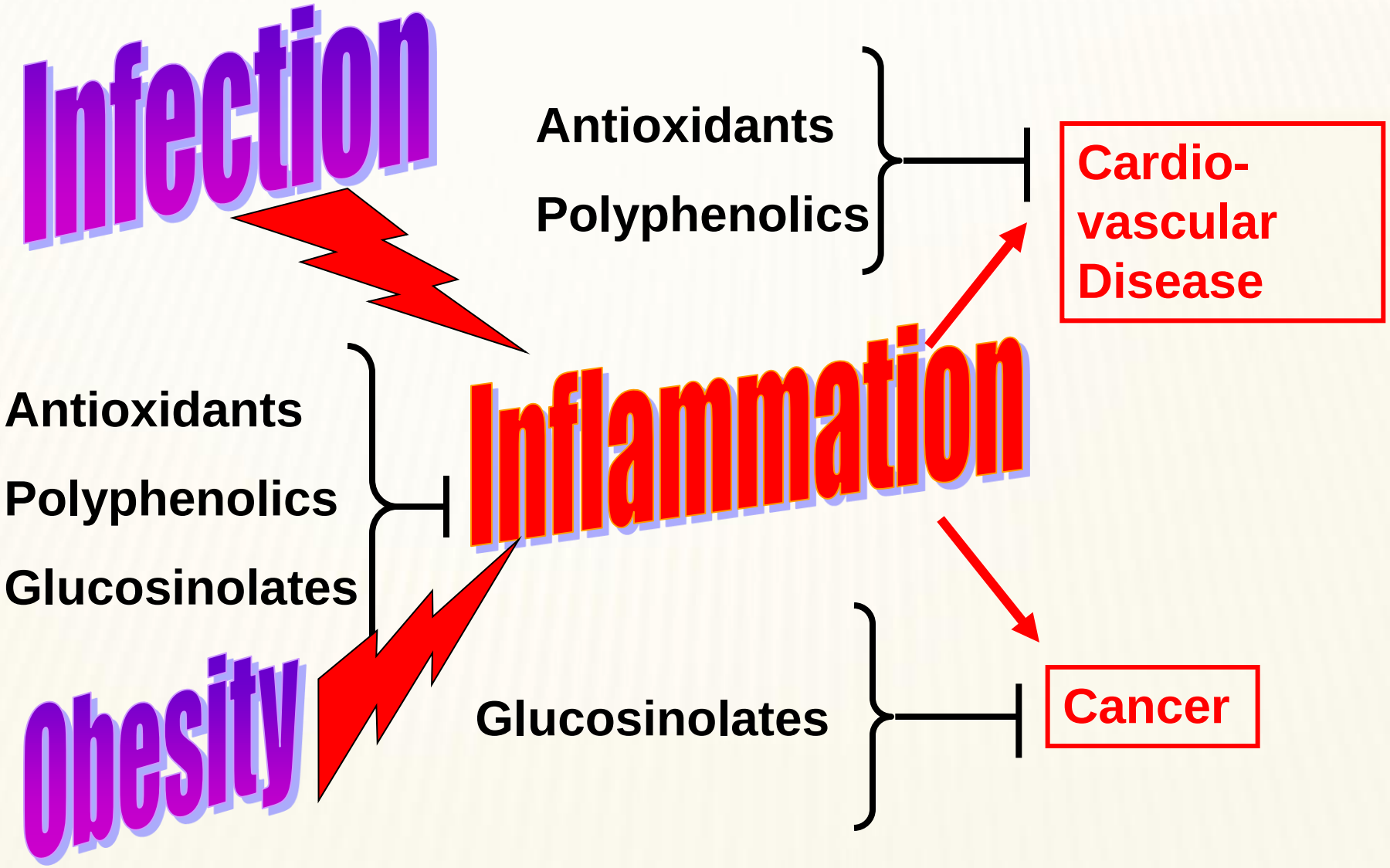
P=0.001

Cornelis et al, 2007

Inflammation may be a common factor



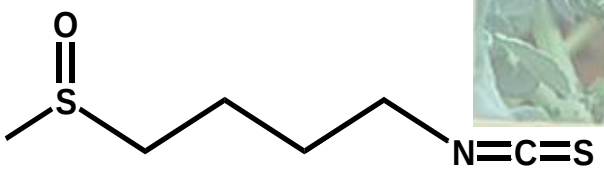

Infection
aging
Antioxidants
Polyphenolics
Glucosinolates
Inflammation
Antioxidants
Polyphenolics
Glucosinolates
Cardio-
vascular
Disease
Cancer

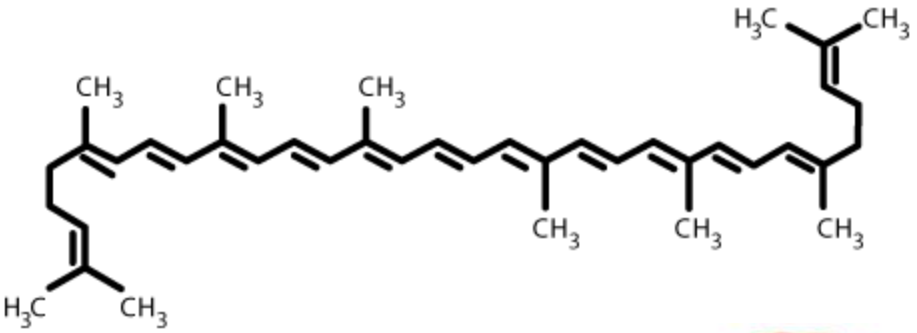

Infection
Antioxidants
Polyphenolics
Cardio-vascular Disease
Antioxidants
Polyphenolics
Glucosinolates
Inflammation
Obesity
Glucosinolates
Cancer

OBESITY: A "GROWING" CONCERN

OBESITY: A "GROWING" CONCERN

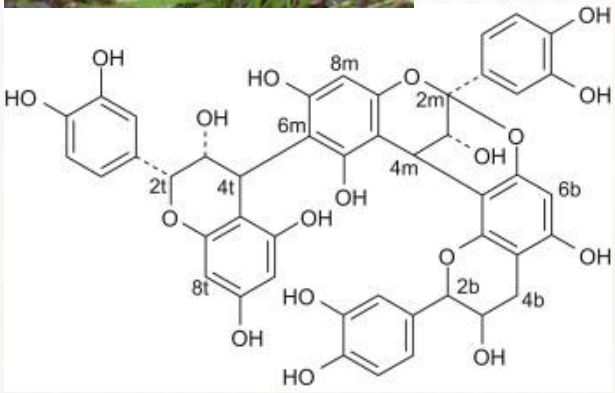
- ~ 1 in 4 dogs and cats seen by practitioners are overweight or obese. Yet, many pet owners do not realize that their pets are overweight or at risk for health problems.
- **Omega-3, crucifers to fight inflammation**
- **Lower-fat, lower-calorie, higher fiber diets**.
- Experimental rats fed "ad libitum" are also fat.



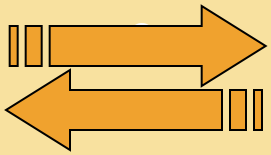


whole foods

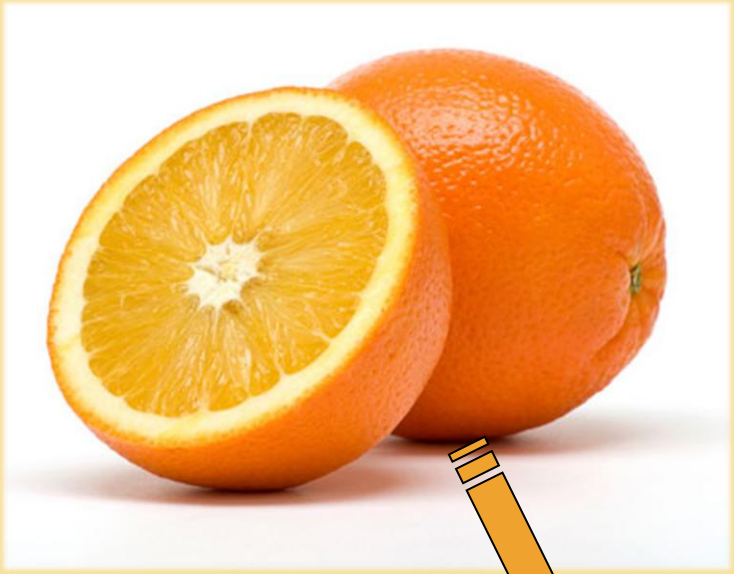
or supplements?



A typical orange contains about 70 mg vitamin C



Recommended Dietary Allowance



Polyphenolics/ Antioxidants

other healthful compounds ?

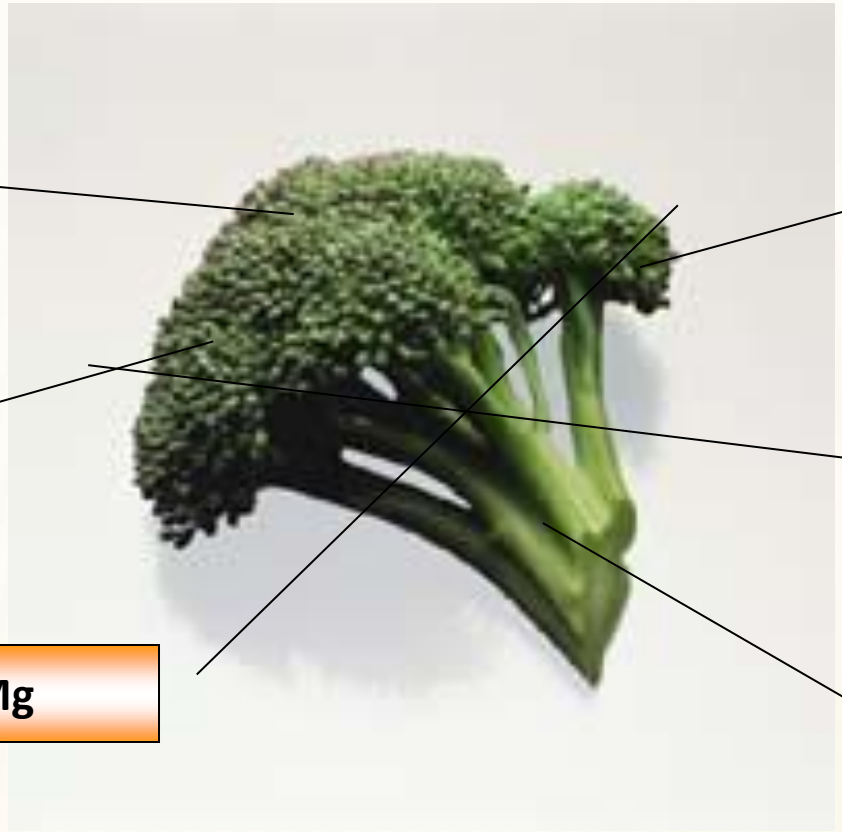
Cruciferous veggies also contain nutrients and other phytochemicals/ bioactives

Nutrients

Vitamins A, C, E, folate

Fiber

Minerals:Ca, Mn, Mg



Bioactives

glucosinolates

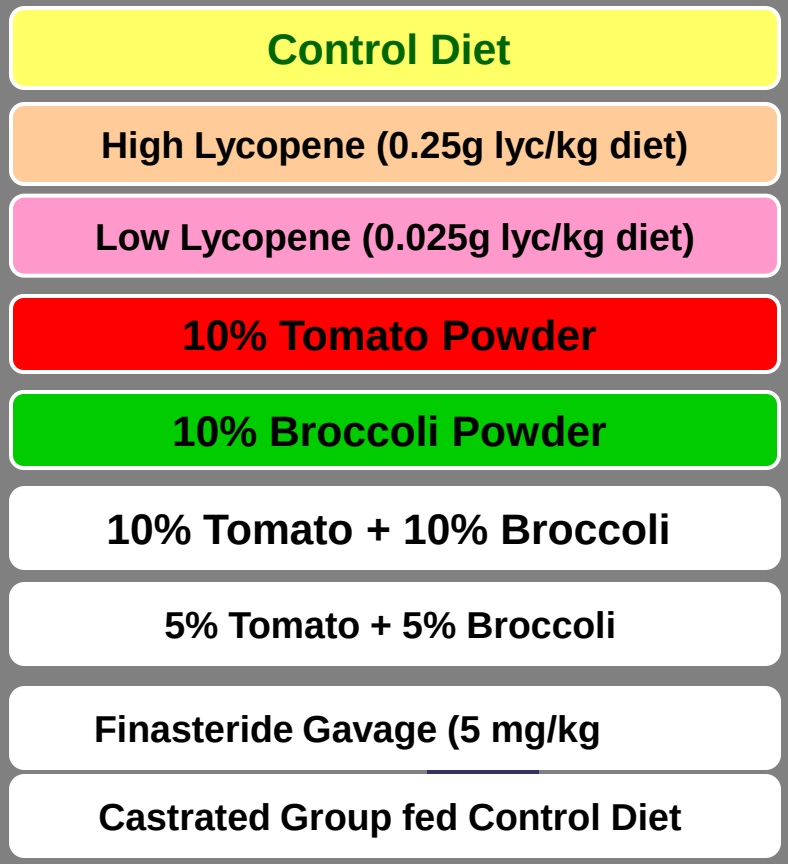
Polyphenolics/ antioxidants

Selenium

Nutrients: for growth & development

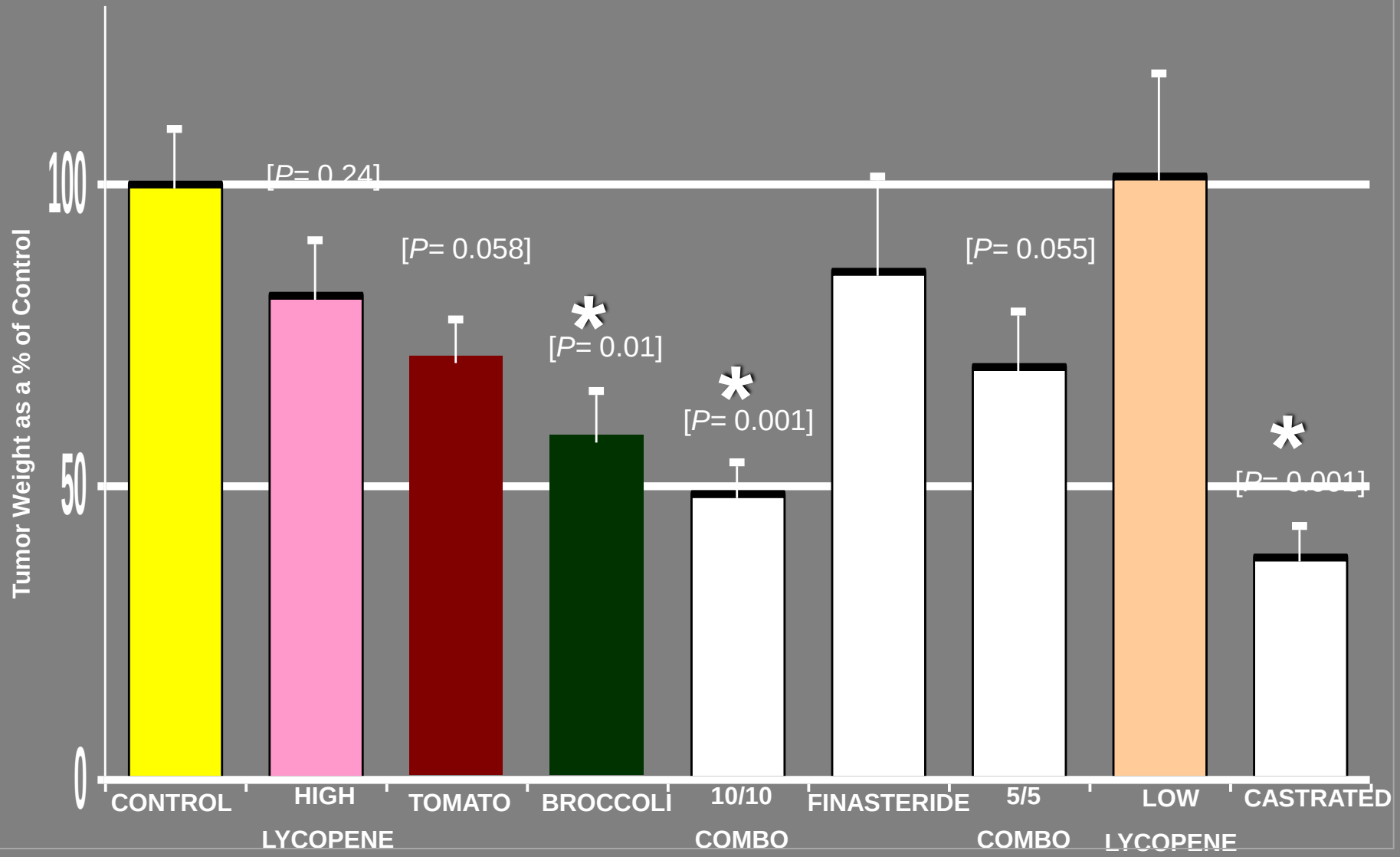
Bioactives: to slow or reverse chronic disease

Effect of feeding whole broccoli, tomato or purified lycopene on rat prostate cancer



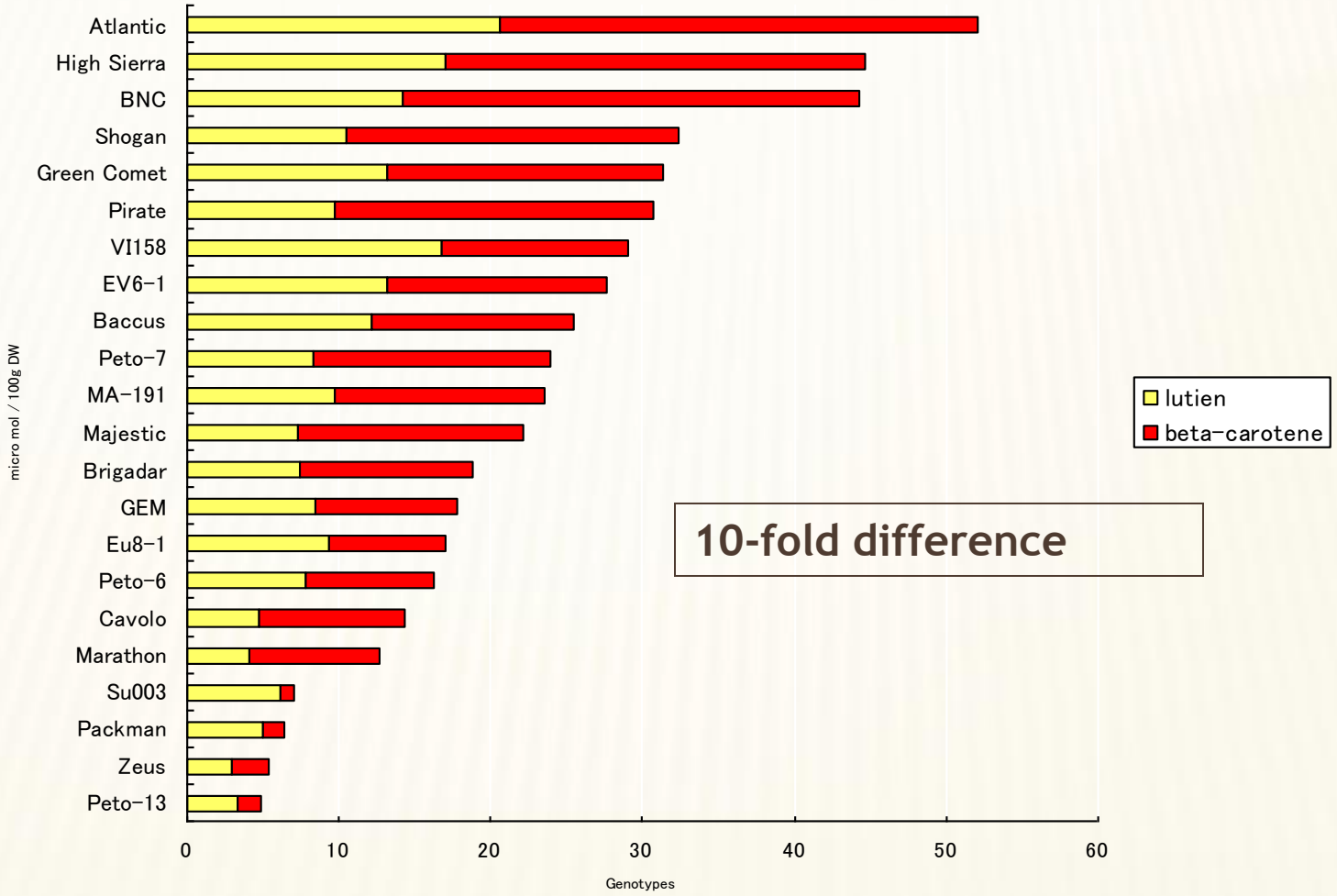
Canene-Adams et al, 2007

Prostate Tumor Weights



P values indicate statistical difference from the control tumor weights.

CAROTENOID CONTENT, 22 BROCCOLIS



Means of carotenoid contents in 22 different broccoli genotypes (μmol/100g DW)

Opportunities and Challenges with Whole Foods

- Less costly for inclusion in food products
- Less likely problems with stability, bioavailability or even safety

- **Variability in content: to control, development involves plant science**
- **Confirming content: development of analytical methods and standards**

Opportunities and Challenges with Purified Components

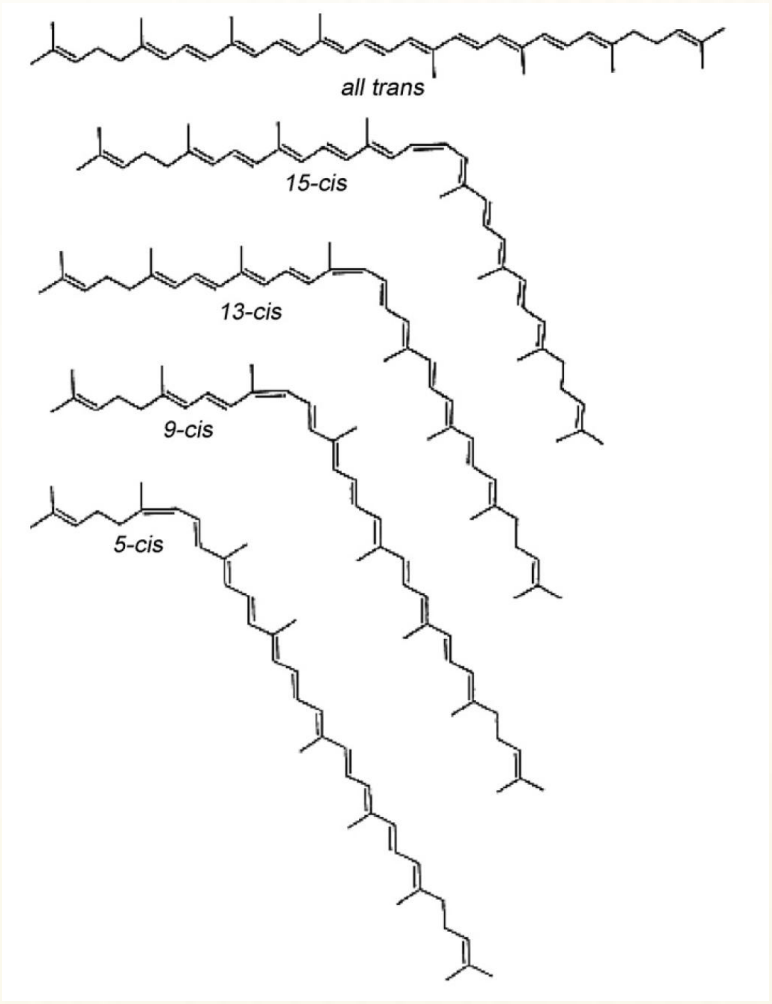
- Once bioactivity is characterized, may be added to many foods and/or be sold as a dietary supplement
- Product content can be standardized

- **Development of cost-effective purification**
- **Development of product with good shelf life, flavor attributes**
- **Determine safety and bioavailability**

Impact of processing on bioavailability of dietary components

- Processing is a bad word today –
  - -Sometimes it helps bioavailability
  - -Sometimes it destroys some nutrients
  - -Sometimes it destroys needed cofactors

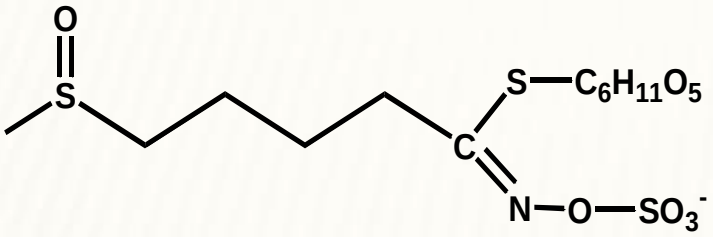
Thermal processing of tomatoes causes some lycopene to be in the cis form, which is more readily absorbed



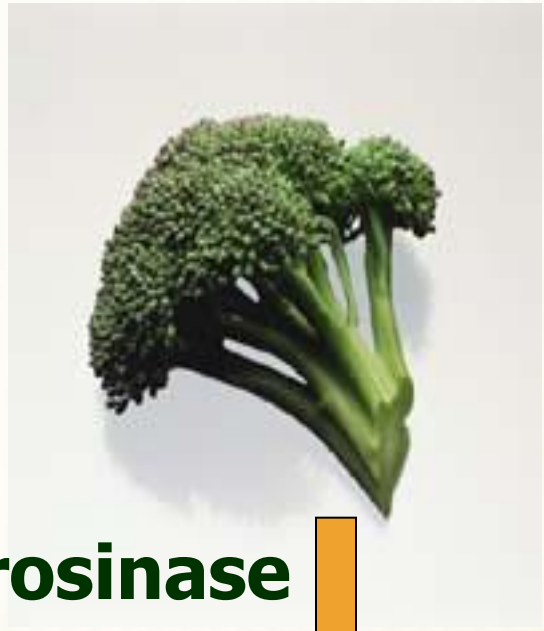
Impact of processing on bioavailability of dietary components

- Processing is a bad word today –
  - -Sometimes it helps bioavailability
  - -Sometimes it destroys some nutrients
  - -Sometimes it destroys needed cofactors
- 'Raw Food' is a fad today -
  - – Sometimes even key nutrients are not as available in raw food, since heat improves digestibility
  - – Sometimes raw improves bioavailability but increases risk of bacterial contamination

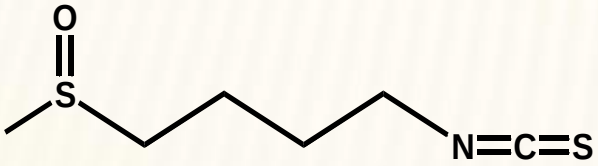
Glucosinolates are metabolized to ITC when plants are crushed or chewed



Glucoraphanin



Myrosinase



Sulforaphane

ITC

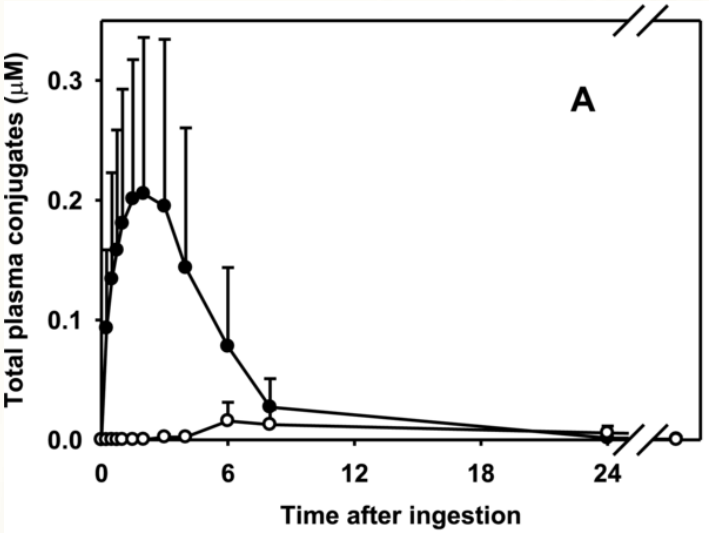
Isothiocyanate

Anticarcinogen

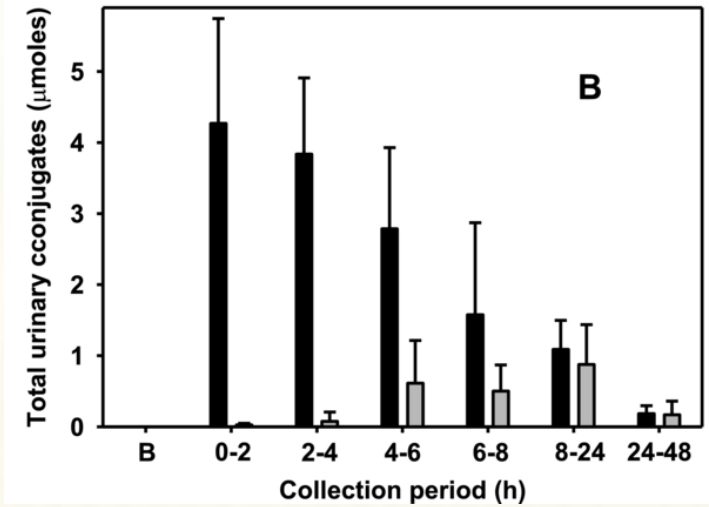
Sulforaphane and metabolites are found in plasma & urine after ingesting cooked broccoli, but very little compared to fresh broccoli.

Fresh: Closed circles and bars

Cooked: Open circles and bars



Plasma sulforaphane

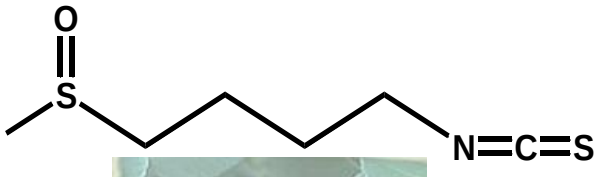


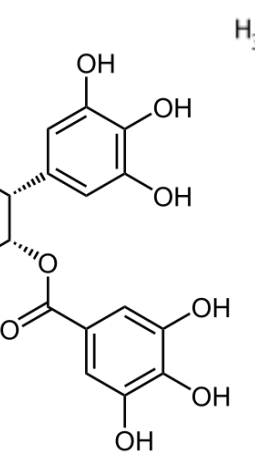
Urinary sulforaphane

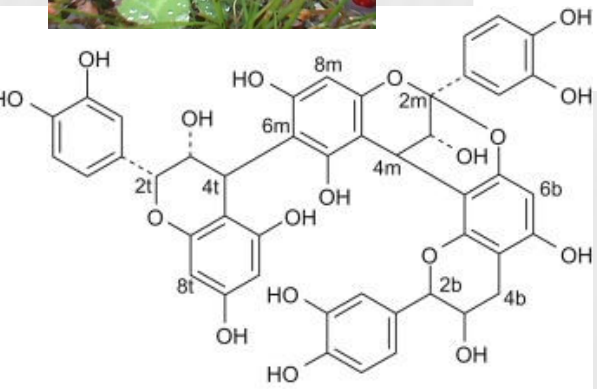
Molecular Nutrition & Food Research
Volume 56, Issue 12, pages 1906-1916, 27 OCT 2012 DOI: 10.1002/mnfr.201200225
http://onlinelibrary.wiley.com/doi/10.1002/mnfr.201200225/full#mnfr1856-fig-0002

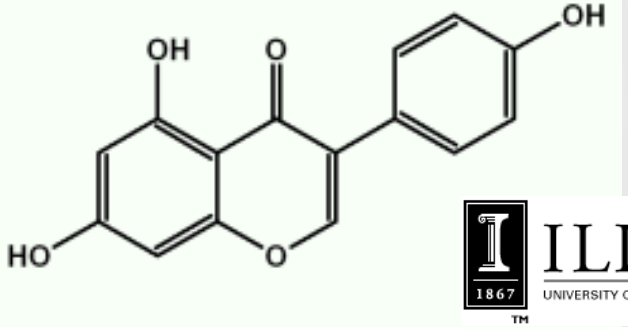
Saha et al, 2012

Addressing the Bioavailability of Bioactive Food Components









ILLINOIS
UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN

Factors affecting bioavailability

BFC in plant (glycoside)

Digestion/
Hydrolysis

Thioglycosides in crucifers are hydrolyzed **by the plant**

A few O-glucosides of flavonoids are hydrolyzed by **mouth enzymes**, many by **gut wall enzymes**[1]

BFC in gut (aglycone)

Microbiome can hydrolyze[2], but may also metabolize

Absorption

Metabolism

Secretion

Enterocytes and Hepatocytes support methylation, sulfation, glucuronidation, GSH conjugation

Efflux: Multidrug resistance proteins, enterohepatic recirculation

Plasma BFC (and metabolites)

[1]Lactate phlorizin hydrolase [2]beta glucosidase

BFC in plant (glycoside)

Digestion/
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Methylation, sulfation, glucuronidation, GSH conjugation

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Plasma BFC (and metabolites)

Microbiota hydrolyze and metabolize

Hydrolysis can form aglycones, often more bioavailable, often more active.

Metabolism can form new compounds that
- may have new, beneficial activities
- may lose the activity of the parent compound

Knowledge of metabolism by microbiota may permit the use of
- prebiotics, probiotics, antibiotics
- modified bacteria

to improve health directly, or by impacting the health benefits of BFC

INTESTINAL MICROFLORA

10^{14} micro-organisms, >500 differentes species

Stomach 10^2 to 10^3

Lactobacilli

Duodenum

Streptococci
Lactobacilli

Jejunum

$<10^{4-5}$

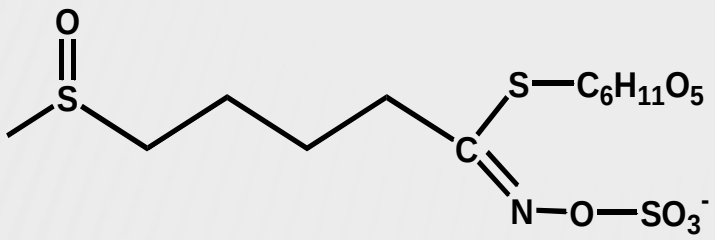
Enterobacteria
Enterococcus
Faecalis
Bacteroides
Bifidobacteria
Peptococcus
Peptostreptococc
Ruminococcus
Clostridia
Lactobacilli

Ileum 10^3 to 10^7

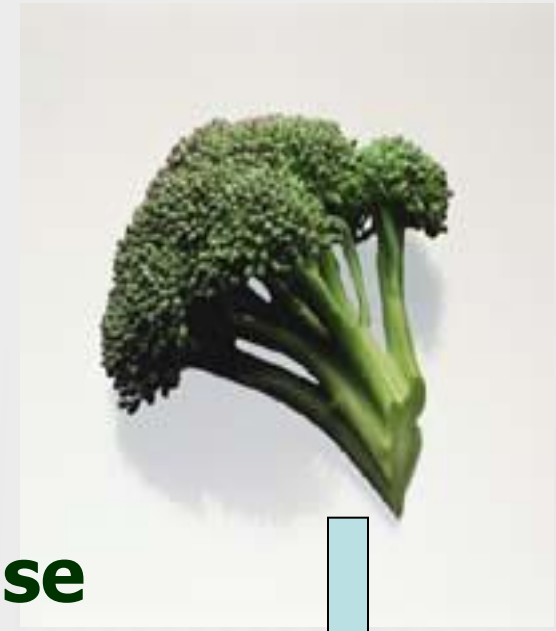
Colon with appendix 10^9 to 10^{12}

and....

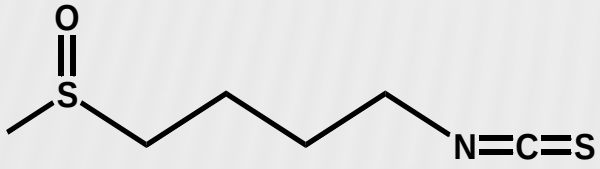
Can gut microbiota release anticarcinogenic isothiocyanates from heat processed broccoli ?



Glucoraphanin



Myrosinase (plant enzyme)



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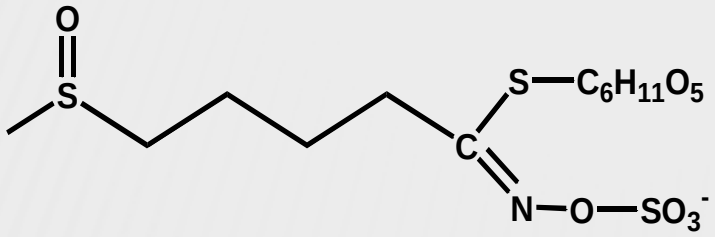
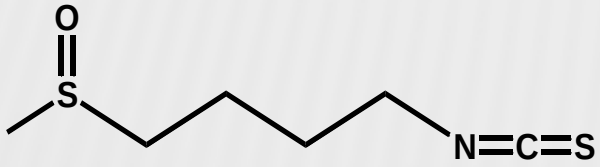


Glucoraphanin

Gut Microbiota?

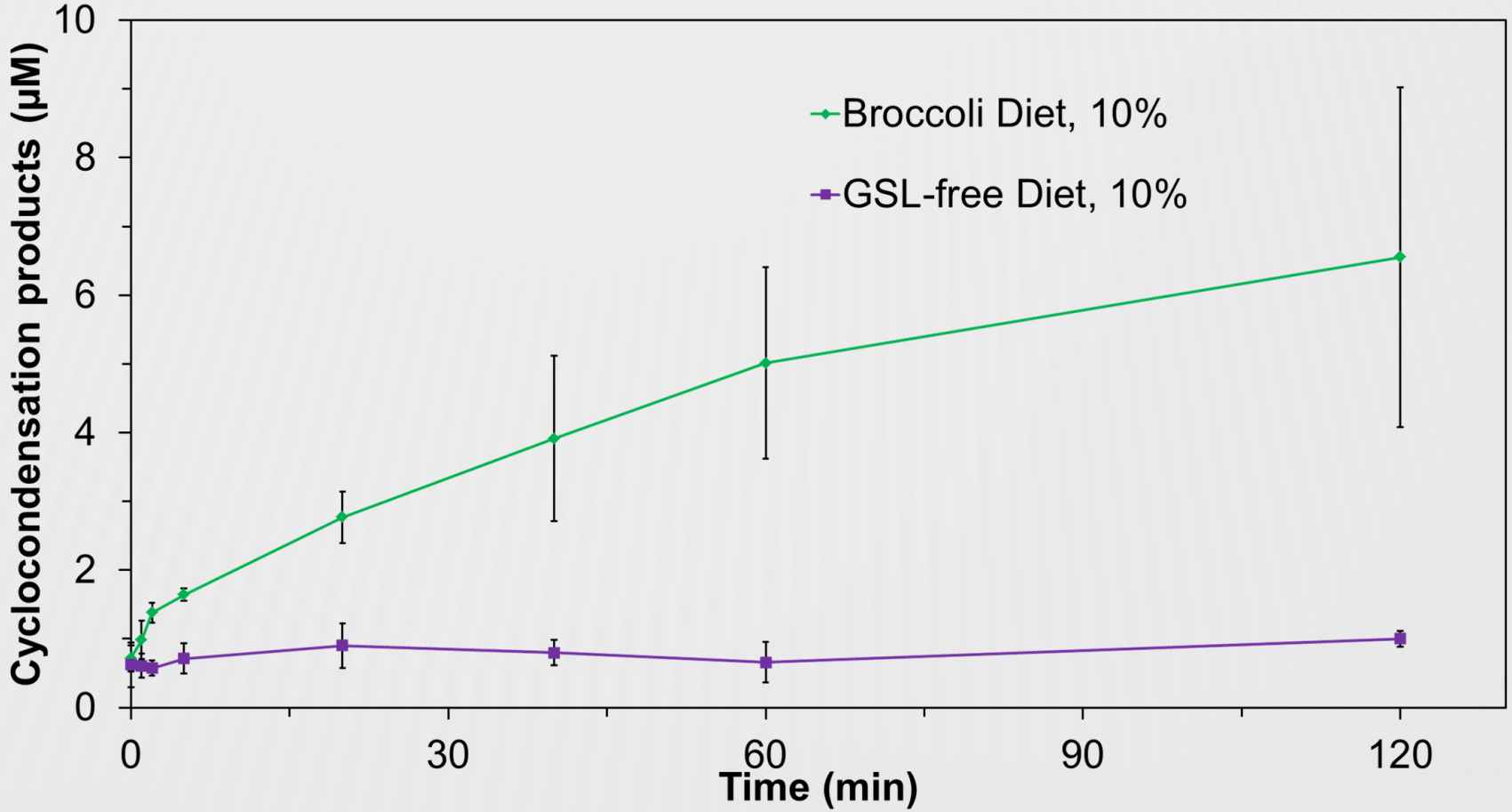


Sulforaphane

ITC

Isothiocyanate
Anticarcinogen

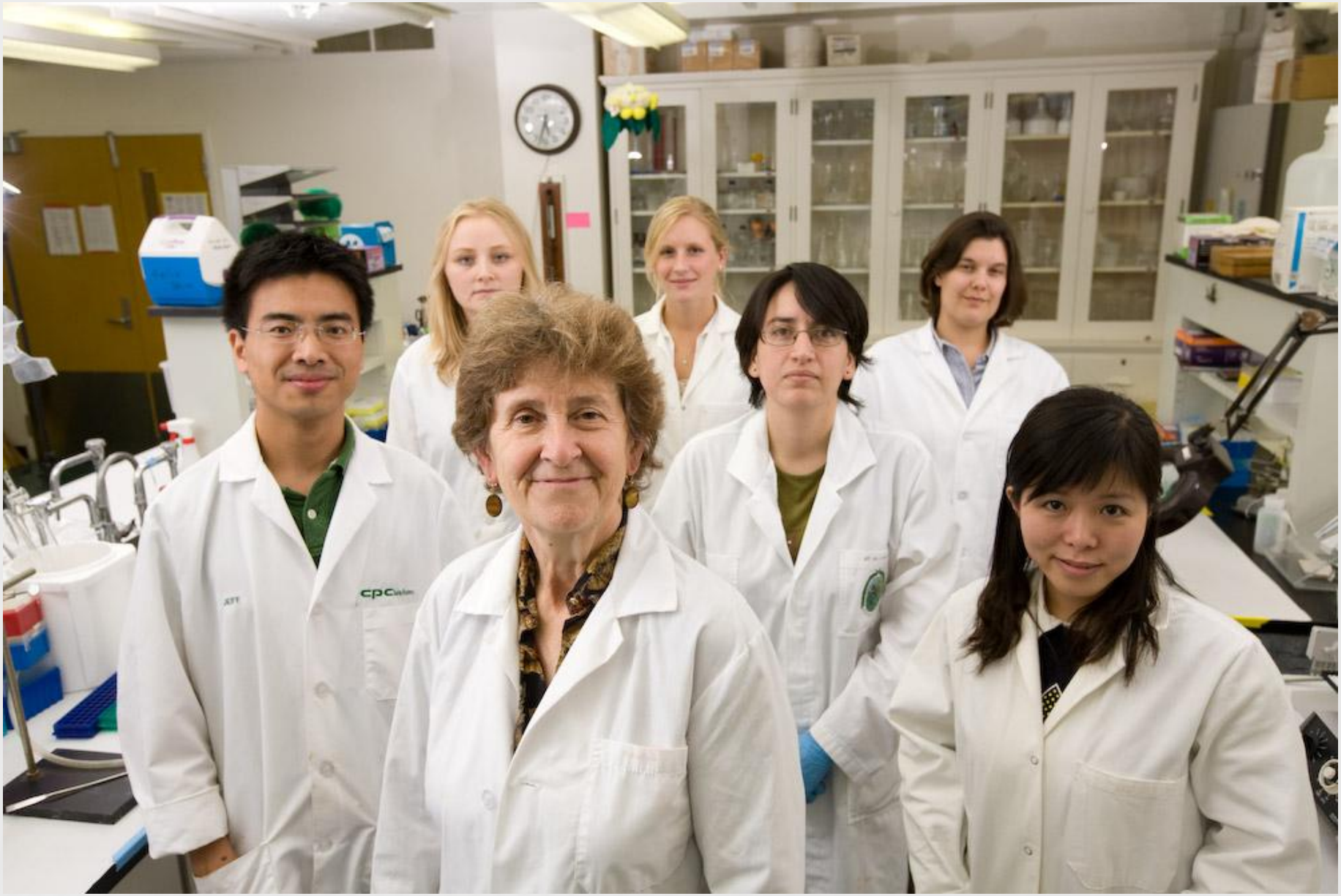
Metabolism of glucoraphanin by rat cecal microbiota ex vivo from rats fed a 10% broccoli diet for 1 week



Microbiota and bioavailability of health-promoting food components

TAKE HOME

- Fruits and vegetables are a great source of vitamins, minerals and phytochemicals.
- Phytochemicals slow or decrease risk for many chronic diseases, particularly through quenching inflammation.
- Advertised antioxidant levels don't always indicate antioxidant effects in the body, but they usually mean there's something good for health in there.
- Bioavailability studies on the product are essential



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