

Inflammation

The Main Etiological Factor in
Most, if not All Disease

Dr. Christopher Hobbs, Ph.D., L.Ac., A.H.G.

Chronic Inflammation is a Silent Public Health Crisis

Top Killers

1. Heart Disease
2. Cancer
3. Lung disease
4. Strokes
5. Accidents
6. Alzheimer's disease
7. Diabetes
8. Flu and Pneumonia
9. Kidney Disease
10. Suicide



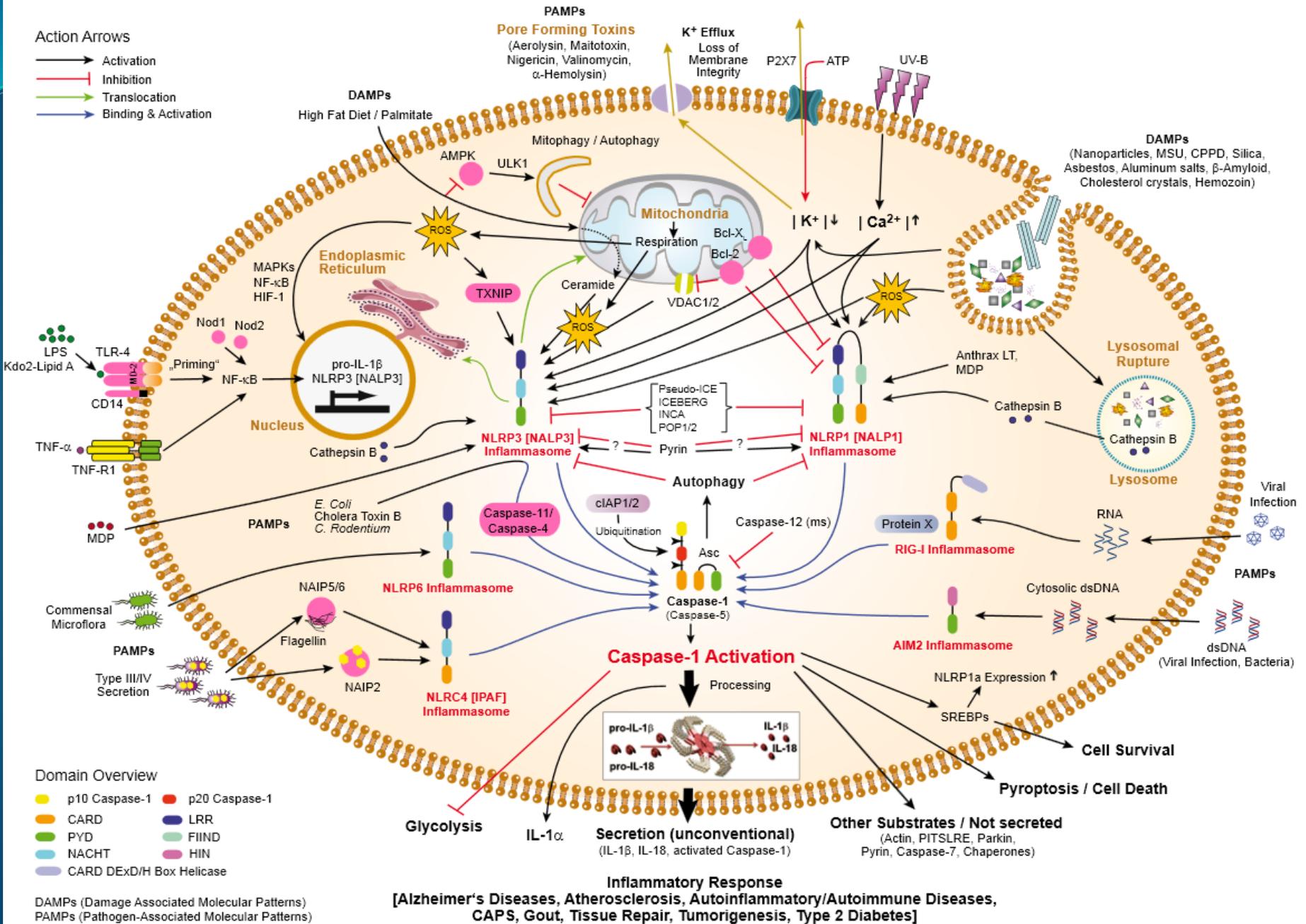
Inflammation and the Inflammasome

Innate Immune Response

- Inflammasome, cellular orchestrator of inflammation
- Multi-protein oligomer
- Expressed in myeloid cells (progenitor of cells of the innate immune system like granulocytes, platelets)
- Caspase (1, 5, 11 and others) are first response signals
- Exact nature and action of the inflammasome depends on initiators (viral, bacterial, cholesterol crystals, asbestos, high-fat diet, etc.)
- End cellular products are cytokines (IL-1beta, IL-18, etc.)
- Mediators = our innate microflora, many dietary factors

Action Arrows

- Activation
- ⊥ Inhibition
- Translocation
- Binding & Activation



Domain Overview

- | | |
|----------------------------|-----------------|
| ● p10 Caspase-1 | ● p20 Caspase-1 |
| ● CARD | ● LRR |
| ● PYD | ● FIIND |
| ● NACHT | ● HIN |
| ● CARD DExD/H Box Helicase | |

DAMPs (Damage Associated Molecular Patterns)
PAMPs (Pathogen-Associated Molecular Patterns)

More about the Inflammasome

- Inflammation as an innate protective response is ancient, and fundamental to many animals
- A number of different kinds have been discovered
- Once active, they carry out and orchestrate processes like induction of natural killer cell activity, cell pore formation (facilitating communication between cell types, and alterations of signaling molecules)
- Formation of tissue repair mediators
- Formation and activation of ligand-recognition (of pathogenic ligands) receptors
- Sensitizes immune effector cells to pathogens, harmful chemicals, etc.

Features of Inflammation

- Acute or chronic
- Orchestrates immune response to pathogens, tissue damage and then removal of wastes
- Alters blood flow, vessel permeability, and many other processes
- Pattern-recognition receptors
- Pathogen-associated molecular patterns
- Migration of leukocytes (macrophages, neutrophils)
- Several other parallel cascades also initiate and promote inflammation (complement, etc.)
- Other mediators = histamine, Leukotriene B4, nitric oxide (NO), prostaglandins, tumor necrosis factor, others

Further--

- Nutritional deficiency can promote chronic inflammation
 - Vitamin A
- Cancer—inflammation produces and alters environment around tumors that contribute to proliferation, migration, metastasis
- Inflammation is shut down by several pathways and mediators such as Resolvins, Protectins, Maresins, some derived from omega-3-polyunsaturated fatty acids
- Obesity and fat cells are modern drivers of inflammation (IL-6,

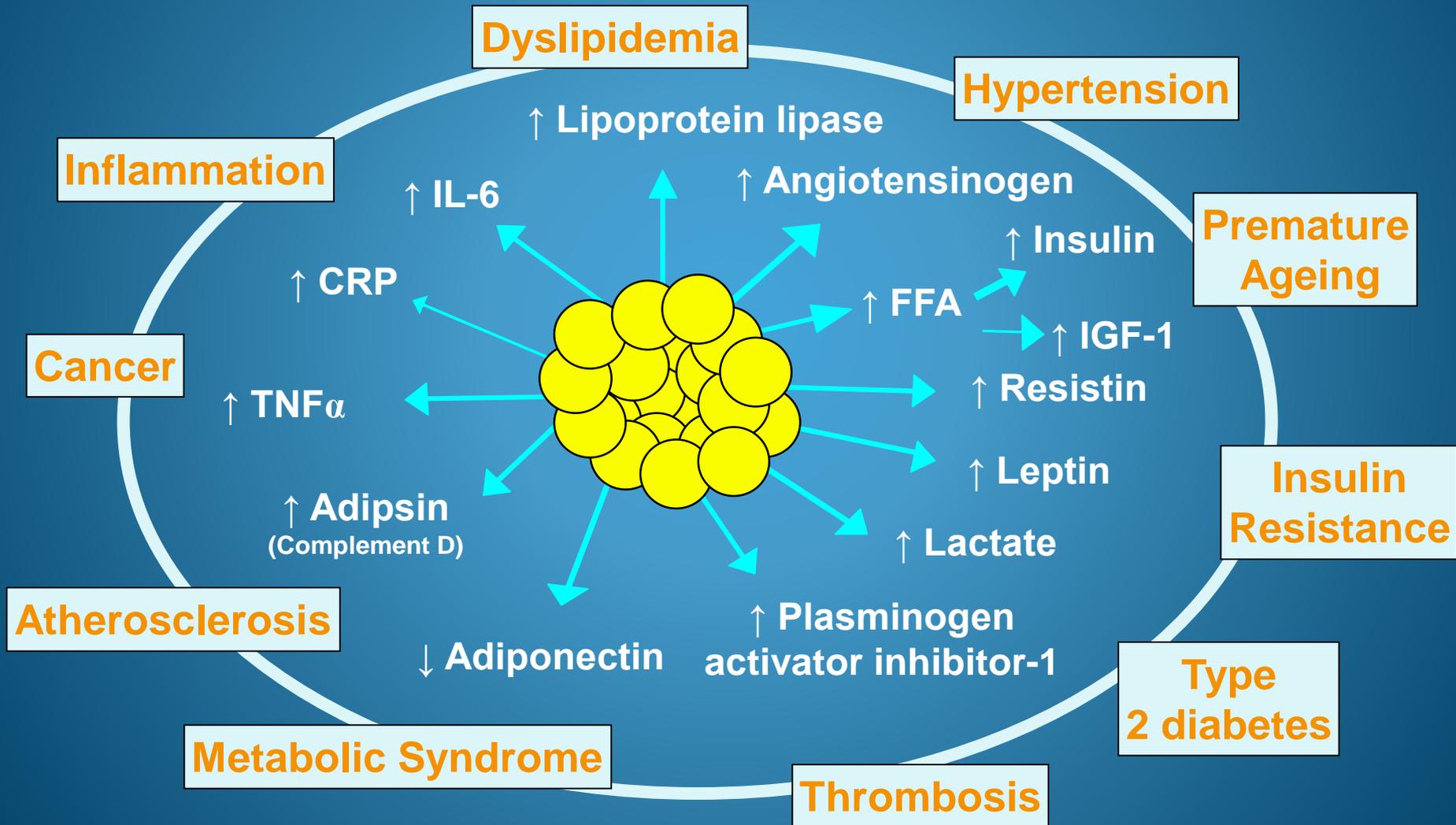
Inflammation and Obesity

- Waist circumference is significantly associated with systemic inflammatory response
- Low-grade chronic inflammation = 2-3 x increase in inflammatory mediators
- Elevated markers associated with obesity-associated inflammation
 - IL-6, IL-8, IL-18
 - TNF-alpha
 - CRP
 - Insulin, insulin-growth factor, blood glucose
 - Leptin

Inflammatory Disease & Obesity

- Obesity, a Chronic metabolic disease
- Adipocyte, fat cell toxicity
 - Releases toxic substances as we gain weight
 - Inflammatory protein signals: Hormones, cytokines
 - FFA's, lipid and cholesterol oxidation, Atherogenic
 - Fuels insulin resistance and beta cell dysfunction
 - Energy storage disease and energy overload
 - Inflammation and metabolic derangement
 - **Dietary carb's the trigger, not dietary fats**

Obesity: A Chronic Metabolic disease



How to Diagnose Inflammation?

- How to identify pro-inflammatory markers to address the root of the problem early, before chronic disease states or pain take hold
- Common signs of inflammation:
 - Impotence (beginning vascular disease)
 - Memory changes/muddled thinking
 - Ringing in the ears
 - Swelling, pain, fatigue, myalgia
 - Chronically sore gums, gum disease, deep “pockets”
 - Sore joints, arthritis
 - Heart disease, lupus, liver disease, diabetes



Inflammation and Traditional Medicine

- Traditional Chinese Medicine (TCM)
 - Long history of understanding inflammation as root cause to disease
 - False & true heat
- Diet, Herbs, Acupuncture
- “Drain the heat”
- “Tonify”



“True Heat”

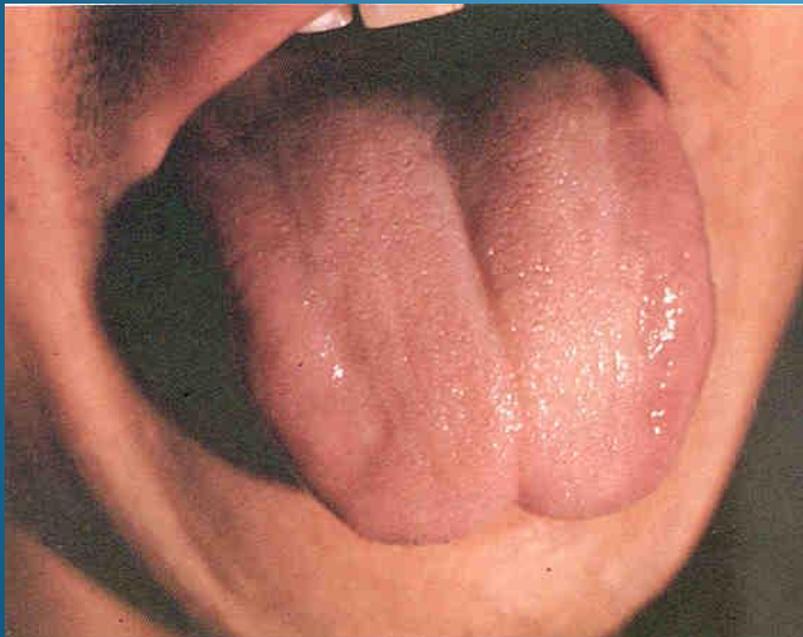
- Thick yellow coat
- Full, fast pulse
- Typically worse when young



“False Heat”

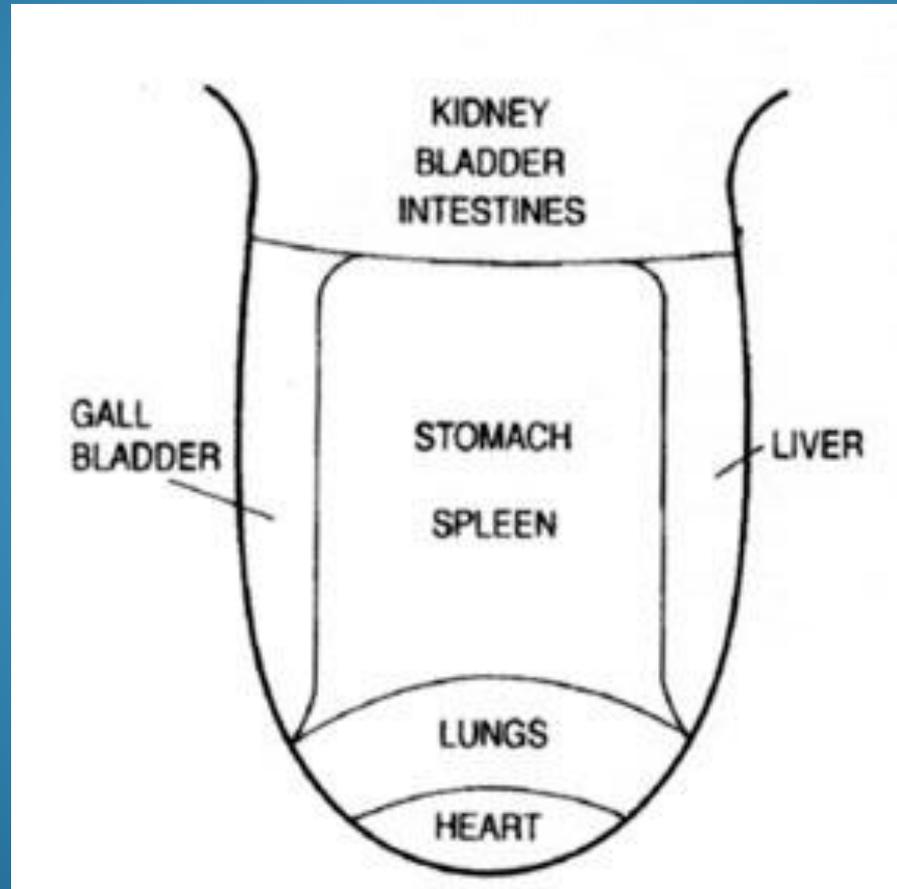
- “Peeled,” red tongue body
- Little or no coat
- Chronic condition
- Worse when older

Normal Tongue



- Good “spirit” (shen)
- Few cracks, even surface
- Thin white, rooted coating
- Not swollen or shrunken
- Not too red or pale (uniform pinkish red)
- No scallops on edges
- Not too dry or wet
- Free of red dots

Tongue Map



Sources of Chronic Inflammation

- Poor lifestyle choices
 - Tobacco abuse
 - Excessive alcohol consumption
 - Unhealthy diet, especially added sugar!
 - Limited exercise
 - Obesity (fat cells – inflammation)
- Environmental exposure
- Genetic factors
- Natural process of aging
- Overeating—big meals (recent research)



Western Medical Treatment for Pain and Inflammation

- Pharmacological
 - Analgesics
 - Non-steroidal anti-inflammatories (aspirin, ibuprofen, naproxen)
 - Opioid analgesics (morphine, hydrocodone, oxycodone)
 - Non-opioid analgesics (Acetaminophen, ibuprofen)
 - Muscle relaxants (cyclobenzaprine)
 - Steroids (cortisone)

- Also surgery, physical therapy

Pharmacological Effects of NSAIDs

- All inhibit cyclooxygenase
- Inhibition of prostaglandin (PG) synthesis is responsible for their therapeutic effects
- Inhibition of PG synthase is responsible for side effect (i.e. in gastric mucosa → GIT damage resulting in dyspepsia, gastritis)

The mechanisms of NSAIDs

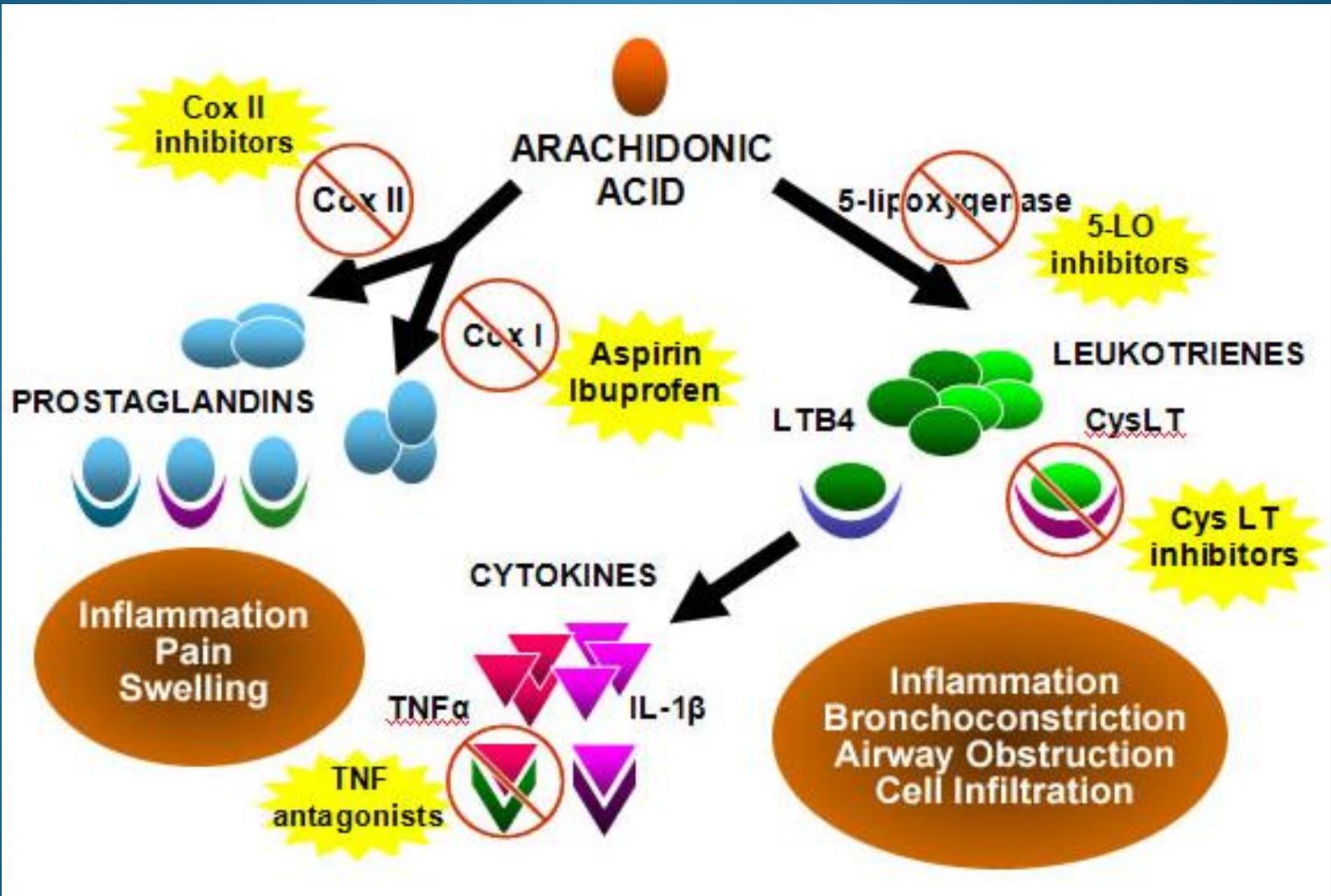
- NSAID inhibition of PG production alleviates most of the pathologic effects associated with inflammation, but it also interferes with the physiologic role of these molecules
- Consequently, long-term therapy with nonspecific NSAIDs is frequently limited by their adverse effects, particularly those caused by erosion of gastric mucosal protection

Can lead to GI bleeding

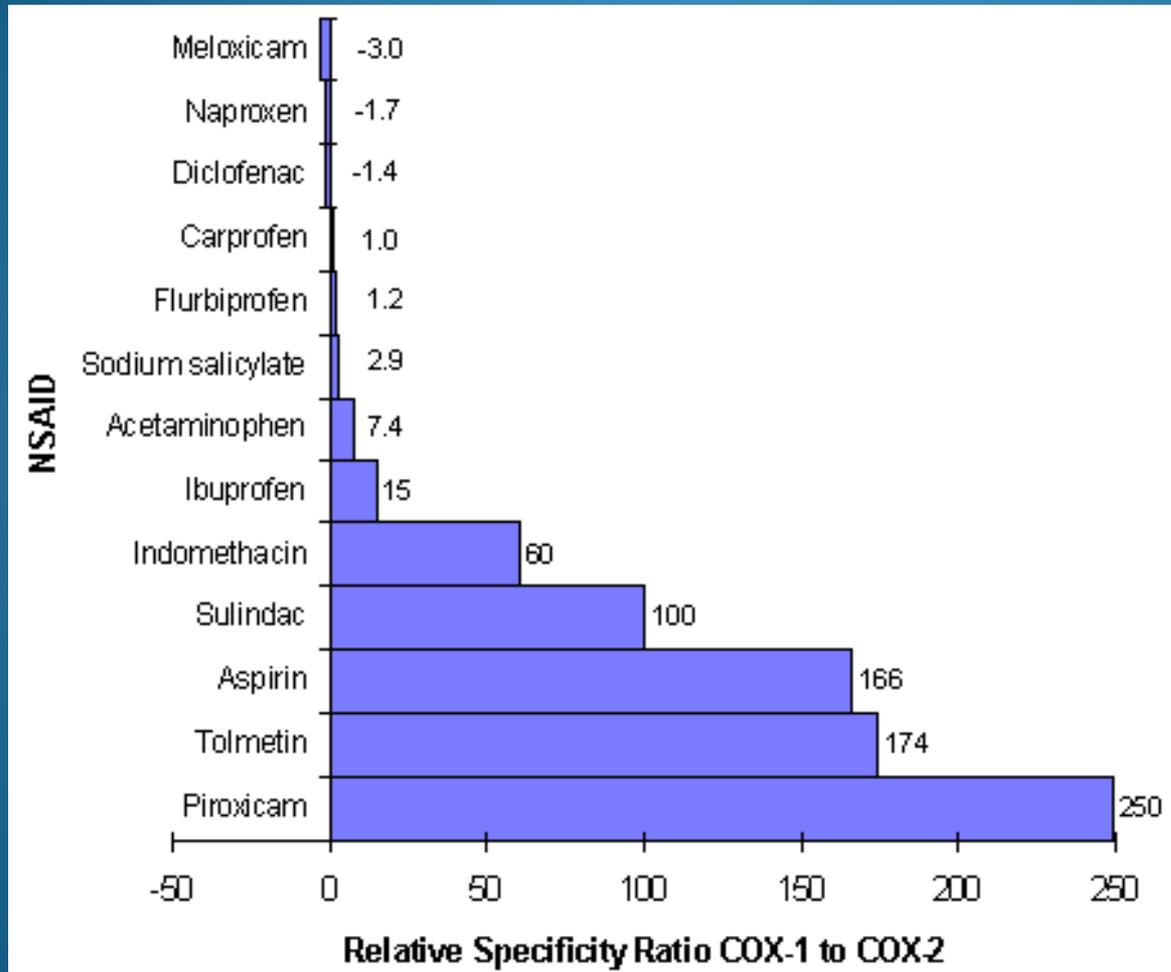
Cox-1, Cox-2 Inhibition

- Two different isoforms (chemical derivatives) of the enzyme cyclooxygenase
- Important to reduce Cox-2 production while not affecting Cox-1
- “Cox-2 specificity” – Cox-1/Cox-2 ratio
 - Aspirin = 0.6 (greater GI distress)
 - Curcuminoids = 3.0
 - Accepted Cox-2 specificity to reduce GI upset = 5.0
 - Hops extract = 29.5 (combinations of turmeric + hops)

Arachidonic Acid Pathways



Cox-1/Cox-2 Specificity, Drugs



Cox-2/Cox-1 Ratio, Botanicals

- Cox-1 and -2 inhibitory potency and selectivity of 17 botanicals (J Clin Nutr, 2004)
- Caco-2 cell line with ibuprofen as an active control
- Hops extract high in alpha acids, showed a Cox-2/Cox-1 IC50 selectivity ratio of 0.06, compared to 4.2 (15) for ibuprofen
- Hops powder or hops resin extract produced a 9-hour Cox-1 / Cox-2 AOC ratio of about 0.4 (i.e., some degree of Cox-1 sparing), compared to 1.5 for ibuprofen (i.e. no Cox-1 sparing).
Conclusion: Hops exhibited Cox-2 inhibition over 9 hours equivalent to ibuprofen 400 mg but had significant Cox-1 sparing activity relative to ibuprofen.

Black Box Warning on all NSAIDs

Common Reactions:

- GI upset and pain
- Nausea
- Fluid retention
- Constipation



Severe side effects that can damage multiple organs:

- GI bleeding
- GI ulceration/perforation
- Cardiovascular damage
- Kidney damage
- Liver damage
- Blood cell damage

Natural Treatment Options for Chronic Pain and Inflammation

Natural therapies are a great first intervention

- Herbal Medicine for pain and inflammation was practiced for many centuries in all systems of traditional healing—for instance **turmeric** and **ginger**
- Antioxidant supplements and antioxidant-rich fruits and vegetables (raw or lightly cooked)
- Omega-3 family Fatty Acids
 - Alpha-linolenic acid (ALA), gamma-linolenic acid (GLA), **EPA, DHA**
- Proteolytic enzymes (**bromelain**, papain)
- Manual therapies – acupuncture, massage, cranial sacral therapy, chiropractic
- Yoga, therapeutic exercises

And of course, Diet

- Without belaboring the point, these are pro-inflammatory:
 - Overeating (new research), obesity, metabolic syndrome
 - Added sugar to drinks, foods
 - High-fat diet
 - Insulin and insulin-binding, insulin growth factor
 - Stimulants (caffeine, etc.)
- Reduces chronic inflammation
 - Intake of spices (i.e. ginger, turmeric)
 - Mediterranean diet, raw foods, fasting (flavonoids, OPCs)
 - Light meals

Herbal Medicine and Inflammation

Medical Research Validates Herbal Therapies

- Numerous clinical trials now support the traditional use of many herbal remedies
- A careful review of the scientific and traditional literature is necessary to determine the most effective and safe uses
 - Database searches, full-text articles
 - Determination of effective types of extracts, active constituents
 - Absorbability of active constituents (pharmacokinetics)
 - Proper dose that follows clinical trials
 - Length of supplementation
 - Safety

Most-Researched Herbs for Inflammation

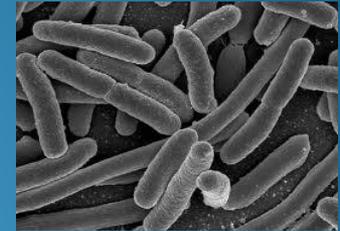
- Turmeric (curcumin)
- Pineapple (bromelain)
- Papaya (papain)
- Frankincense (Boswellia)
- Hops (hops bitter acids)
- Buckeye (escin)
- Onions, apples, berries (quercetin)
- Anthocyanins (berries, etc.)
- Willow bark extract (salicin)
- Berberine-containing herbs



In Regards to Products

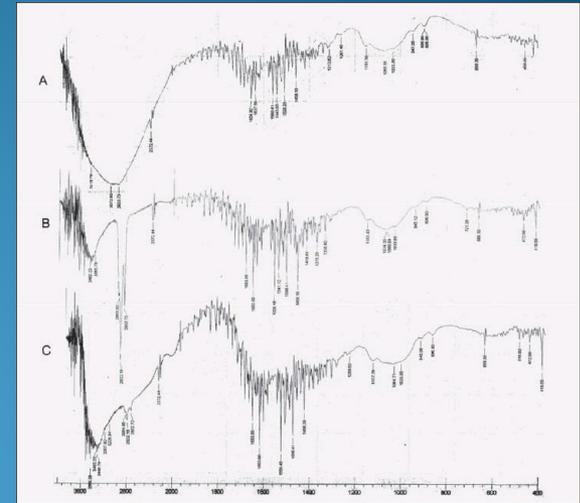
Drugs and Toxins Contribute to Inflammation

- Research shows toxins, contaminants, bacteria are implicated in systemic inflammation
- Purity of herbal products important
 - Microbial activation of immune response and inflammation
 - Heavy metals
 - Pesticides, herbicides
 - Substitution with toxic herbs (Aristolochia as an example)
- Testing and some form of standardization is essential for ensuring effectiveness and safety of all herbal products
- Test frequently!



Testing and Authentication Methodologies

- Purity tests conducted using ICPMS (Inductively Coupled Plasma Mass Spectrometry) methodology
 - Guarantees herbs to be free of most common heavy metals
- HPTLC (High Performance Thin Layer Chromatography) is the gold standard of herbal authentication
- For identity—DNA (next-gen sequencing)



FTIR Identification



HPTLC Authentication

Methods of Extraction besides tinctures

Pressure Vessel Extraction based on the Tea Method

- Uses only pure water as the solvent – the most effective solvent for the broadest range of plant constituents!
- Whole plant tea extract provides full spectrum plant constituents
- Over 2,000 years of applied history and science that ensure both efficacy and safety

Other extraction processes such as the Supercritical CO2 process or alcoholic extraction can be used for specific herbs

- Examples include Supercritical CO2, a cold-extraction process for extracting delicate fatty acids from saw palmetto



Pressure Vessel Extraction

Boswellia



- Frankincense in the bible, used as a spice for many centuries
- Boswellic acids shown to inhibit inflammation – In vitro, in vivo studies and clinical trials
- Clinically-effective in 47 clinical trials– patients with asthma, rheumatoid arthritis, Crohn’s disease, osteoarthritis, and colitis (studies vary in quality)
- Seven of these trials were controlled, and all showed positive effects

Curcumin



- Curcumin inhibits inflammation via 6 distinct pathways—most hotly researched ingredient
- Down-regulates activity of COX-2, lipoxygenase, iNOS enzymes, inhibits inflammatory cytokines TNF-alpha, interleukins (Jurenka, 2009)
- In vivo studies show benefits for models of ulcerative colitis, rheumatoid arthritis, osteoarthritis, cancer, etc.
- Pilot controlled studies and Phase III, IV clinical trials—many underway
 - Cancer prevention (many)
 - Arthritis (OA, RA), ulcerative colitis, IBS
- Liver metabolism limits bioavailability—piperine or phosphatidylcholine-curcumin complex

Hops



- Traditionally used by clinical herbalists to ease insomnia and infections
- Widely used to give beer and ale a bitter taste, stronger effects
- Some beers and ales contain up to 100 mg/L bitter hops acids
- Non-alcoholic beers show similar cardio-protective effects to alcoholic beers (Clausthaler)
- Nine in vitro and in vivo studies demonstrating anti-inflammatory and anti-cancer effects

Proteolytic Enzymes Address Inflammation



Proteolytic enzymes from traditional foods show strong antiinflammatory effects

- Pineapple stem juice = Ca. 30 mg/L; up to 40% absorbed from gut
- More than 70 in vitro and in vivo studies demonstrate immunomodulating, antiinflammatory, antidiarrheal, anticancer, and digestive-enhancing effects [*Alternative Medicine Review* 15(4), 2010]
- In a small controlled trial in patients with osteoarthritis of the knee, diclofenac and proteolytic enzymes had statistically-similar pain score outcomes (Klein and Kullich, 1999)
- In a 6-week, RDBPC clinical trial (n=90) Bromelain 90 mg, along with trypsin and rutin, reduced WOMAC dimensions pain, stiffness and physical function, and along with other tests, could find no difference between PE and the NSAID diclofenac (DC) 100 mg/day in pain (Klein et al, 2006)

Meadowsweet



- Contains salicylate derivatives that provide natural analgesic action
- Analgesic, anti-rheumatic and anti-inflammatory
- Flower extracts of meadowsweet possess pronounced complement-inhibiting effects, an immune process involved with inflammation and pain
- Soothes digestion, unlike many salicin (aspirin-based) products

Corydalis



- Strong analgesic and anti-spasmodic with approx 1% the strength of opium
- Alkaloids in corydalis 40% as effective as morphine – strongest component is corydaline
- Alleviates pain, esp traumatic pain, chest pain, abdominal pain, menstrual pain and epigastric pain
- Controlled human trial in 2004 (Yuan, C.S. et al) showed positive results for treating mild to moderate pain

Treating Inflammatory Diseases with Western Herbs and TCM Principles



- Traditional Chinese medicine is an intact system of healing of continuous development using holistic principles for over 4,000 years
- Chinese herbs are shipped from overseas, quality issues exist
- Western herbs are often local, fresher, wild in some cases
- Western herbalism was founded on energetic principles: Galen identified over 150 pulse types

Inflammatory Conditions According to TCM

- Yin = vital essence; Yang = vital function, Qi = vital energy
- Pathogenic heat accompanies:
 - Yin deficiency (= chronic inflammation!)
 - Yang excess
 - Fire poison
- Associated with Liver, Heart, Spleen, Stomach, LI, Lung

Deficiency/Excess

- A lack of necessary nutritive or functional substances
- A depletion of necessary fluids or substances like blood, hormones, neurotransmitters, enzymes
- Deficiency is made up with difficulty, and it takes time
- More chronic conditions
- Accumulation or flourishing of pathogenic influence
- Excess can be removed or drained through kidneys, bowels, skin, breath
- Excess can be reduced by calming hyperactive system
- More acute conditions

Excess and deficient heat

Cold/Heat

- Cold signs:
 - Slow pulse
 - Pale or normal tongue
 - Thick white coating
 - Clear mucus
 - Withdrawal
 - Fear of cold
 - Yang deficiency
- Heat signs:
 - Fast pulse
 - Red tongue
 - Yellow coating
 - Thick, yellow or green mucus
 - Irritability
 - Infections
 - Elevated WBC
 - Yin deficiency, yang excess

Herbs for Deficient Heat Conditions

- Treat deficient heat by tonifying the Kidney yin, plus Liver, Heart, or Lung system
 - Give about 100-120 grams (10-12 g 10:1 extract) of an herb formula total in tea or dried tea form (alcohol breaks down polysaccharides and proteins); doesn't capture minerals
 - 1 "00" cap = 500 mg
- *Panax quinquefolius*
 - *Ligustrum lucidum*
 - *Arctium lappa* (spring)
 - *Ganoderma lucidum*
- *Ample protein, fat: fish, well-cooked small beans (aduki), ketogenic diet, reduce refined carbs

Yin Tonifying Herbs



- American ginseng root
 - Identification suspect
- Rehmannia tuber
 - Cooked form
- Ophiopogon tuber
 - “turf lilly”
- Ligustrum fruit
 - Common ornamental
- Wolfberry (Lycium)
 - Goji—widely researched
- Solomon seal
- Asparagus tuber

Ligustrum lucidum—nuzhen zi



- Common street tree
- Weed in California
- Ripe fruits are extracted with water
- See my new book, *Grow It, Heal It* (Rodale Press) for instructions
- Excellent kidney yin, heart yin, liver yin tonic
- Sexual debility
- Weakness, fatigue
- Counteract chronic inflammation

Goji Berry—*Lycium*



- long history of use as a kidney tonic in traditional Chinese medicine,
- Crossed over into world markets as a longevity herb and tonic with restorative and protective properties
- Anti-aging, antioxidant, neuroprotection, cardiovascular, eyesight (Zeaxanthin, lutein) benefits, blood sugar balance, immune balance, anti-cancer, antiinflammatory

Other Antiinflammatory herbs

- Willow bark (*Salix* spp.) salicin, tannins
- Meadowsweet (*Filipendula ulmaria*) salicylates, flavonoids, tannins
- Cottonwood buds (*Populus fremontii*, *P.* spp.) populin
- Yucca root (*Yucca* spp.) saponins
- Aloe gel (*Aloe vera*) polysaccharides, sterols, saponins, fatty acids
- Feverfew (*Tanacetum parthenium*) sesquiterpenes
- *Urtica urens*, *Urtica* spp. Histamines, 5-HT, sterols
- *Taraxacum officinale* (intestinal tissue) sterols
- *Actaea racemosa* alkaloids, terpenoids, isoflavones

Administration of Herbs

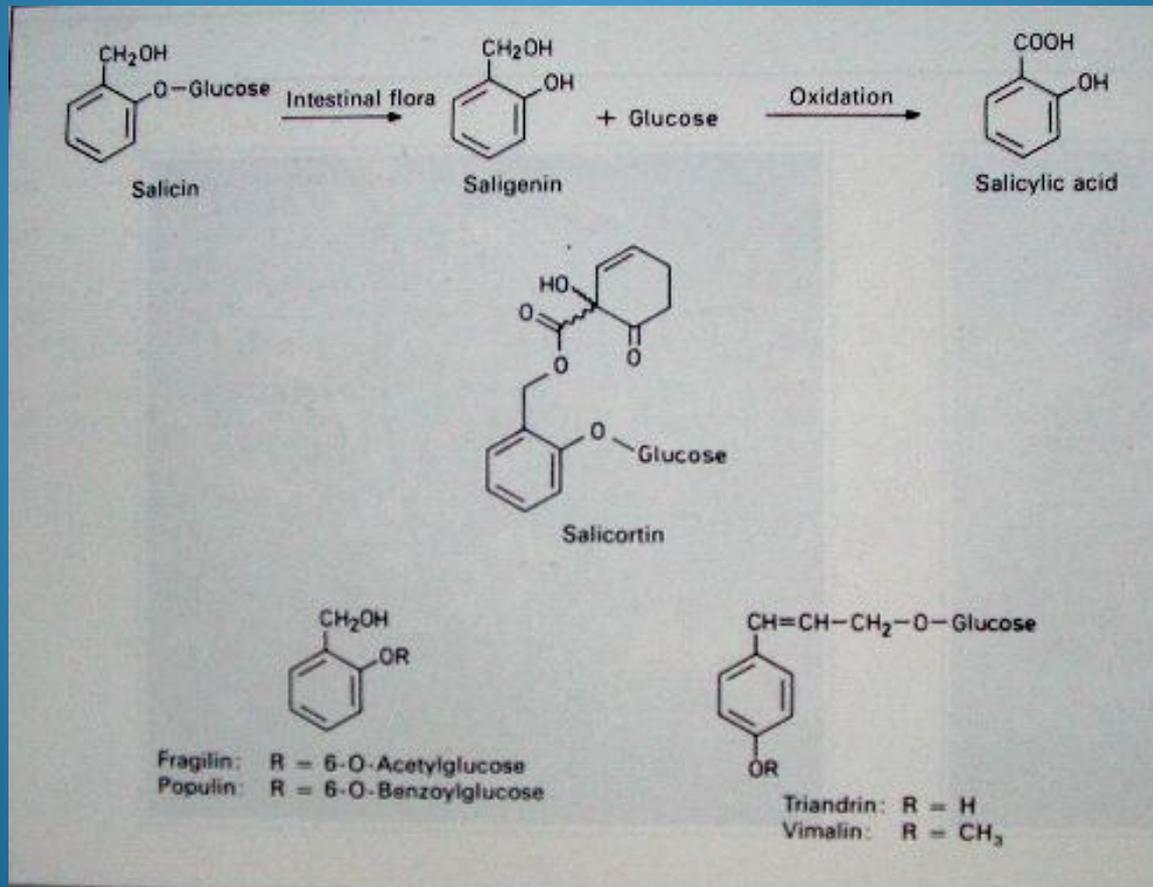
Containing Salicin (Willow bark)

- **Filipendula flos**
 - Flowering tops
 - Tincture or tea
 - Dose: 4-7 g/day (dried), 3-5 ml tinc. t.i.d.
- **Populus buds**
 - Tincture
 - Dose: 2-4 ml t.i.d.
 - Warming for cold-damp types
- **Willow bark**
 - 2-3 year old bark before leaves emerge
 - Cool macerate or tincture (48 hours)
 - Tannins irritate GI tract
 - Dose: 3-5 g/day (dried), 3-5 ml, capsules or tablets with 200-300 mg salicin

Salicylates

- Use described by Dioscorides, 56 A.D.
- COX1, COX2- prostaglandin inhibitors
- Salicin is a glycoside that does not cross the blood-brain barrier as well as acetylsalicylic acid
- Side effects probably nil
- Found in *Betula* spp. (leaves, bark, buds)
- *Filipendula ulmaria*
- *Gaultheria procumbens*
- *Populus* spp.
- *Salix* spp.
- *Actaea racemosa*
- [Salicin metabolism](#)

Salicin metabolism in humans

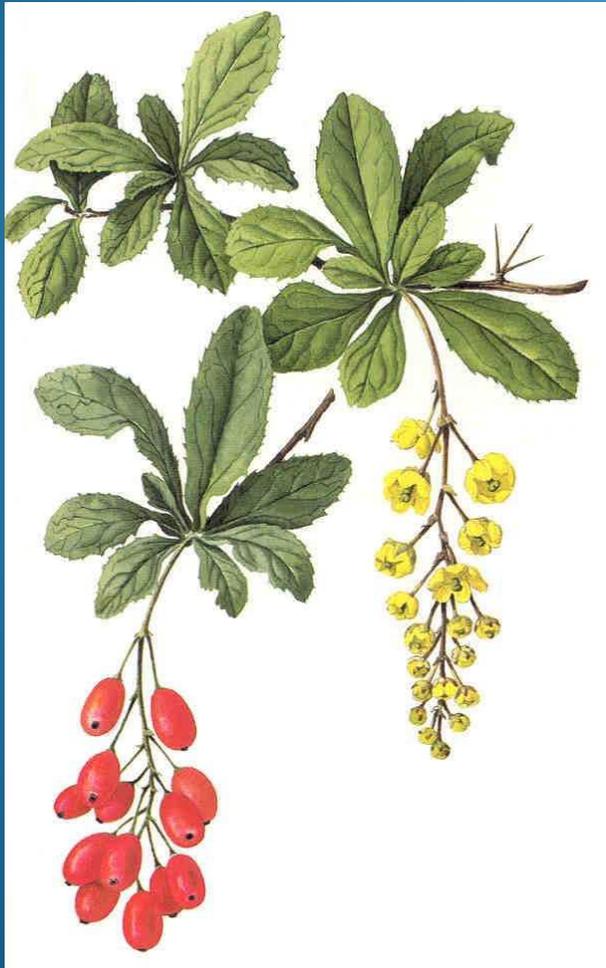


Willow bark extract--Salicin



- 39 volunteers with osteoarthritis took extract with 240 mg salicin, 39 a placebo for 2 weeks
- The willow bark showed moderate superiority over placebo for pain (2% increase in WOMAC pain score vs. 14% reduction in Salix group)
- Several show effectiveness for chronic low back pain

Berberine-Containing Herbs



- Berberidaceae
- Ranunculaceae
- Rutaceae

- *Coptis chinensis*
- *Mahonia* spp.
- *Berberis* spp.
- *Phellodendron amurense*
- *Hydrastis canadensis*

Berberine

- Moderately absorbable from GI tract.
- Relatively safe
- Effective against *E. coli*, *Mycobacterium phlei*, *Staphylococcus aureus* (methicillin-resistant) (equicocal), at the concentration of 20.0 microliters/disc (J. Ethnopharm. 1992; 37(3):213-223.
- Effective against *H. pylori* (*Biol Pharm Bul* 21:990. 1998.)
- As effective as sulfa drugs or chloramphenicol for bacterial dysentery with few side effects
- Strong antiviral and antifungal effects
- Strong effect in vitro against hemolytic *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Shigella dysenteriae*, *S. flexneri*. More effective than sulfa drugs, but less so than streptomycin or chloramphenicol against some of these pathogens. Sometimes effective against bacteria that have developed resistance to streptomycin, chloramphenicol, and oxytetracycline hydrochloride.

Coptis chinensis (huang lian)

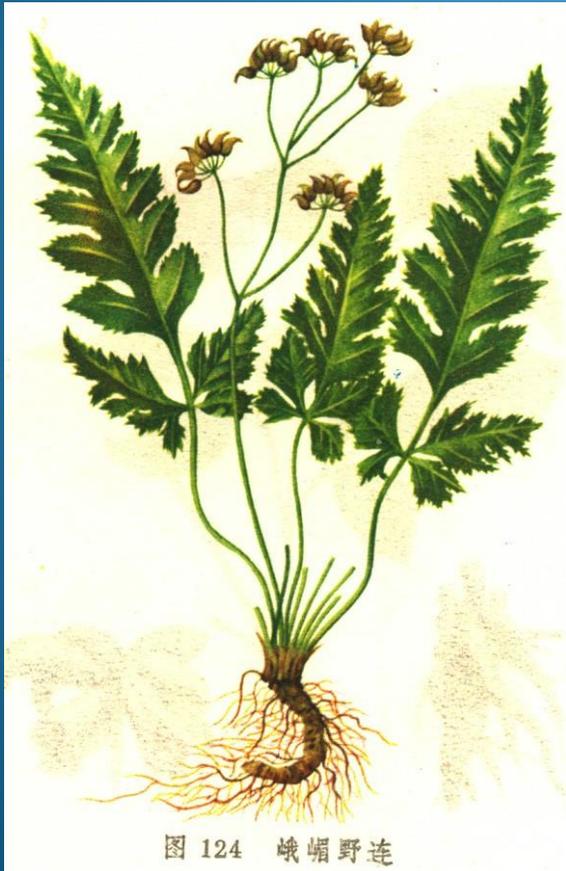


图 124 峨嵋野连

- Coptis is a good source of berberine because it is cultivated
- Huang lian is indicated especially for infections of the gut, urinary tract, liver
- Clears “Heart” heat for insomnia, mania
- Externally for conjunctivitis
- Huang lian su is berberine sulfate tablets from Coptis

Huang Lian Su



- Huan Lian Su is berberine sulfate
- 100 mg tablets
- Take 1-2 tablets t.i.d.
- Useful for acute and chronic allergic rhinitis
- Dilute in saline nasal spray
- UTI, URI
- Colitis, traveler's diarrhea