



**FREE WEBINAR**

## **Incorporating Herbal Supplements into Your Practice:**

The Science and Regulations Behind Five Popular Botanicals

With integrative medicine expert

**Tieraona Low Dog, M.D.**

**JUNE 16 • 1 pm EDT**



Presented by:



**Council for Responsible Nutrition**

*The Science Behind the Supplements*

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**This is a reminder that this webinar is intended for healthcare practitioners only. Dr. Low Dog will be presenting scientific research on five herbal ingredients and drawing on her medical knowledge and experience as an M.D. familiar with these ingredients. In the U.S., companies are restricted from selling dietary supplement products with claims to prevent, treat, or mitigate disease. However, the law does not restrict healthcare practitioners from evaluating the science and long history of use of these ingredients for use in their practice with individual patients.**

# Incorporating Herbal Supplements into Your Practice:

## Practice:

### The Science and Regulations Behind Five Popular Botanicals



**Tieraona Low Dog, MD**

# Disclosures

Tieraona Low Dog, MD has the following disclosures to make:

- Health Advisory Board: Pharmaca
- Director Scientific & Regulatory Affairs: Healthy Lifestyle Brands

This talk will not discuss off-label and/or investigational use of pharmaceuticals or devices not yet approved by the FDA.

# Patient Centered Care

- Take time to understand the patient's attitudes and beliefs around conventional and complementary therapies.
- When possible use therapies that are gentle and aligned with patient's values and suitable for level of complexity of condition.
- Explain in simple terms risks and benefits of all treatments. Be watchful of herb-drug interactions. Document in the patient chart.

# Herbal Medicine

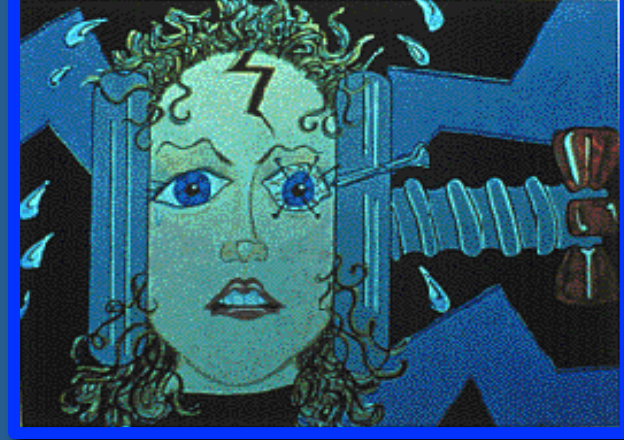
- Herbal medicine is part of our lineage as clinicians and pharmacists.
- Widely used around the world as primary forms of medicine and are popular as natural medicines and dietary supplements in many countries.
- Herbal remedies can play an important role in the treatment of minor conditions with fewer adverse effects and at a lower cost than many conventional alternatives.

# Migraine in USA



- 30,000,000 migraine sufferers
- 1 in 10 persons is a migraineur
- 1 of 4 households include a migraineur
- 9<sup>th</sup> leading disability, more common than diabetes or asthma





*“Almost half of people with migraine are undiagnosed.”*

American Migraine Prevalence and  
Prevention Study (AMPP)

# Butterbur

## (*Petasites hybridus*)

- Long history of use in ***migraine and allergy treatment***: anti-inflammatory, vasodilatory, and smooth muscle relaxant properties.
- Reduction in mast cell activation, thus less histamine and leukotriene release.
- Butterbur well studied in children over six years with wide margin of safety.

Utterback G, et al. Complement Ther Clin Pract, 2014; 20(1): p. 61-4.

# Butterbur Extract

- Butterbur has a Level A (highest) recommendation for **migraine prevention** in adults from the American Academy of Neurology and American Headache Society and is “***strongly recommended***”
  - Children 6-9 years: 25 milligrams BID
  - Children 9-13: 50 milligrams BID.
  - Children > 13 yrs. and adults: 75 mg BID



Holland S, et al. Neurology 2012; 78(17): 1346-53

# Butterbur: Safety Considerations

- Use only *standardized extracts* containing ~7.5% petasin and *free of pyrrolizidine* alkaloids (hepatotoxic and carcinogenic).
- Safety has not been established in pregnancy or lactation or for children younger than six years of age.

# Tamiflu: Derived from Star Anise





*Katie Collins/Press Association Images*

Stocks of the antiviral drug Tamiflu at an undisclosed location in the United Kingdom.

# Tamiflu

- In 2009, widespread concern about a new flu pandemic, caused billions to be spent stockpiling Tamiflu globally. Sales that year hit \$3 billion.
  - WHO recommends Tamiflu, but did not vet data.
  - EMA approved Tamiflu, but did not review the full Tamiflu dataset.
  - CDC and ECDC encourage the use and stockpiling of Tamiflu, but did not vet the Tamiflu data.
  - The majority of Roche's Phase III treatment trials remain unpublished over a decade after completion.
  - In 2009, scientists requested Roche to hand over data for evaluation.....

# The Findings

- In October 2013, Cochrane reviewers received the full Clinical Study Reports for 107 studies from Roche and GlaxoSmithKline. Here were their findings:
  - Reduction in time to first alleviation of symptoms from 7 days to 6.3 days compared with the control group.
  - No evidence it reduces hospitalizations or complications of flu: pneumonia, bronchitis, sinusitis, ear infections in adults or kids
  - In prophylaxis trials, reduced flu-like symptoms in adults but did not prevent person-to-person spread.
  - Increases risk of vomiting, headaches, psychiatric syndromes and a statistically significant increase in renal events.

Jefferson T, et al. *British Medical Journal* 2014; 348: g2545



# Concluding Thoughts

- The stated intentions of governments to distribute Tamiflu to healthy people to prevent complications and interrupt transmission of influenza on the basis of a published evidence base that has been affected by reporting bias, ghost authorship, and poor methods is worrisome.
- *“We believe these findings provide reason to question the stockpiling of oseltamivir, its inclusion on the WHO list of essential drugs, and its use in clinical practice as an anti-influenza drug.”*

Jefferson T, et al. *British Medical Journal* 2014; 348: g2545.

# Elderberry

(*Sambucus nigra*)



- The flowers and berries have long been used for colds, sore throat, fever and sinus congestion.
- A rich source of anthocyanidins, which are thought to be responsible for antiviral and immune priming effects.

# Elderberry Extracts

- Possesses antimicrobial activity against Gram-positive bacteria *Streptococcus pyogenes*, and the Gram-negative bacterium *Branhamella catarrhalis*.
- One study found standardized elderberry extract could shorten the duration of flu by about 3 days.
- Cyanidin-3-sambubioside, derived from elderberry extract, has been found to be a potent inhibitor of sialidase(neuraminidase) activity.
- Safety profile is excellent.

Swaminathan K, et al. Anal Bioanal Chem 2013; 405(20):6563-72.  
Krawitz C, et al. BMC Complement Altern Med 2011 Feb 25;11:16.



# *Elderberry*

- *In vitro*, elderberry flavonoids inhibited H1N1 to same degree as Tamiflu and amantadine.
- Elderberry extract reduces symptoms when administered to patients with influenza A or B.
- Greatest benefit when started within 24-48 hours of symptom onset.
- Take elderberry extracts as instructed on label (crude equivalent 5000-6000 mg) 1-4 times per day

Krawitz C, et al. BMC Complement Altern Med 2011; 11:16.

Roschek, et al. Phytochemistry 2009; 70(10):1255-61.

Zakay-Rones Z, et al. J Int Med Res 2004; 32(2):132-40.

## Supplement Facts

Supplement Facts		
Serving Size: 2 teaspoons (10 ml)		
Servings Per Container: 24		
	Amount Per Serving	% DV
Calories	20	
Total Carbohydrate	6 g	2%†
Standardized Elderberry BioActives Extract (berry) from 6.4 g (6,400 mg) of premium cultivar berries	100 mg	**

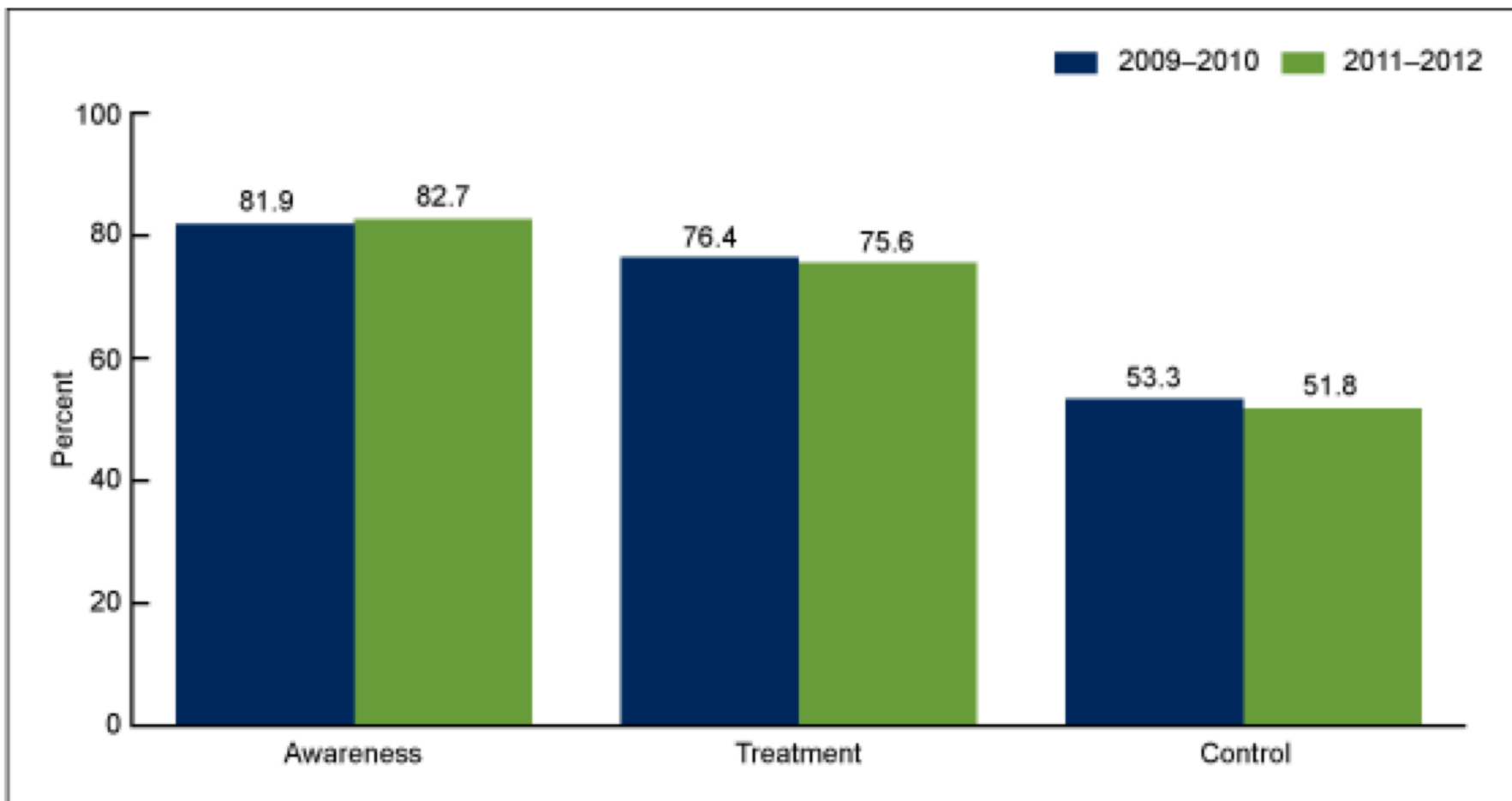
Supplement Facts		
Serving Size: 2 Capsules		
Servings Per Container: 30		
Amount Per 2 Capsules	mg	%DV
Calories	30	
Alcohol Free Concentrated Extract Of: Black Elderberry berries (Sambucus nigra)◆	800 mg	†
†Daily Value not established. ◆ = Organic Ingredient Each 2 capsules contain 5,000 mg crude herb equivalent.		

# Hypertension

Increases the risk for:

- Stroke
- Myocardial Infarction/ coronary artery disease
- Heart Failure
- Atrial Fibrillation
- Aortic Dissection
- Peripheral Vascular Disease
- Kidney Disease

**Figure 2. Age-adjusted awareness, treatment, and control of hypertension among adults with hypertension: United States, 2009–2012**



NOTE: Age-adjusted prevalence of awareness, treatment, and control of hypertension were calculated using the subpopulation of persons with hypertension in 2011–2012.

SOURCE: CDC/NCHS, National Health and Nutrition Examination Survey, 2011–2012.



# Hibiscus

(*Hibiscus sabdariffa*)

- In India, Africa and Mexico – the calyces are used in traditional medicine for a variety of conditions.
- Dried roselle calyces are sold in plastic bags in Mexico, labeled "*Flor de Jamaica*", leading many to believe that they are flower petals. Actually, the flower falls before the red calyx enlarges and becomes fit for food use.
- Calyces are high in calcium, niacin, riboflavin and iron.
- Commonly used in many countries for treatment of hypertension and elevated cholesterol.



# Hibiscus Tea & Extract

- Low degree of toxicity: LD50 ranging from 2,000 to over 5,000 mg/kg/day.
- Animal studies consistently show hibiscus extract reduces BP in a dose dependent manner.
- In RCTs, tea or extract significantly lowered SBP and DBP in adults with pre to moderate essential hypertension and type 2 diabetes; half of RCTs showed favorable influence on lipid profiles including reduced total cholesterol, LDL-C, triglycerides, increased HDL-C.

Hopkins A, et al. *Fitoterapia* 2013; 85:84-94

Herrera-Arellano, et al. *Planta Med.* 2007 Jan;73(1):6-12.

Wright CI, et al. *J Ethnopharmacol.* 2007 Oct 8;114(1):1-31.

Mozaffari-Khosravi H, et al *J Hum Hypertens.* 2009 Jan;23(1):48-54



# *Hibiscus*

- Tuft's study (n=65) found at 6 weeks that 240 ml tisane taken 3 times/d lowered systolic BP compared with placebo (-7.2 +/- 11.4 vs. -1.3 +/- 10.0 mm Hg; P = 0.030). Those with higher SBP at baseline had most benefit.
- Hibiscus tisane (tea) can be a useful lifestyle option.
- Dose of extract used in most studies 1 gram BID

# As Tea/Tisane

## Supplement Facts

Serving Size 1 Cup Brewed Tea    Servings Per Container 16

Amount Per Serving    %DV

### All Herbal Ingredients:

Organic hibiscus flower\*\* (PhEur)\*\*    1260 mg    †

Proprietary blend:    490 mg

Organic blackberry leaf, fermented    †

Organic West Indian lemongrass leaf    †

† Daily Value (DV) not established.

## Supplement Facts

Serving Size 2 Capsules

Servings Per Container 30

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AMOUNT PER 2 CAPSULES

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Calories 20

---

TOTAL ALCOHOL FREE EXTRACT . . . . 1,070 mg†

Hibiscus flower (*Hibiscus sabdariffa*) ▲

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†Daily Value not established.

### Other ingredients:

Vegetable glycerin, capsule (vegetable cellulose)

▲ = Certified Organic Ingredient

Each 2 capsules contain 1,300 mg dry herb equivalent.

# Peppermint

*(Mentha x piperita)*



- Peppermint leaf popular for minor digestive and respiratory complaints.
- FDA approved use of mentholated ointments, lozenges and steam inhalants for alleviating coughs.
- Topical analgesic

## Treatments for IBS

Therapy	Trials	NNT
Peppermint oil	8	2
Hycosamine	22	11
Alosetron	6	7
Tegaserod	8	17
Tricyclics	8	4

- Studies estimate that IBS affects 10 to 15 percent of U.S. adults, twice as many women as men, and most often occurs in people < age 45
- Peppermint oil highly effective for treating IBS. Significantly prolongs orocecal transit time and directly inhibits smooth muscle contractions by interacting with calcium channels.
- Dose is 0.2 ml enteric coated caplet TID. Heartburn and loss of anti-spasmodic effect will occur if preparation is not enteric coated.

Grigoleit HG Phytomedicine. 2005 Aug;12(8):607-11

Goerg KJ. Aliment Pharmacol Ther 2003;17(3):445-51

Ford AC, et al. British Medical Journal 2008; 337:a2313

# Enteric Coated Soft Gel

## Supplement Facts

Supplement Facts		
Serving Size: 1 Softgel		
Servings Per Container: 60		
	Amount Per Serving	%Daily Value
Peppermint Oil	0.2 ml	**
Soybean Oil (organic, non-GMO)	0.1 ml	**
** Daily Value not established.		

# Turmeric

(*Curcuma longa*)





# Curcumin

- Curcumin is the yellow pigment in turmeric and has powerful health benefits. Human and animal data suggest it may be beneficial for:
  - Brain health
  - Inflammation
  - Heart disease
  - Cancer
  - Depression
  - Skin Conditions



# Curcumin

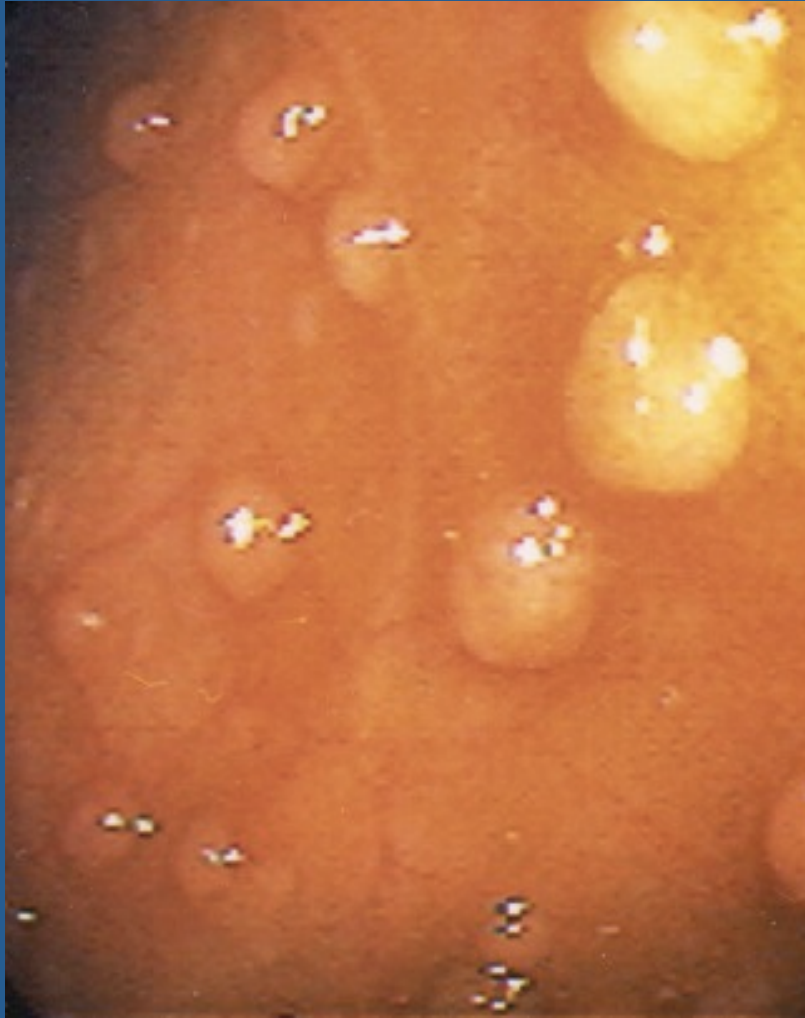


- Effective anti-inflammatory; strong inhibitor NF- $\kappa$ B very favorable clinical trials in knee osteoarthritis.
- 25 clinical trials using curcumin in a variety of cancers, curcumin is the most promising polyphenol as possible future adjuvant in colorectal cancer management.

Irving GR, et al. *Cancer Prev Res* 2013; 6(2):119-28.

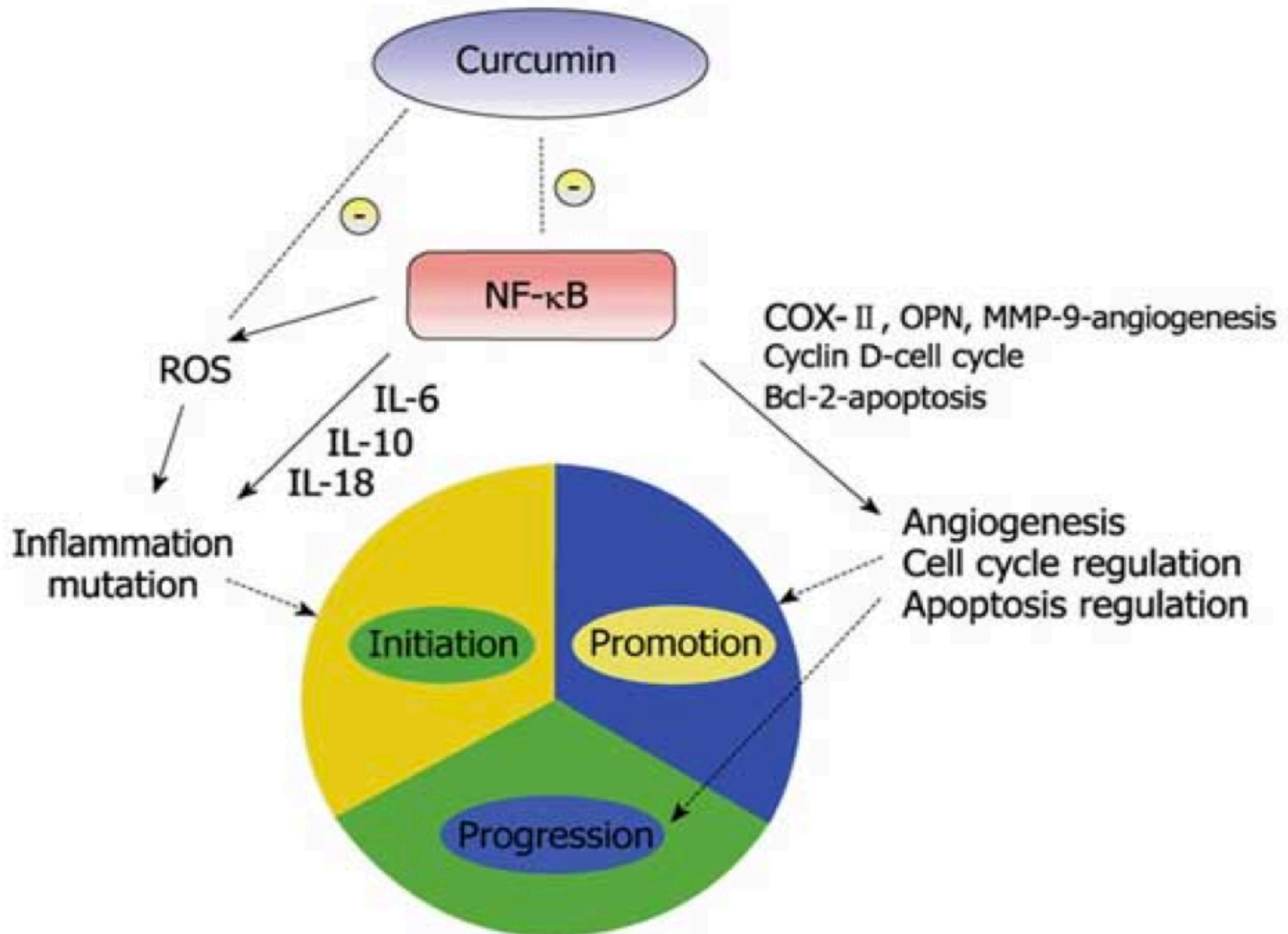
Shanmugam MK, et. Al. *Molecules* 2015, 20(2), 2728-2769

## Early Investigation

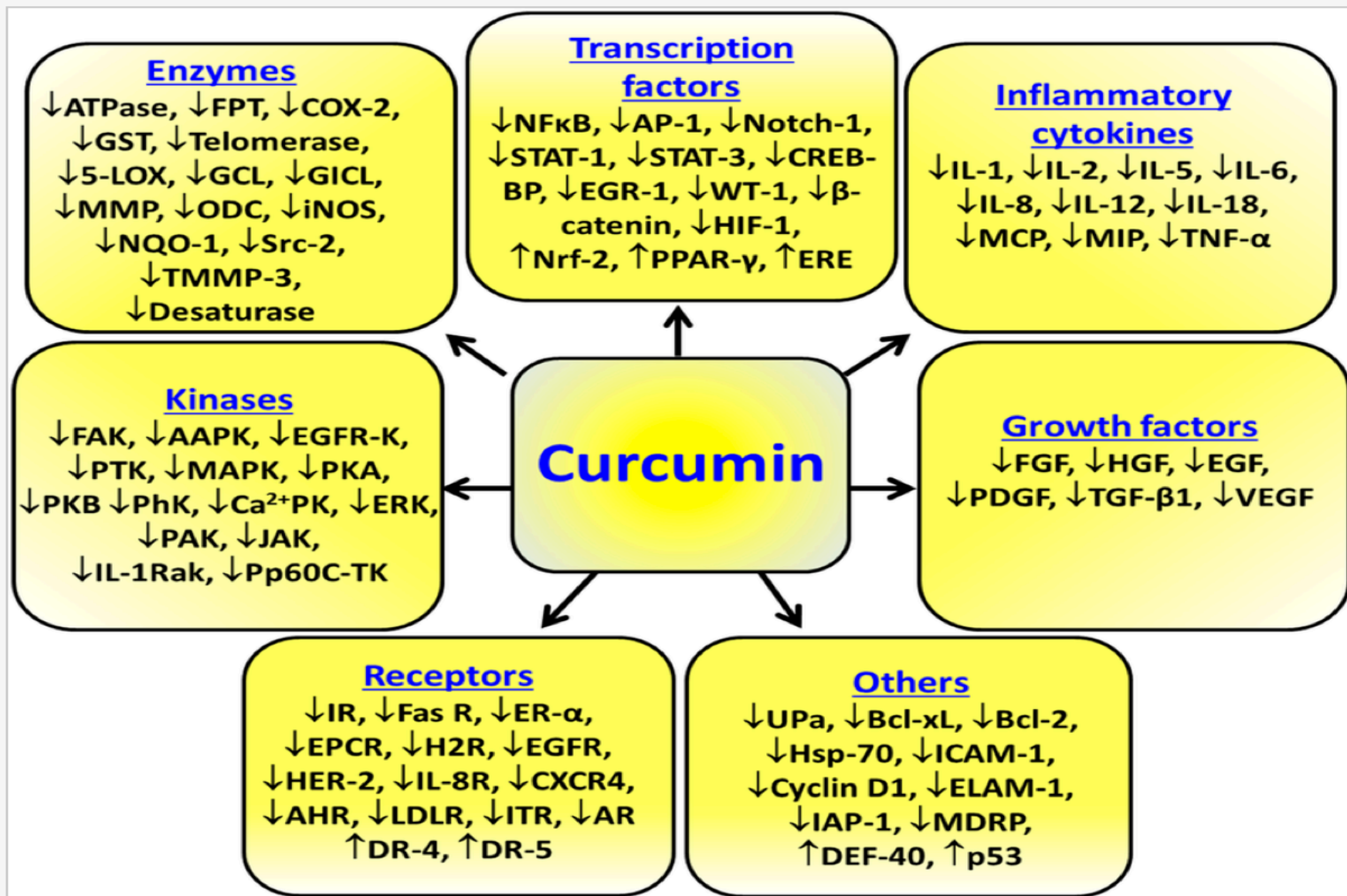


- Colonic polyps are a precursor to colorectal cancer.
- A small pilot study of 5 patients with familial adenomatous polyps found that after six months of taking 480 mg of curcumin and 20 mg quercetin taken three times a day, polyp numbers were reduced by 60%.

Cruz-Correa M, Clin Gastroenterol Hepatol. 2006;4:1035–1038



**Figure 2.** Molecular targets modulated by curcumin. ↓ Down-regulated targets; ↑ Up-regulated targets.



# Beneficial Effects in the Gut

- Distribution studies show curcumin preferentially accumulates in intestine, colon and liver.
- Early research is promising in cases of ulcerative colitis, NAFLD, FAP. Strong hepatoprotectant.
- For systemic absorption consider using phytosome bound curcumin. Peak plasma approximately 5-fold higher than traditional curcumin products.

Dulbecco P, et al World J Gastroenterol 2013; 19(48): 9256–9270.



# Absorption



- Most research has used range of 1200-6000 mg of *curcumin*.
- Doses up to 12 grams per day for three months not associated with toxicity HOWEVER, GI upset is common complaint.
- Curcumin is poorly absorbed from the GI tract.
- Preparations that increase absorption include: nanoformulations, phytosome, and those with piperine (alkaloid from black pepper).

Kanai M. World J Gastroenterol 2014; 20(28):9384-91.

Kakarala M, et al. Breast Cancer Res Treat 2009; 122:777-785

# Label: Curcumin with Piperine

## Suggested Use

As a dietary supplement, take 1-3 capsules daily, in divided doses, between meals.

## Supplement Facts

Supplement Facts		
Serving Size: 1 Capsule		
Servings Per Container: 60		
	Amount Per Serving	% Daily Value
Vitamin C (ascorbyl palmitate)	10 mg	7%
Turmeric (curcuma longa) Extract (root) (standardized to contain 95% curcuminoids)	500 mg	*
Bioperine (piper nigrum) Extract (fruit) (standardized to contain 95% piperine) ←	5.3 mg 5 mg	*



# Curcumin Bound to Phytosome

**Serving Size:** Two Capsules

**Servings Per Container:** 60

**Two Capsules Contain:**

**Amount  
Per  
Serving**

**% DV**

Curcumin Phytosome† (Curcuma longa extract (root) /  
Phosphatidylcholine complex)

500 mg

\*

# Resources

- NIH National Center for Complementary and Integrative Health (NCCIH): [www.nccih.nih.gov](http://www.nccih.nih.gov)
- NIH Dietary Supplement Label Database  
[www.dsld.nlm.nih.gov](http://www.dsld.nlm.nih.gov)
- Office of Dietary Supplements:  
[www.dietary-supplements.info.nih.gov](http://www.dietary-supplements.info.nih.gov)
- Natural Standards Research Collaboration:  
[www.naturalstandard.com](http://www.naturalstandard.com)
- Natural Medicines Comprehensive Database:  
[www.naturaldatabase.com](http://www.naturaldatabase.com)
- Council for Responsible Nutrition: [www.crnusa.org](http://www.crnusa.org)
- American Botanical Council: [www.herbalgram.com](http://www.herbalgram.com)
- Consumer Labs: [www.consumerlabs.com](http://www.consumerlabs.com)