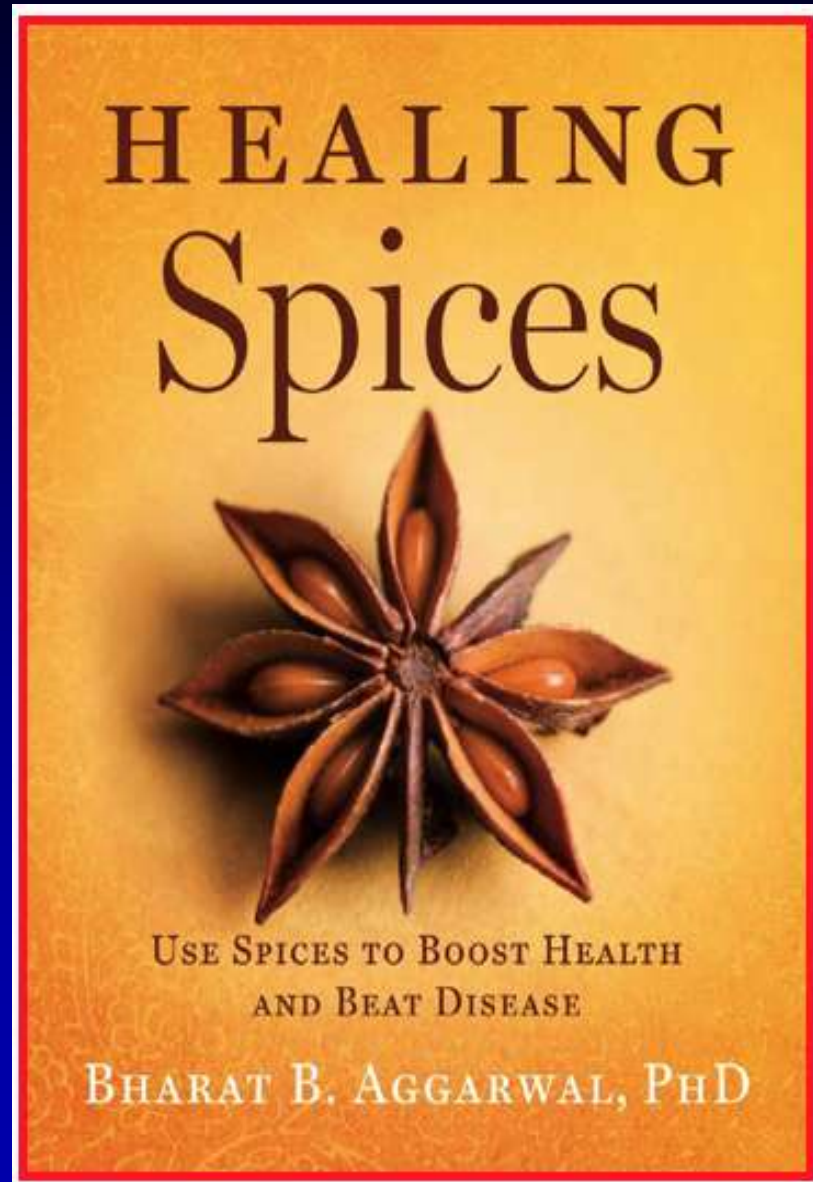


# TNF blockers



# ***Targeting Inflammatory Pathways by Dietary Spices for Prevention and Therapy of Cancer & Other Chronic Diseases***

**Bharat B. Aggarwal, Ph.D.**

**Cytokine Research Laboratory,  
Department of Experimental Therapeutics,  
The University of Texas, M.D. Anderson Cancer Center,  
Houston, Texas, U.S.A.**

***Cancer Strategies: Improving Outcomes and Quality of Life***

***Organized by Healthy Medicine Academy***

***March 25-27, 2011,***

***FireSky Resort, Scottsdale***

***(Hosted by Robert Zieve, MD)***

# ***Inflammation, Chronic Diseases and Nutrition: A Silent Link***

**Bharat B. Aggarwal, Ph.D.**

Cytokine Research Laboratory,  
Department of Experimental Therapeutics,  
The University of Texas, M.D. Anderson Cancer Center,  
Houston, Texas, U.S.A.

***Public seminar,***  
***Department of Nutritional Sciences Series***  
***AT&T Executive Education and Conference Center,***  
***The University of Texas in Austin;***  
***March 3rd, 2011 (6:00-7:00 PM)***  
***(Hosted Drs. Kimberly Kline and Linda deGraffenried )***

# ***Inflammation, Lifestyle and Chronic Diseases: The Silent Link***

***Bharat B. Aggarwal (Editor),  
Sunil Krishnan (Editor),  
Sushovan Guha (Editor)  
(Francis and Taylor)***

# ***Working Hypothesis:***

***Dysregulated chronic inflammation caused by life style factors mediate chronic diseases including cancer!***

# What is Inflammation?

Cornelius Celsus,  
a physician in first century Rome:



Heat (*calor*)

Pain (*dolor*)

Redness (*rubor*)

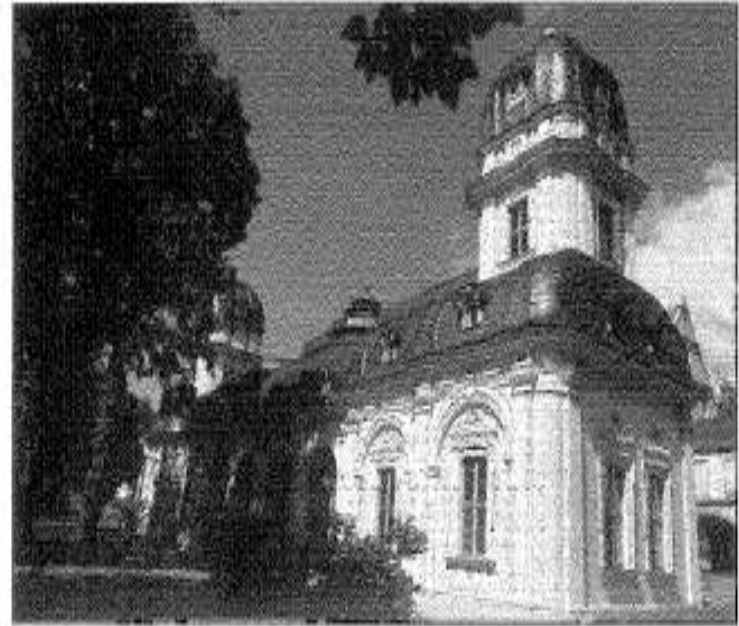
Swelling (*tumour*)

# *Inflammation and cancer*

*Redness, swelling, heat and pain*



*Rudolf Virchow  
(1821-1902; in 1850)*



*Fig. 3 - Jullusspital-Pavilion, Virchow's working place in Würzburg (1849-1854).*

*His Pathology laboratory in  
Würzburg, Germany*

*Linked Inflammation with atherosclerosis, rheumatoid arthritis, multiple sclerosis, cancer, asthma, Alzheimer's*

# ***Inflammation is “itis”***

***Arthritis is inflammation of the joints***

***Bronchitis..... Bronchus***

***Sinusitis..... Sinus***

***Gastritis..... Stomach***

***Esophagitis..... Esophagus***

***Pancreatitis..... Pancreas***

***Meningitis..... Brain***

***Rhinitis..... Rhina***

***Gingivitis..... Gum***



# Inflammation as a risk factor for most cancers

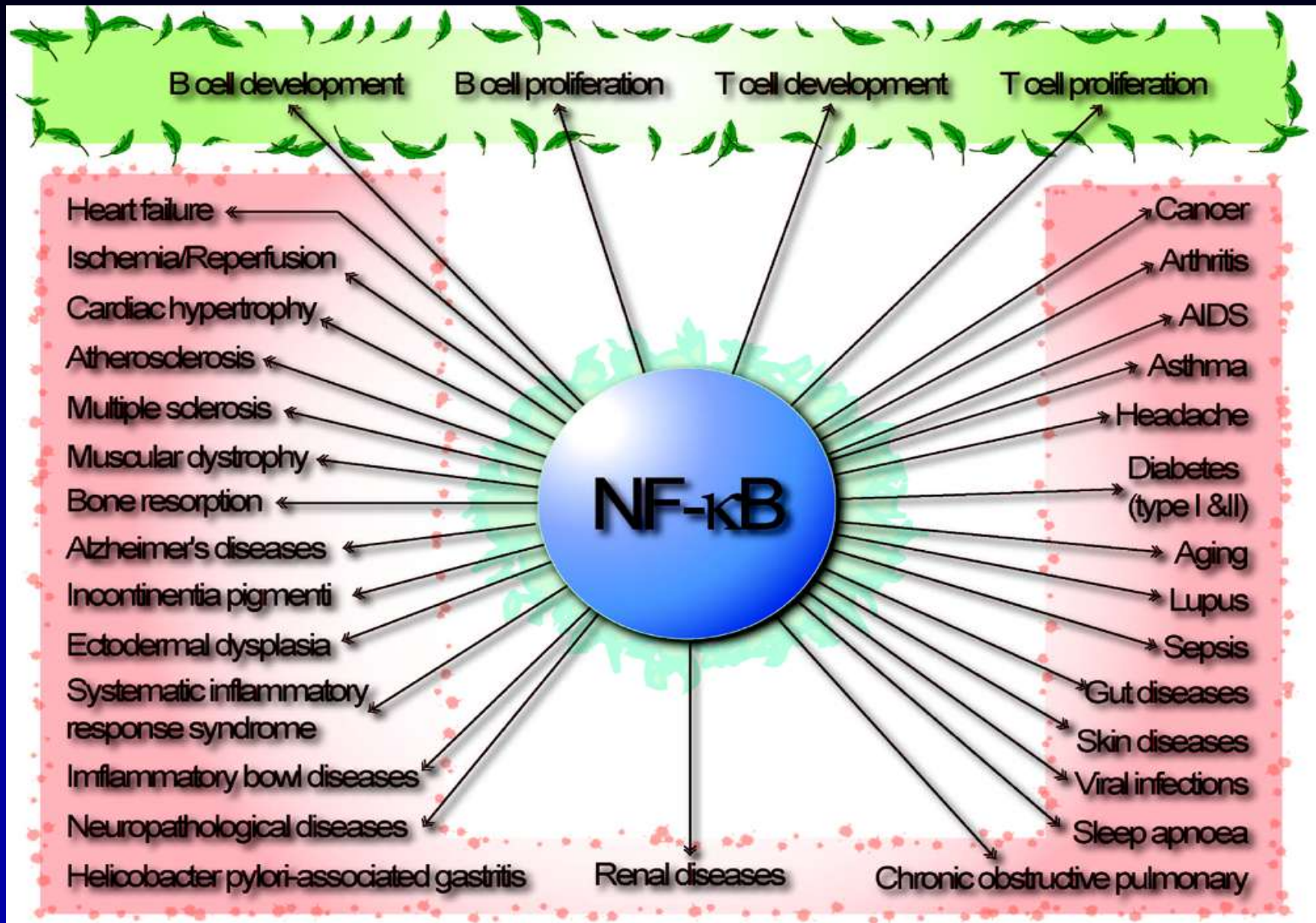
<i>Inducer</i>	<i>Inflammation</i>	<i>Cancers</i>	<i>% predisposed progress to cancer</i>
<i>Tobacco smoke</i>	<i>Bronchitis</i>	<i>Lung Cancer</i>	<i>11-24</i>
<i>Helicobacter pylori</i>	<i>Gastritis</i>	<i>Gastric Cancer</i>	<i>1 - 3</i>
<i>Human papilloma virus</i>	<i>Cervicitis</i>	<i>Cervical cancer</i>	<i>&lt;1</i>
<i>Hepatitis B &amp; C virus</i>	<i>Hepatitis</i>	<i>HCC</i>	<i>10</i>
<i>Bacteria, GBS</i>	<i>Cholecystitis</i>	<i>Gall bladder cancer</i>	<i>1 – 2%</i>
<i>Gram- uropathogens</i>	<i>Cystitis</i>	<i>Bladder cancer</i>	<i>&lt;1</i>
<i>Tobacco, genetics</i>	<i>Pancreatitis</i>	<i>Pancreatic cancer</i>	<i>≤10%</i>
<i>GA, alcohol, tobacco</i>	<i>Esophagitis</i>	<i>Esophageal cancer</i>	<i>15</i>
<i>Asbestos fibers</i>	<i>Asbestosis</i>	<i>Mesothelioma</i>	<i>10–15</i>
<i>Epstein-Barr virus</i>	<i>Mononucleosis</i>	<i>Burkitt's lymphoma</i>	<i>&lt;1</i>
	<i>Hodgkin's disease</i>		
<i>Gut pathogens</i>	<i>IBD</i>	<i>Colorectal cancer</i>	<i>1*</i>
<i>Ultraviolet light</i>	<i>Sunburn</i>	<i>Melanoma</i>	<i>≤9%</i>
<i>Infections, STD</i>	<i>PIA</i>	<i>Prostate cancer</i>	<i>?</i>

*GA, gastric acid; GBS, gall bladder stones; HCC, hepatocellular carcinoma; STD, sexually transmitted diseases; PIA, prostate inflammatory atrophy.*

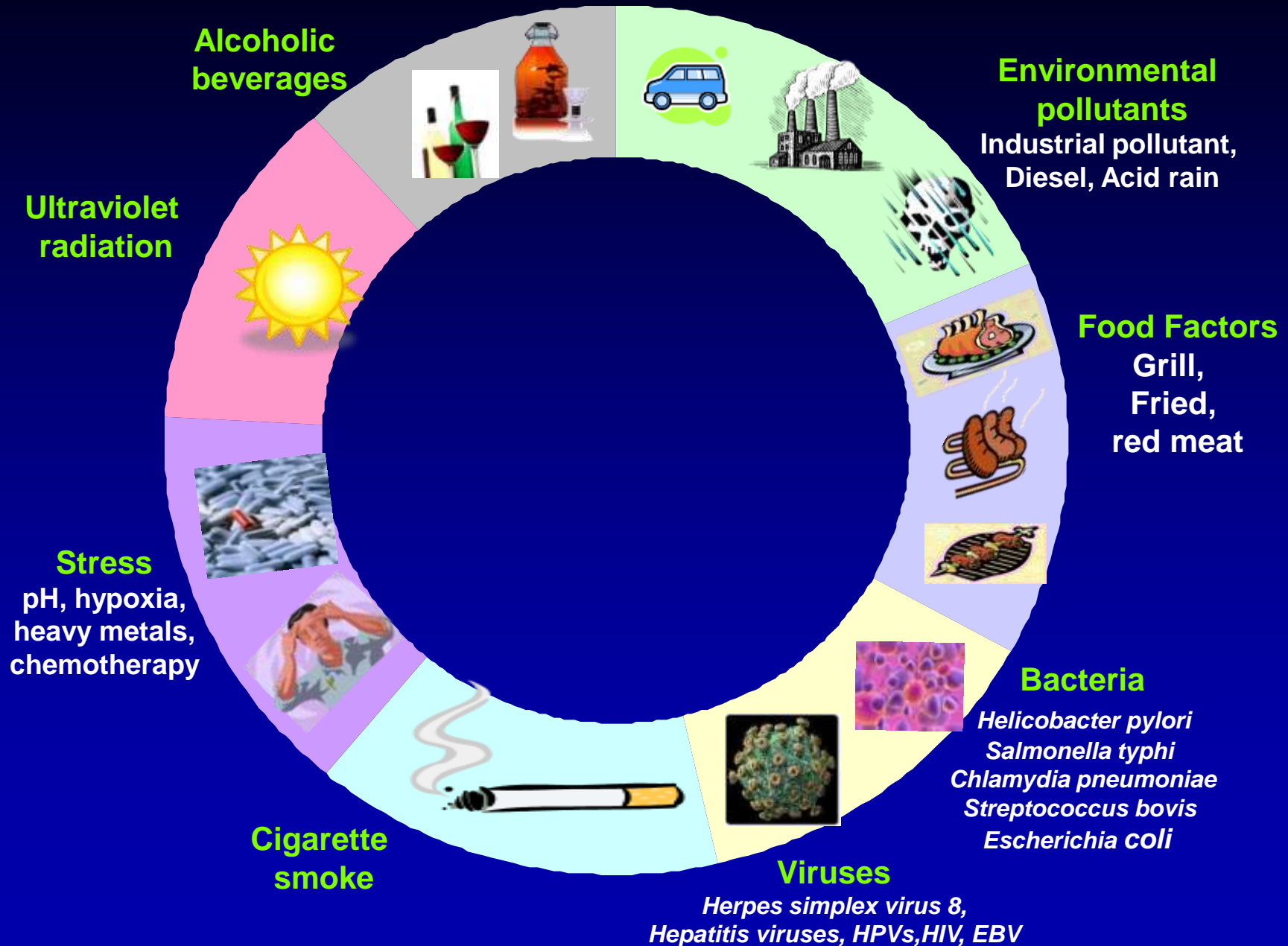
# *Hypothesis!*

*NF- $\kappa$ B activation is a major mediator of inflammation in most chronic diseases (including cancer) & inhibition of NF- $\kappa$ B can prevent/delay the onset of the chronic diseases!*

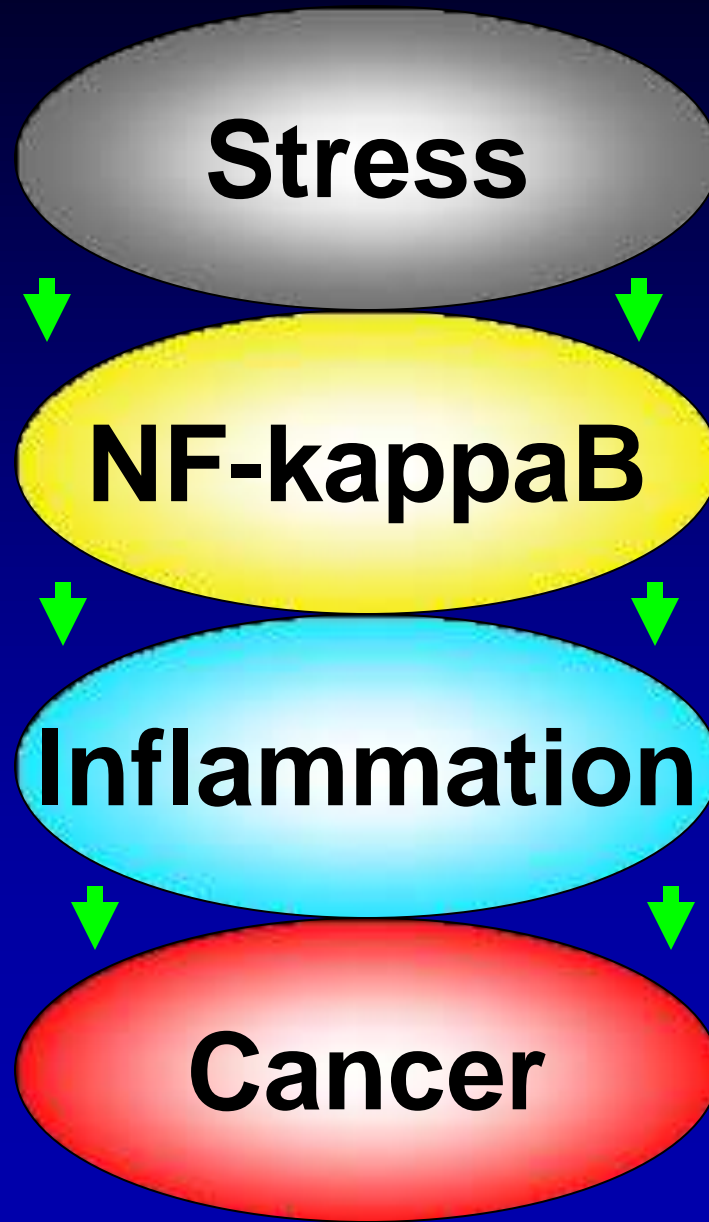
# NF-kappa B activation has been linked to most major diseases



# Potential Sources of Inflammation



# Working Hypothesis



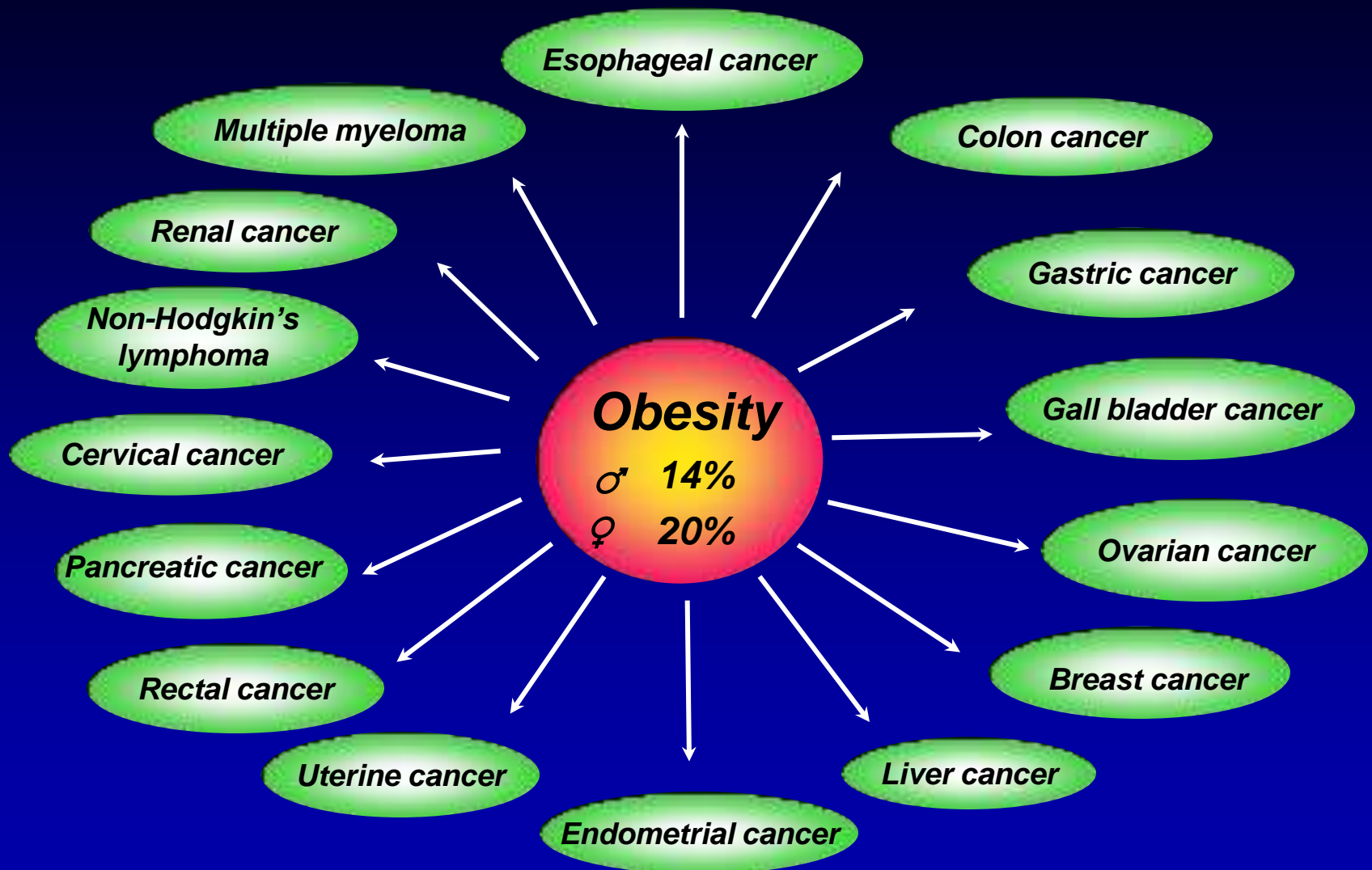


# **Cigarette Smoke Activates Nuclear Factor- $\kappa$ B and Induces Cyclooxygenase-2**

*Anto R. J., Mukhopadhyay A., Gairola C. G. and  
Aggarwal B. B.,*

*Carcinogenesis, 23, 1511, 2002*

# Obesity and Cancer



***Increase in intranuclear NF-  $\kappa$ B  
and decrease in I $\kappa$ B in  
mononuclear cells after a  
mixed meal:  
evidence for a proinflammatory effect.***

*Aljada A, Mohanty P, Ghanim H, Abdo T, Tripathy D, Chaudhuri A, Dandona P.*

*American Journal of Clinical Nutrition.*

*2004 Apr;79(4):682-90.*

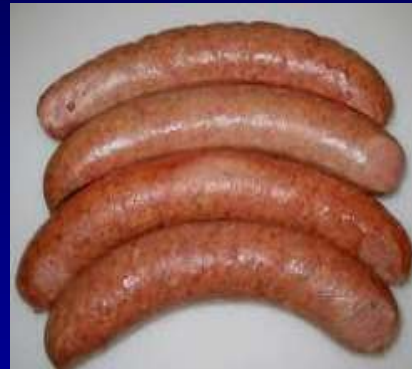


# Protocol

➤ *Expt subjects: (N=9; BMI=25; non-diabetic; 29-38y) fasted overnight, came to clinic between 8-9 AM.*

➤ **Mixed meals:**

*Egg muffin,  
sausage,  
muffin sandwiches,  
2 hash browns*

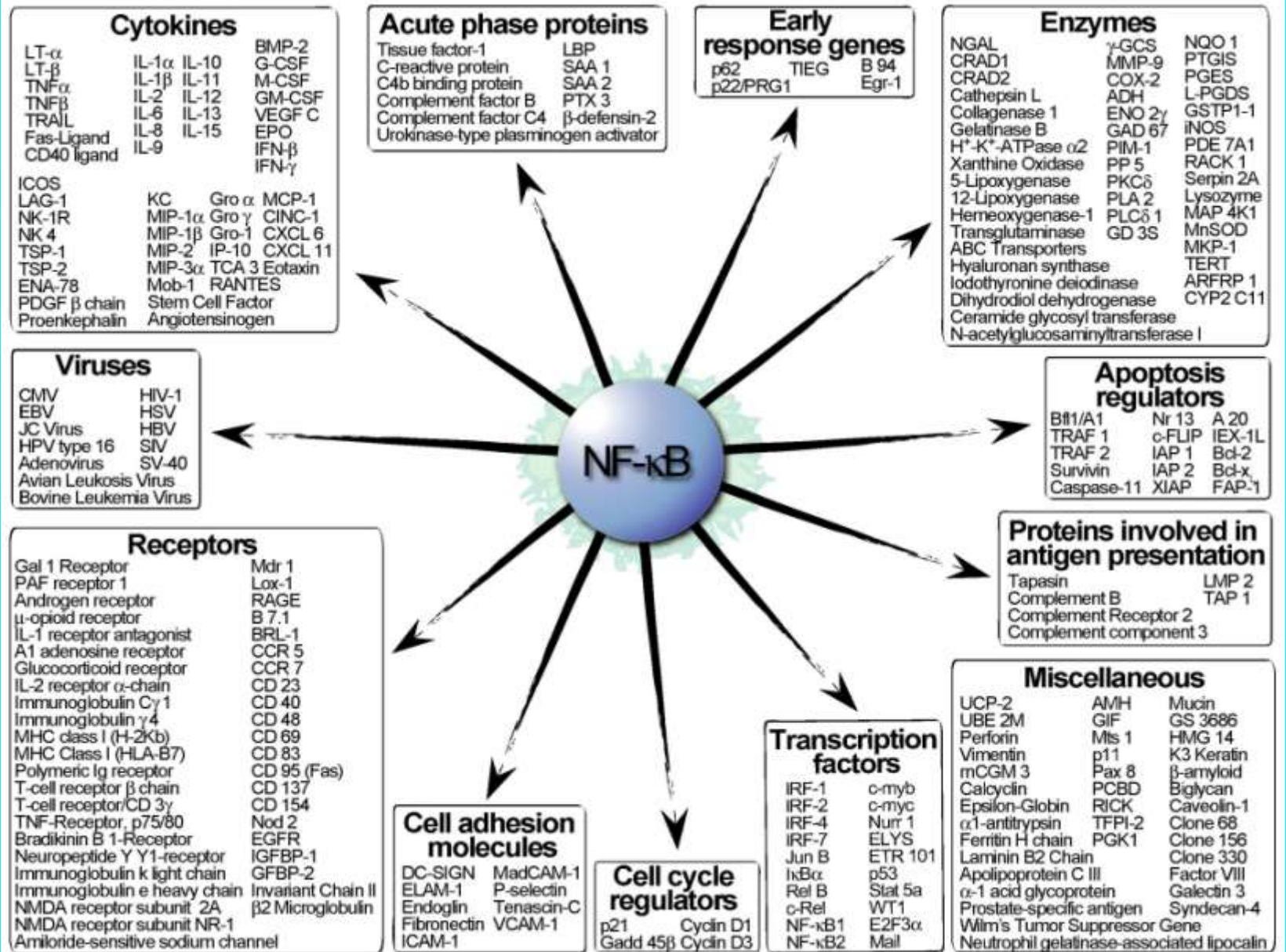


*(81g CHO, 51g fat; 32 g protein=910 kcal) finished in 15 min.*

➤ *Control subject: (N=8; BMI=24.3; 26-50 y) given 300ml water*

➤ *Blood samples: 1, 2, 3 h after the meal.*

# NF- $\kappa$ B -regulated genes



**How to suppress  
NF- $\kappa$ B activation  
safely!**

***Chronic diseases  
caused by chronic  
inflammation  
requires chronic  
treatment!***

***.....Sloan School of  
Management at M.I.T. and  
the Harvard Business  
School has created  
Pharmer's Market,  
however, we need a  
Farmer's Market...***

***New York Times, November, 2009***



# Farmer's Market



**Fruits**



**Spices & condiments**



**Vegetables**



**Cereals**

***Hippocrates proclaimed  
~2500 years ago***

***“Let food be thy  
medicine  
and medicine be  
thy food”***

*To treat/prevent  
most chronic  
diseases, we need to  
“dial down” but not  
“turn off” of  
“multiple”, not  
“single” gene*



# ***Change in Paradigm!***

- *Most diseases including cancer is due to dysregulation of **multiple genes**.*
- ***Mono-targeted** drugs are unlikely to be an effective therapy.*
- ***Multi-targeted** drugs are needed*
- *Most natural products are designed for multi-targeting, **naturally**.*

# ***From exotic spice to modern drug?***

***Singh S.***

***Cell. 2007 Sep 7;130(5):765-8.***

***The global demand for more affordable therapeutics and concerns about side effects of commonly used drugs are refocusing interest on Eastern traditional medicines, particularly those of India and China.***

***Add spices to your life!***

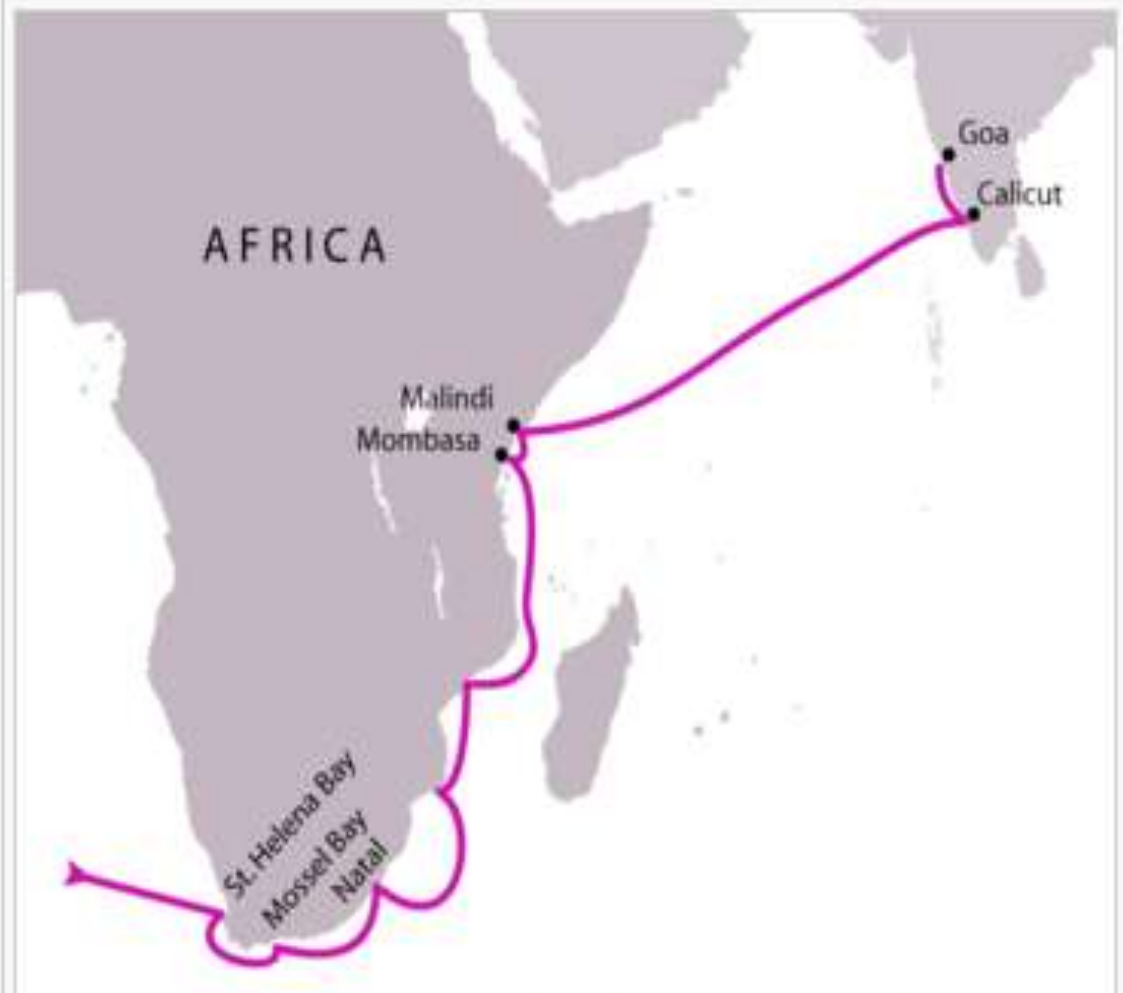




# Spice Route



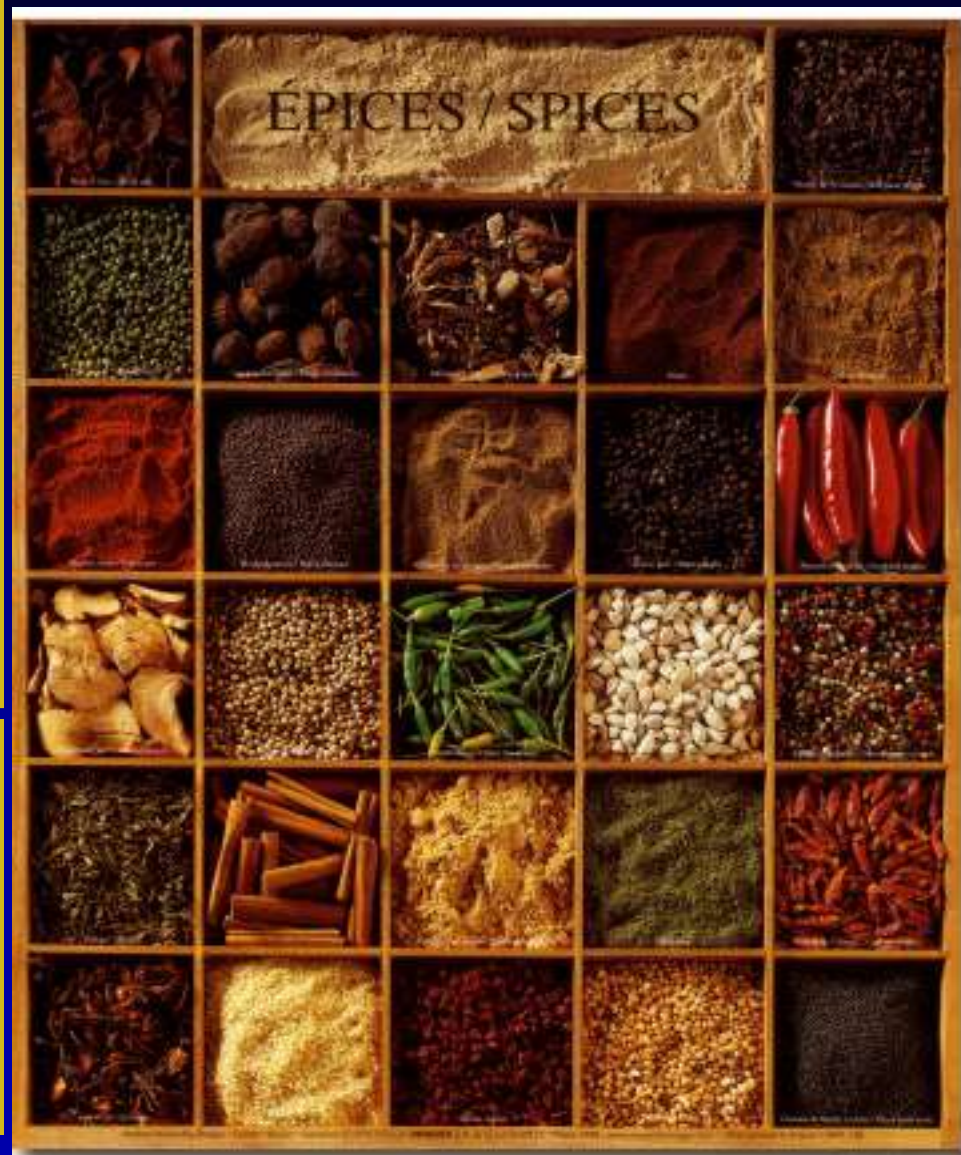
Vasco da Gama lands at Calicut,  
May 20, 1498.



The route followed in Vasco da Gama's first voyage (1497 - 1499).

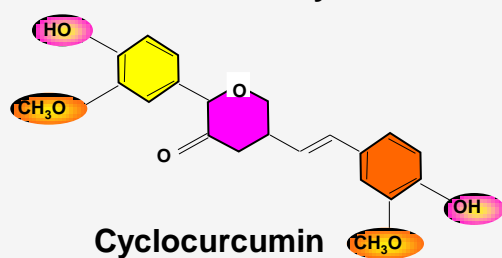
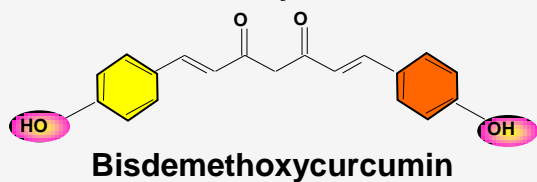
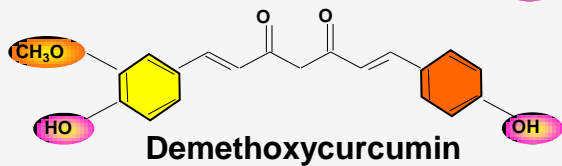
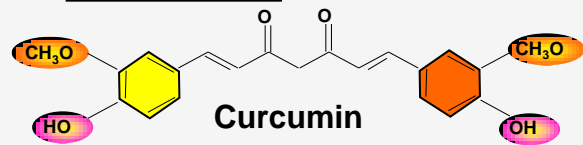


# ***Dietary Spices***

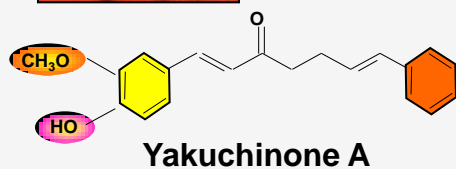




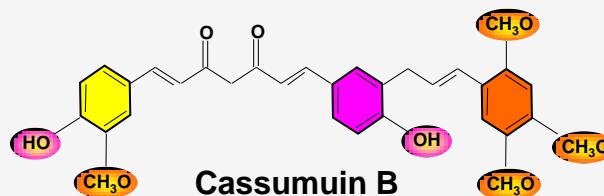
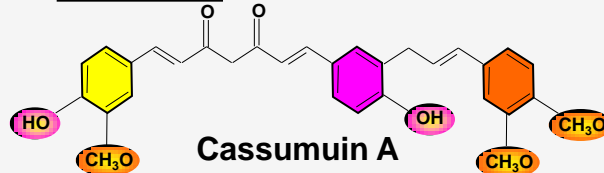
**Turmeric**



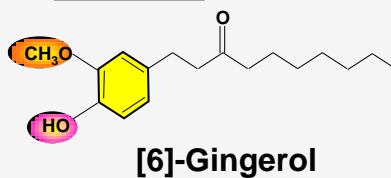
**Alpinia**



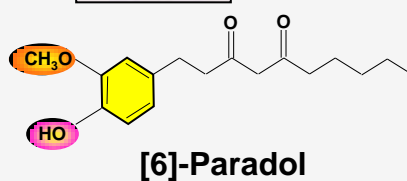
**Zingiber  
cassumunar**



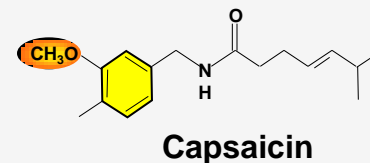
**Ginger**



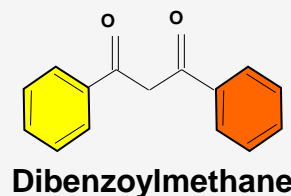
**Guinea  
pepper**



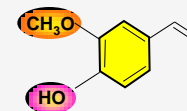
**Red chilli**



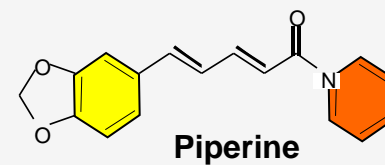
**Glycyrrhiza**



**Clove**



**Black  
Pepper**





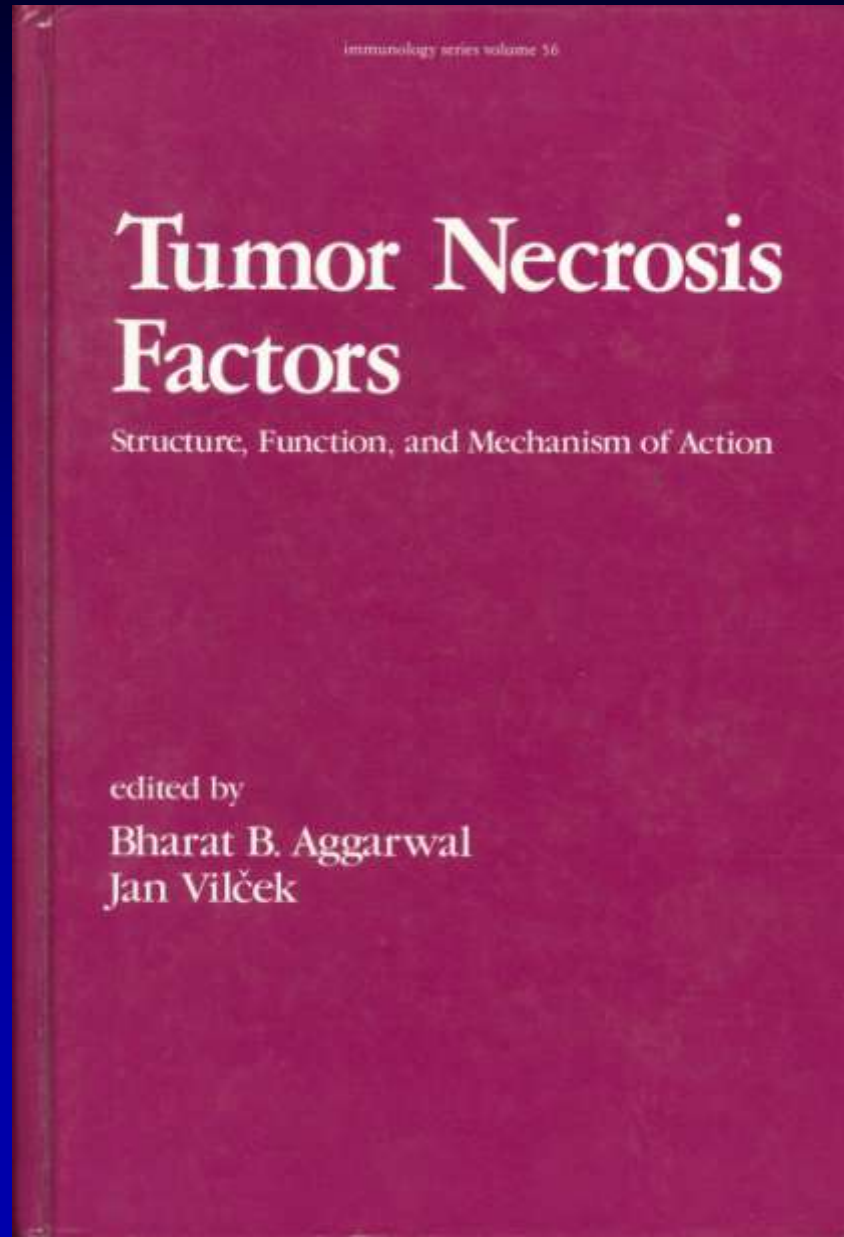
# ***Molecular Targets of Nutraceuticals Derived from Dietary Spices***

***Potential Role in Suppression of Inflammation and Tumorigenesis***

***Aggarwal B, Van Kuiken ME,  
Iyer LH, Harikumar KB, Sung B***

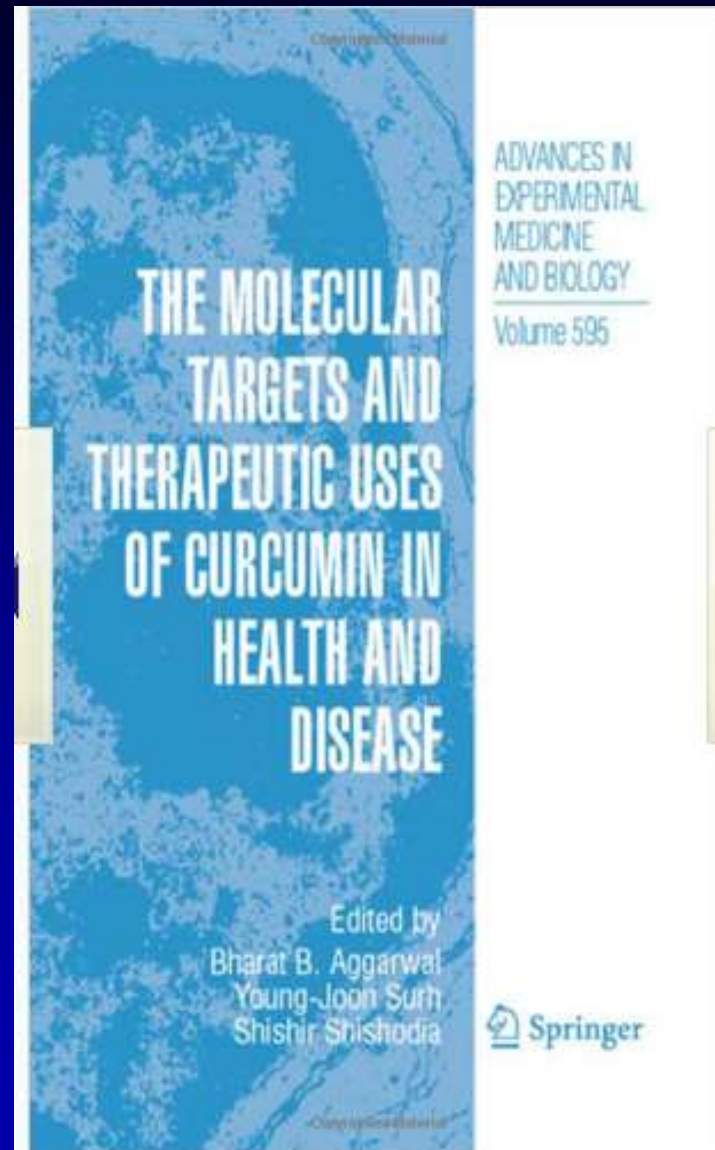
***Experimental Biology & Medicine  
2009 234(8):825-49.***

# TNF blockers

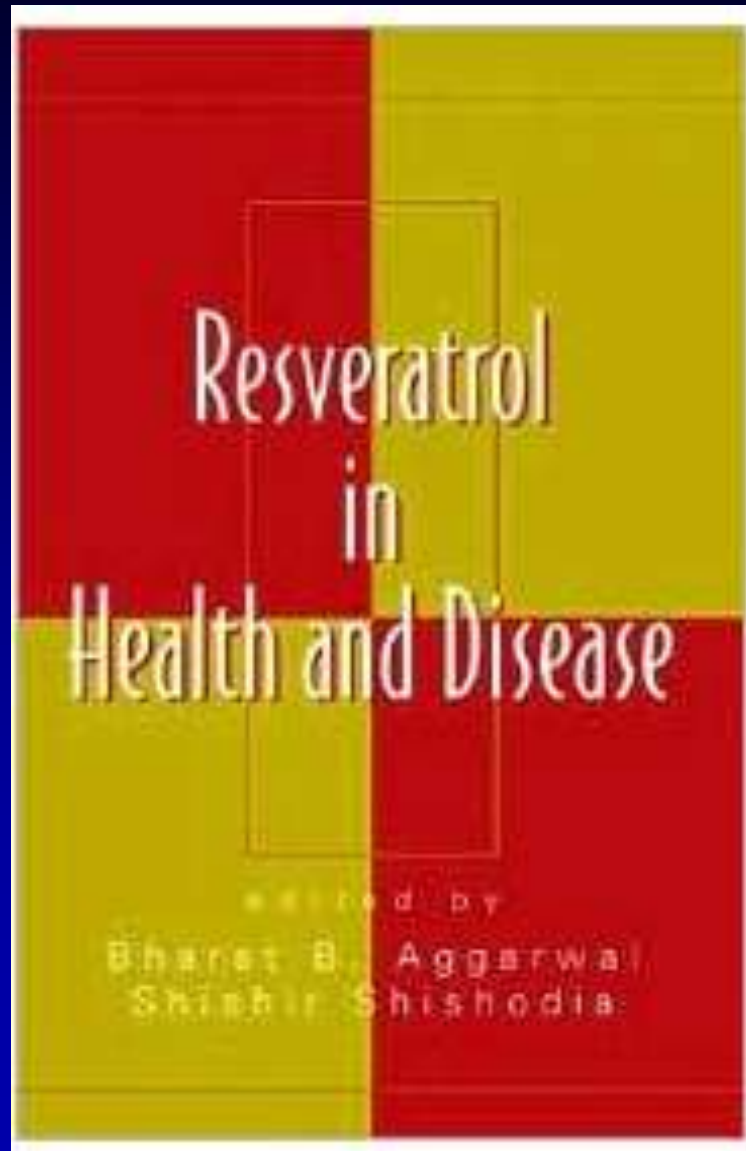




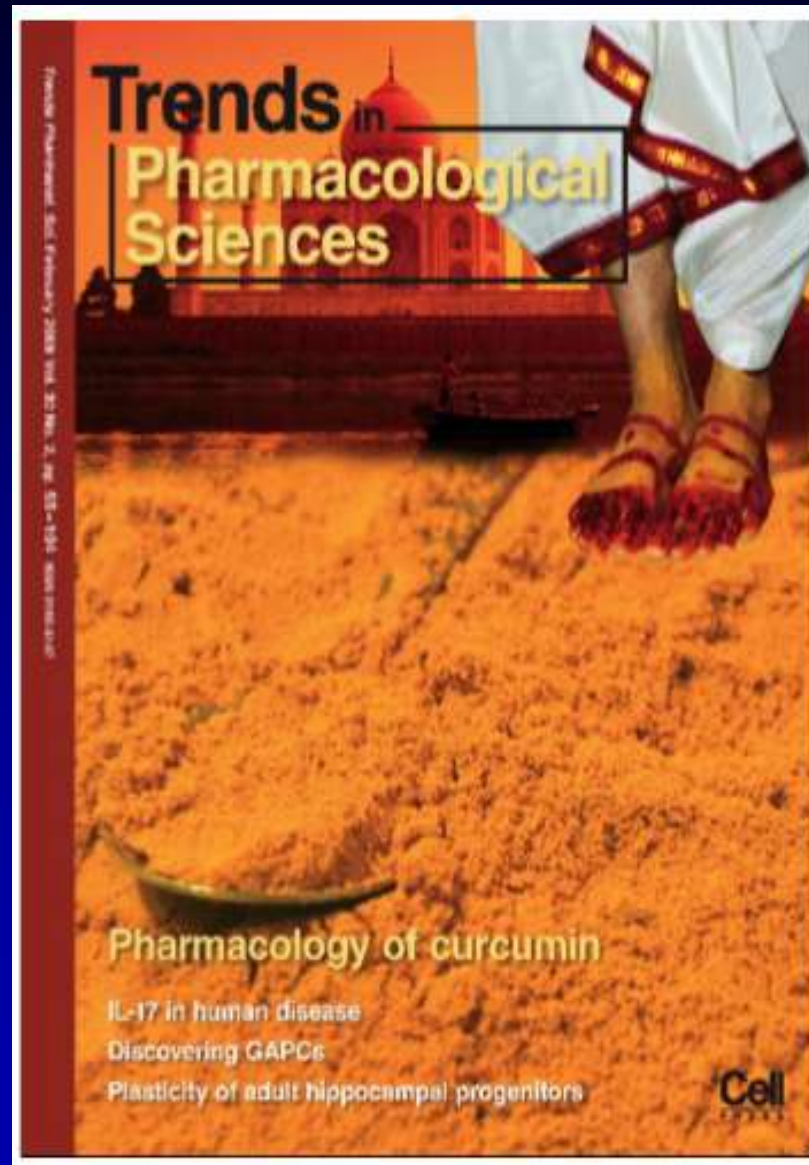
# TNF blockers



# TNF blockers



# TNF blockers



# TNF blockers

## INFLAMMATION, LIFESTYLE, AND CHRONIC DISEASE THE SILENT LINK

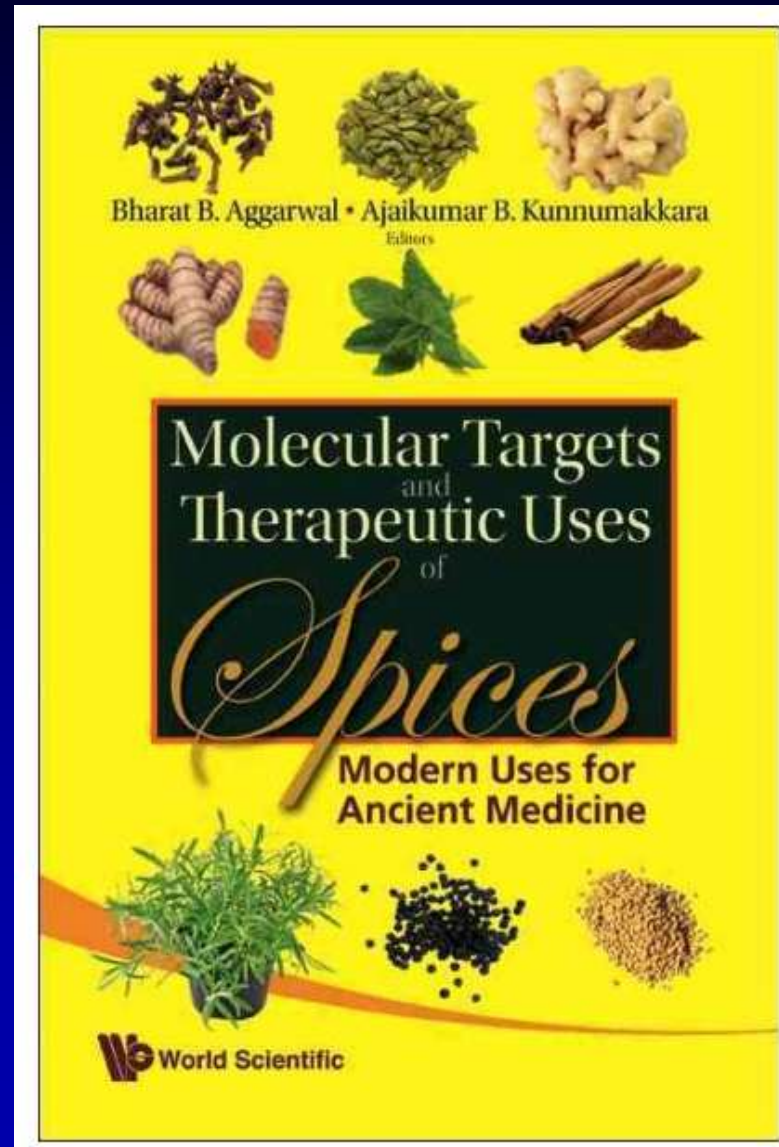


EDITED BY

BHARAT B. AGGARWAL • SUNIL KRISHNAN • SUSHOVAN GUHA

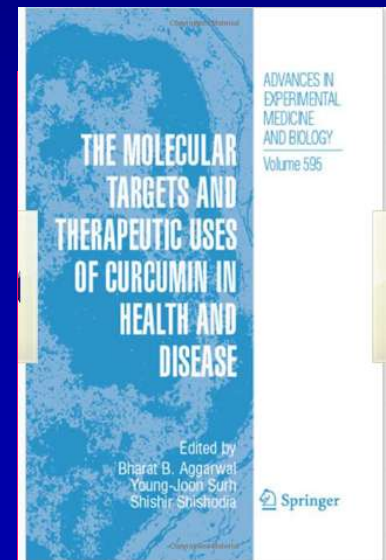
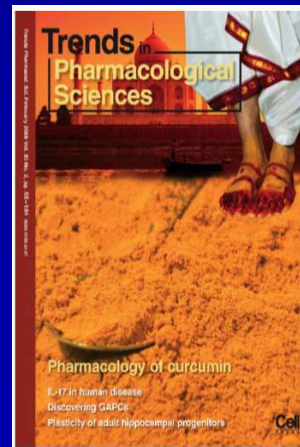
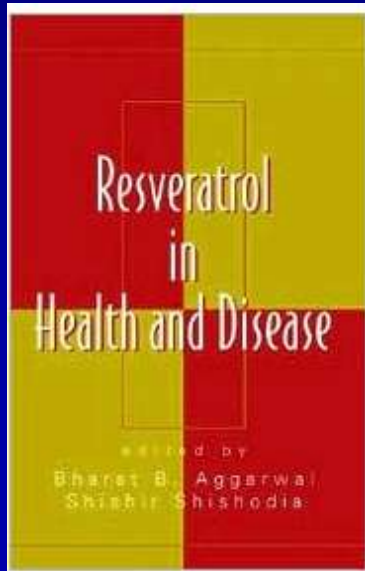
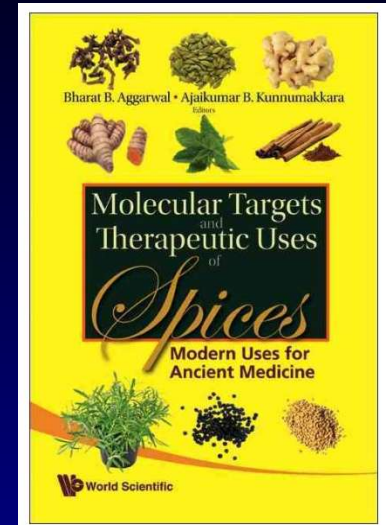
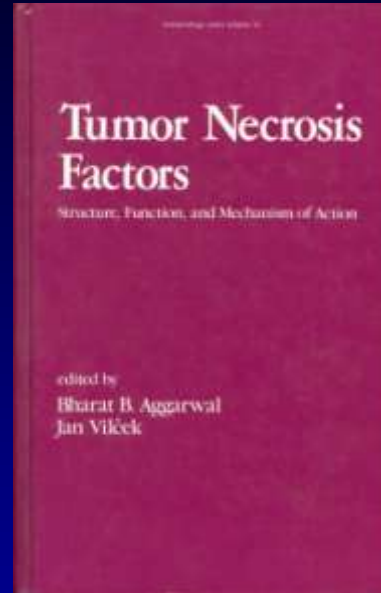
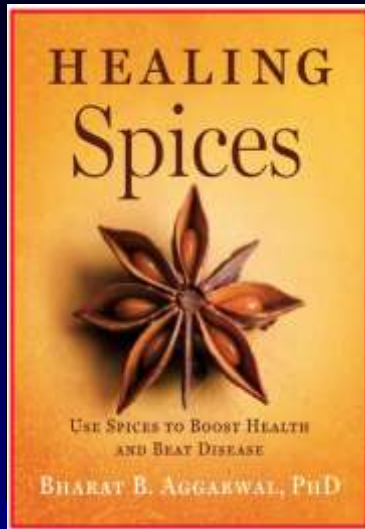
 **CRC Press**  
Taylor & Francis Group

# TNF blockers

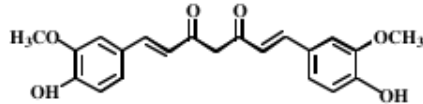




# TNF blockers

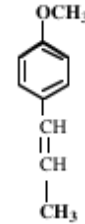


# Spices as NF-κB Inhibitors

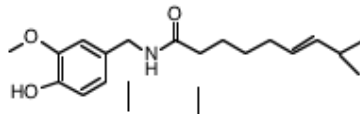


*Curcuma longa*  
Turmeric

Curcumin

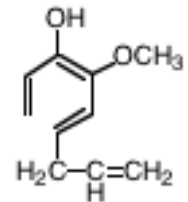


*Foeniculum vulgare* Anethole  
Fennel

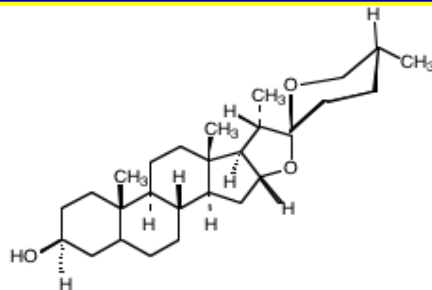


*Capsicum annum*  
Red chilli

Capsaicin

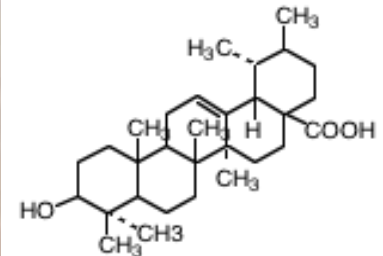


*Eugenia caryophyllata* Eugenol  
Cloves



*T. foenum-graecum*  
Fenugreek

Diosgenin



*Ocimum sanctum*  
Holi basil

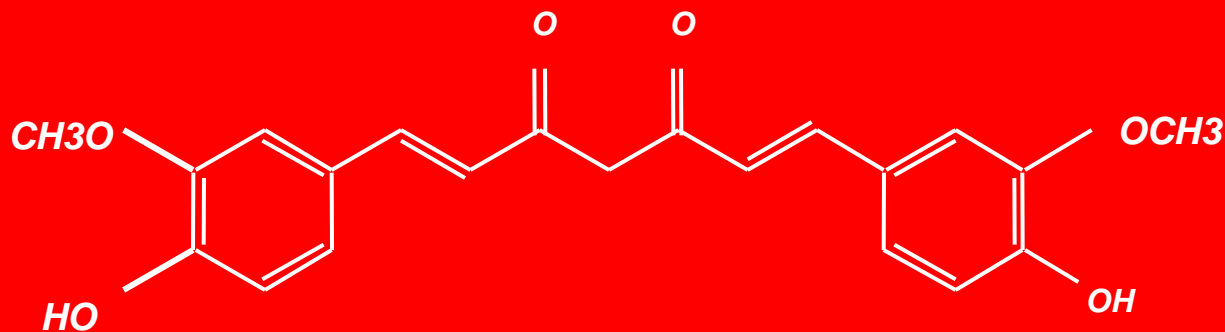
Ursolic Acid

***Curcumin:***  
***Getting Back***  
***to Our Roots!***



# Structure of Curcumin

## From turmeric (curry powder)

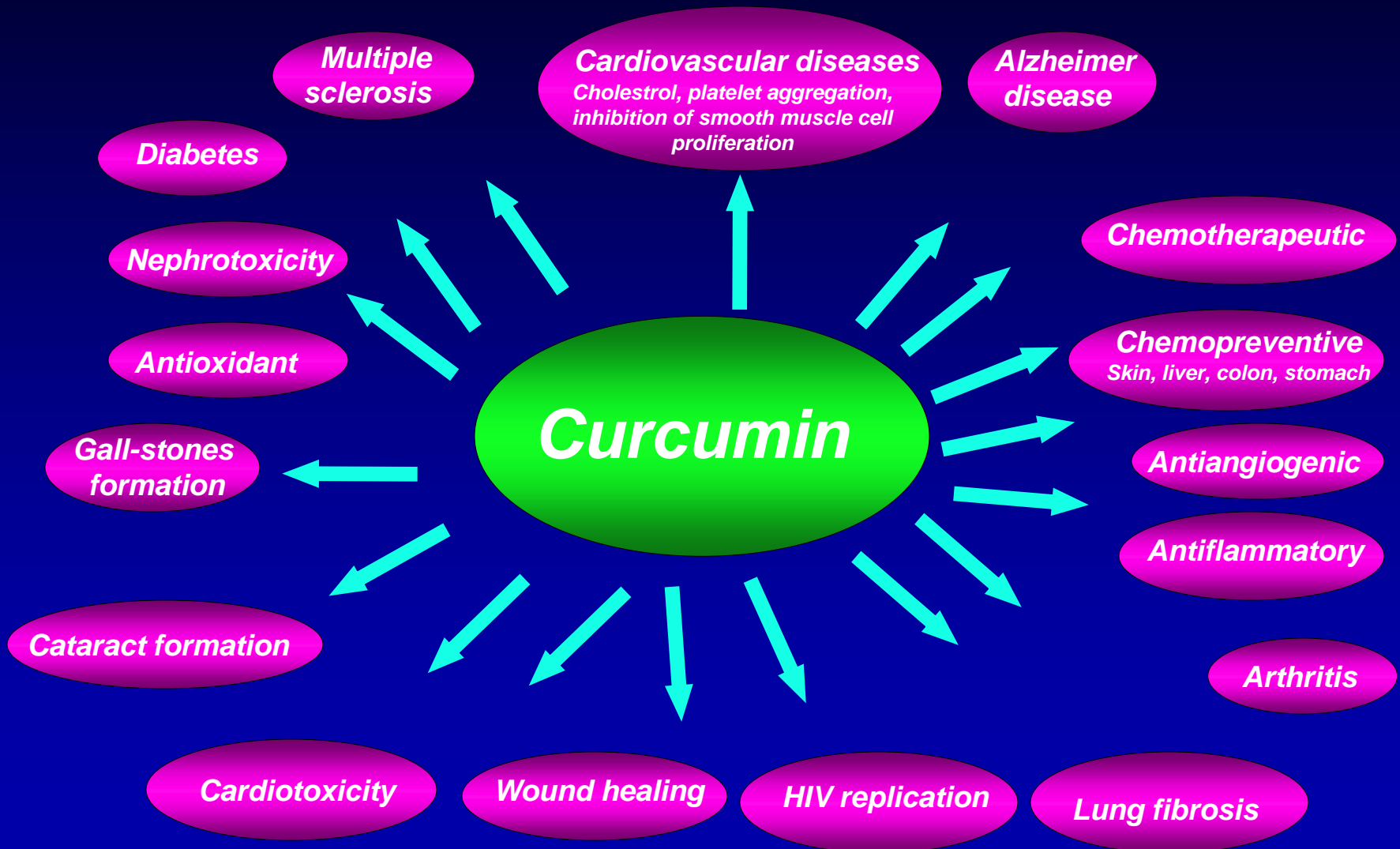


***Diferuloylmethane***

Milobedzka J., von Kostnecki St, and Lampe V: Zur Kenntnis des curcumins. Ber Deutsch Chem Ges, 1910, 43, 2163-2170



# ***Turmeric in India***

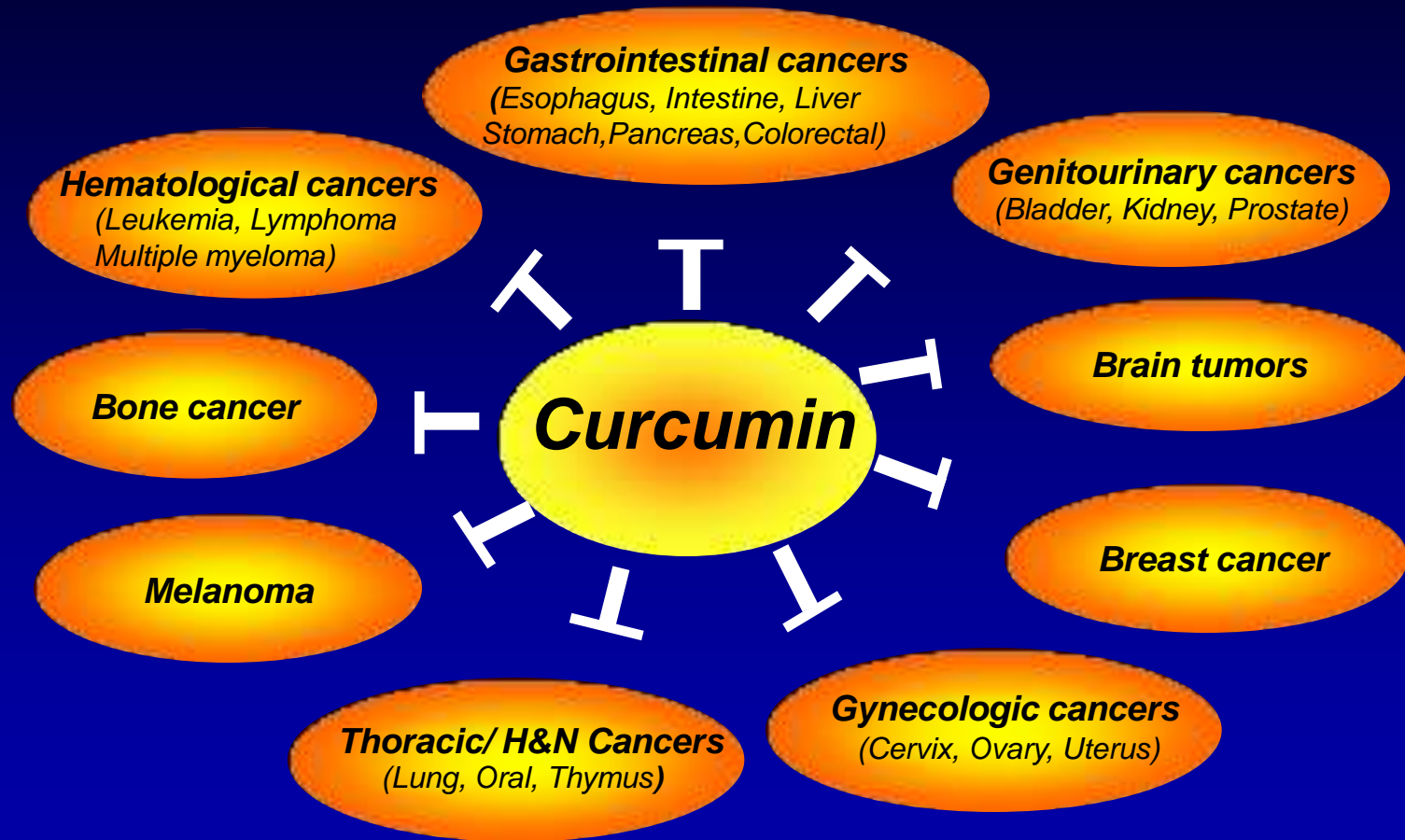


***Pharmacological basis for the  
role of curcumin in chronic  
diseases: an age-old spice with  
modern targets.***

***Aggarwal BB, Sung B.***

***Trends in Pharmacological Sciences  
2009 Feb;30(2):85-94.***

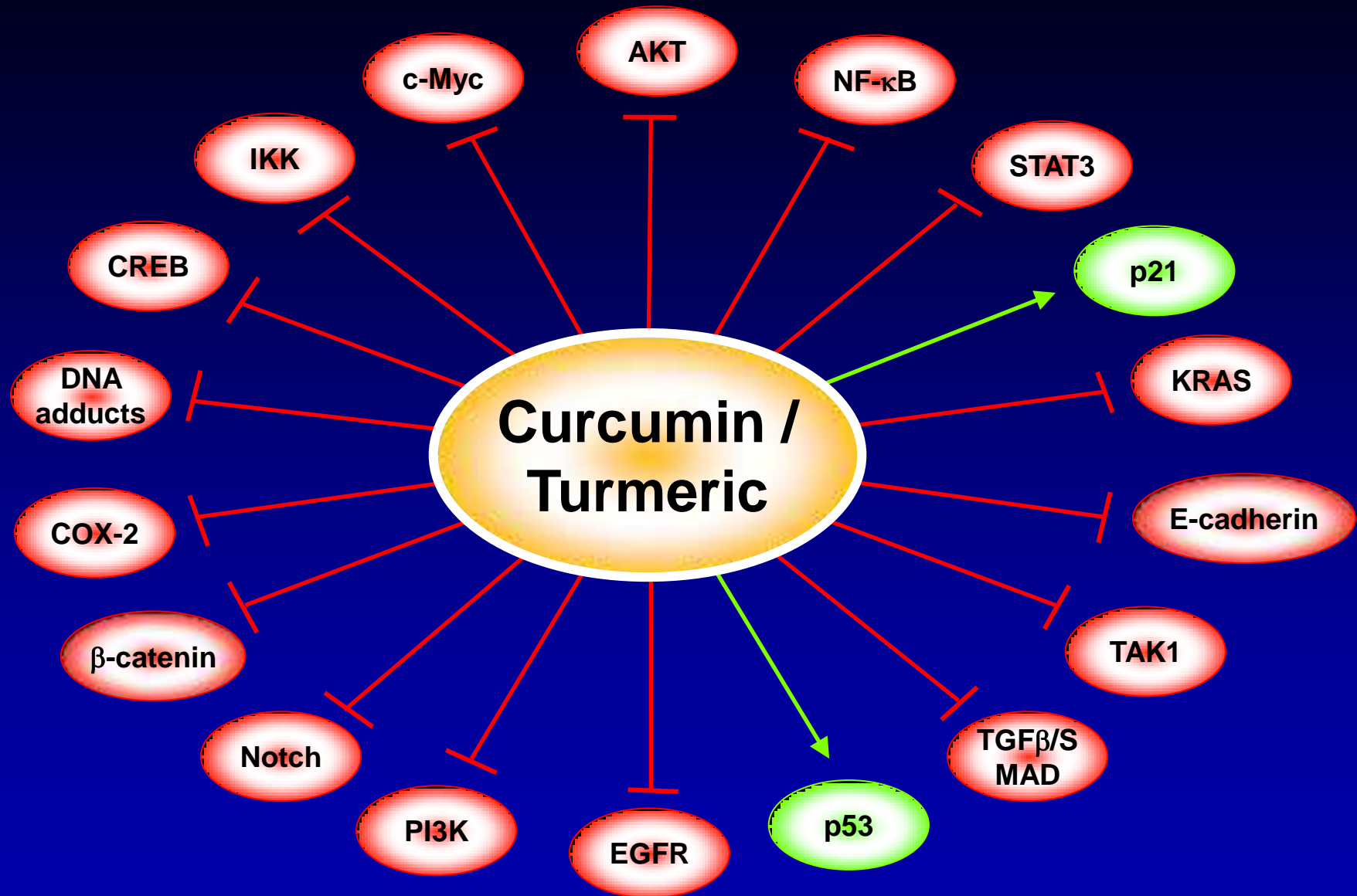
# ***Preclinical data with curcumin against various cancers***



***Curcumin in  
animal models!***



## *Multi-targeted Approach to Prevention of Colorectal Cancer by Curcumin/Turmeric*



# ***Curcumin as a chemo- sensitizer***

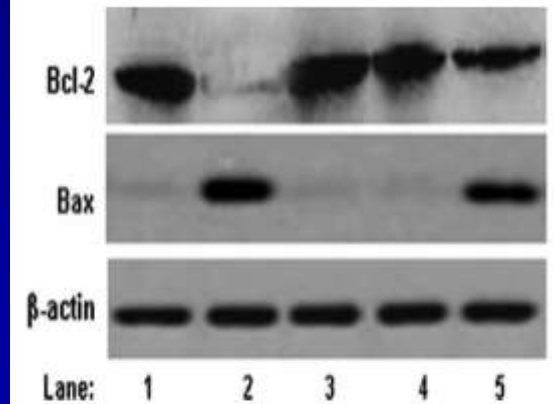
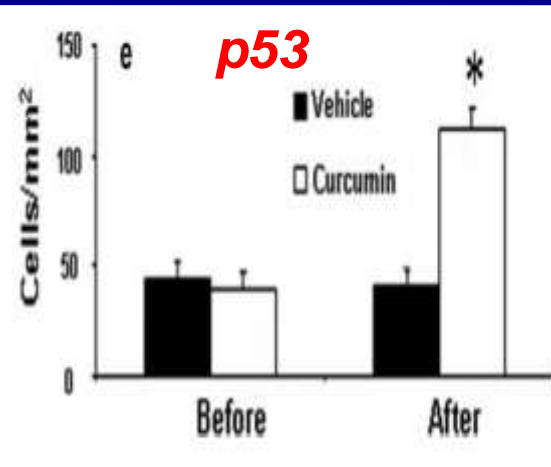
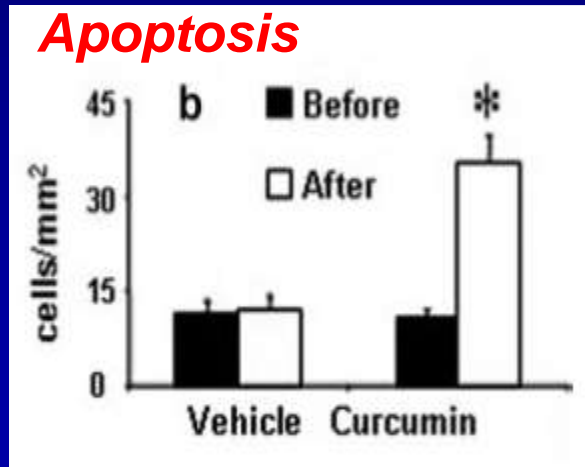
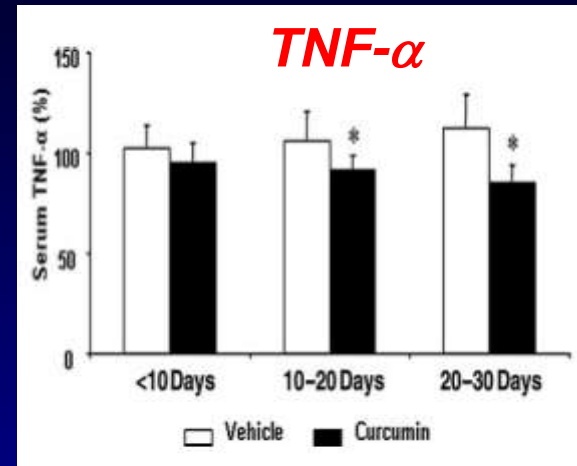
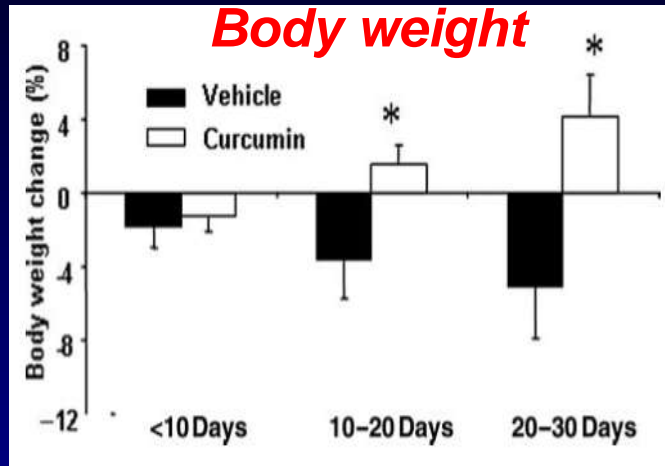
***Curcumin,***  
***the golden spice from Indian***  
***saffron, is a chemosensitizer and***  
***radiosensitizer for tumors and***  
***chemoprotector and radioprotector***  
***for normal organs.***

***Goel A, and Aggarwal BB.***

***Nutrition and Cancer***  
***2010 Oct;62(7):919-30.***

# Curcumin & CRC patients

126 pts; 360 mg curcumin; thrice/day



(He et al, 2011)



# ***Allspice***



***Allergies,***

***Asthma,***

***Cough,***

***Diarrhea,***

***Flatulence,***

***High blood pressure***





# ***Almonds***



***High cholestrol,  
Diabetes,  
Cardiovascular disease,  
High blood pressure,  
Obesity,  
Stroke***



# ***Amchur***



***Benign prostatic hypertrophy,***

***Cancer,***

***Diabetes,***

***Periodontal disease,***

***Cardiovascular disease,***

***Thyroid***



# ***Aniseeds***

***Asthma,***

***Bad breadth,***

***Colic,***

***Constipation,***

***Flatulence,***

***Ulcer,***

***Dehydration***



# ***Asafoetida***



***Cancer,***  
***Flatulence,***  
***Flu,***  
***Irritable bowel syndrome***



# ***Basil***



***Stress,***

***Cancer,***

***Cholestrol,***

***Conjunctivities,***

***Diabetes,***

***Cardiovascular diseases,***

***Malaria,***

***Pain***





# ***Bay leaves***



***Arthritis,***

***Cancer,***

***Diabetes,***

***Food poisoning,***

***Mosquito bites,***

***Ulcer,***

***Wounds***



# ***Black cumin***



***Immune decline,***

***Allergies,***

***Asthma,***

***Cancer,***

***Low-density lipoprotein,***

***Dermatitis,***

***Eczema,***

***Epilepsy,***



# ***Black pepper***



***Alzheimer's disease,***

***Arthritis,***

***Cancer,***

***Constipation,***

***Depression,***

***High blood pressure,***

***Memory loss,***

***Thyroid,***



# ***Caraway***



***Cancer,***

***Low-density lipoprotein,***

***Constipation,***

***Diabetes,***

***Food poisoning,***

***Heartburn,***

***Indigestion,***

***Tuberculosis***



# ***Cardamom***



***Asthma, bad breadth,***

***Blood clots,***

***Colon cancer,***

***Diarrhea,***

***Cardiovascular disease,***

***High blood pressure,***

***Indigestion,***

***Sinusitis,***

***Ulcer***





# ***Celery***

***Arthritis,***

***Low-density lipoprotein,***

***Gout,***

***High blood pressure,***

***Liver disease,***

***Menstrual cramps,***

***Stroke,***

***Ulcer,***

***Vaginal yeast infection***





# ***Chili***

***Arthritis,***

***Blood clots,***

***Cancer,***

***Low-density lipoprotein,***

***Diabetes,***

***Headache,***

***Tension,***

***Cardiovascular disease,***

***Indigestion,***

***Overweight,***





# ***Cinnamon***



***Cancer,***

***Low-density lipoprotein,***

***Diabetes,***

***Food poisoning,***

***Cardiovascular disease,***

***High blood pressure,***

***Stroke,***

***Ulcer,***

***Polycystic ovarian syndrome,***



# **Cloves**



*Bad breadth,*

*Blood clots,*

*Cancer,*

*Cold sores,*

*Food poisoning,*

*Genital herpes,*

*Gingivitis,*

*Hepatitis C,*

*Ulcer*



# Cocoa



*Alzheimer's disease,  
Low-density lipoprotein,  
Dementia,  
Diabetes,  
Fatigue,  
Cardiovascular disease,  
High blood pressure,  
Memory loss,  
Stroke,*



# ***Coconuts***



***Acne,***  
***Alzheimer's disease,***  
***Cancer,***  
***Crohn's disease,***  
***Infection,***  
***Overweight,***  
***Pain,***  
***Vaginal yeast infection.***





# ***Coriander***



***Bloating,***  
***Cardiovascular disease,***  
***Colon cancer,***  
***Diabetes,***  
***Diarrhea,***  
***Eczema,***  
***High blood pressure,***  
***Inflammatory bowel disease,***  
***Liver disease,***  
***Psoriasis,***



# ***Cumin***



***Cancer,***  
***Diabetes,***  
***Epilepsy,***  
***Food poisoning,***  
***Osteoporosis,***  
***Tuberculosis***



# ***Curry leaf***



***Alzheimer's disease,  
Low-density lipoprotein,  
Colon cancer,  
Diabetes,  
Memory loss***



# ***Fennel***

***Alzheimer's disease,***

***Arthritis,***

***Cancer,***

***Colitis,***

***Dementia,***

***Glaucoma,***

***Heart disease,***

***High blood pressure,***

***Stroke***





# ***Fenugreek***



***Cancer,***

***Cataracts,***

***Low-density lipoprotein,***

***Diabetes,***

***Gallstones,***

***Infection,***

***Insulin resistance (pre-diabetes),***

***Kidney stones,***

***Liver diseases,***



# ***Galangal***



***Allergies,***

***Arthritis,***

***Cancer,***

***Diabetes,***

***Ulcer***





# ***Garlic***



***Alopecia,***  
***Benign prostatic hypertrophy,***  
***Cancer,***  
***Low-density lipoprotein,***  
***Colds, Flu,***  
***Diabetes,***  
***Cardiovascular disease,***  
***Sickle cell disease,***  
***Stroke,***  
***Wrinkles and Aging***



# ***Ginger***

*Arthritis,*

*Asthma,*

*Cancer,*

*Low-density lipoprotein,*

*Heart attack,*

*Heartburn,*

*Indigestion,*

*Nausea,*

*Stroke*





# ***Horseradish***



***Bronchitis,***

***Cancer,***

***Low-density lipoprotein,***

***Ear infection,***

***Flu,***

***Pneumonia,***

***Sinusitis,***

***Urinary tract infection***



# ***Juniper berry***

***Arthritis,***

***Osteo and rheumatoid,***

***Bronchitis,***

***Breast cancer,***

***Diabetes,***

***Fungal infection,***

***Heart failure,***

***Hemorrhoids,***

***Hypertension,***





# ***Kokum***



***Cancer,  
Indigestion,  
Overweight,  
Rash,  
Ulcer***



# ***Lemongrass***



*Anxiety,*

*Cancer,*

*Low-density lipoprotein,*

*Diabetes,*

*Epilepsy,*

*Insomnia,*

*Thrush,*

*Vaginal yeast infection*





# ***Marjoram***



***Alzheimer's disease,***

***Blood clots,***

***Cancer,***

***Fungal infection,***

***Heart disease,***

***Indigestion,***

***Stroke,***

***Ulcer***



# ***Mint***



***Allergies,***

***Anxiety,***

***Breastfeeding problem,***

***Cancer,***

***Chronic obstructive pulmonary disease,***

***Menopause problems,***

***Nausea,***

***Stress,***

***Tooth decay***



# ***Mustard seed***



***Benign prostatic hypertrophy,***

***Cancer,***

***Low-density lipoprotein,***

***Chronic obstructive pulmonary  
disease,***

***Diabetes,***

***Heart disease,***

***Insulin resistance (pre-diabetes)***



# ***Nutmeg***



***Anxiety,***

***Cancer,***

***Low-density lipoprotein,***

***Depression,***

***Diarrhea,***

***Epilepsy,***

***Memory loss,***

***Sexual desire low***



# ***Onion***



***Allergies,***

***Benign prostatic hypertrophy,***

***Cancer,***

***Low-density lipoprotein,***

***Diabetes,***

***Heart attack, Heart disease,***

***Hypertension,***

***Osteoporosis,***

***Scars***



# ***Oregano***



*Age spots,  
Alzheimer's disease,  
Cancer,  
Low-density lipoprotein,  
Colitis,  
Heart disease,  
Parasitic infection,  
Insulin resistance (pre-diabetes),  
liver disease,*



# ***Parsley***



***Cancer,  
Constipation,  
Diabetes,  
Heart disease,  
Ulcer***





# ***Pomegranate***

*Alzheimer's disease,*

*Angina,*

*Arthritis,*

*Osteo and Rheumatoid,*

*Atherosclerosis,*

*Cancer,*

*Colitis,*

*Diabetes,*

*Hypertension,*





# ***Pumpkin seed***



***Anemia,***

***Arthritis,***

***Rheumatoid,***

***Benign prostatic hypertrophy,***

***Low-density lipoprotein,***

***Heart disease,***

***Urinary incontinence,***



# ***Rosemary***



***Anxiety,***

***Arthritis,***

***Osteo and rheumatoid, Dermatitis,***

***Cancer,***

***Depression,***

***Diabetes,***

***Heart disease, Liver disease,***

***Memory loss,***

***Stress, Ulcer,***



# ***Saffron***

***Alzheimer's disease,***

***Anxiety, Insomnia,***

***Atherosclerosis,***

***Cancer,***

***Depression,***

***Infertility,***

***Memory loss,***

***Parkinson's disease,***

***Premenstrual syndrome***





# ***Sage***



***Alzheimer's disease,***

***Anxiety,***

***Cancer,***

***Dermatitis,***

***Diabetes,***

***Eczema,***

***Heart disease,***

***Memory loss,***

***Psoriasis,***



# ***Sesame seed***



***Alzheimer's disease,***

***Cancer,***

***Low-density lipoprotein,***

***Heart disease,***

***Hypertension,***

***Huntington's disease,***

***Wounds***



# ***Star anise***



***Cancer,***

***Cold sores,***

***Flu,***

***Hepatitis B,***

***HIV/AIDS,***

***Mononucleosis,***

***Septic shock,***

***Tooth decay***





# ***Tomato***



***Cancer,***  
***Low-density lipoprotein,***  
***Dementia,***  
***Heart disease,***  
***Hypertension,***  
***Infertility (male),***  
***Osteoporosis,***  
***Parkinson's disease***



# ***Tamarind***



***Cancer,***

***Cataracts,***

***Low-density lipoprotein,***

***Conjunctivitis,***

***Diabetes,***

***Eye infection,***

***Heart disease,***

***Hypertension,***



# ***Thyme***



***Aging,  
Alcohol abuse,  
Cancer,  
Bronchitis (acute),  
Colitis,  
Cough, Flu,  
Heart attack,  
Bacterial infection,  
Stroke,***



# ***Turmeric***



***Acne,***

***Allergies,***

***Alzheimer's disease,***

***Arthritis,***

***Osteo and rheumatoid,***

***Asthma,***

***Cancer,***

***Dermatitis,***

***Diabetes,***

***Depression,***



# ***Vanilla***



***Cancer,  
Sickle cell disease***



# ***Wasabi***



***Blood clots,***  
***Cancer,***  
***Low-density lipoprotein,***  
***Eczema,***  
***Food poisoning,***  
***Osteoporosis,***  
***Tooth decay,***  
***Ulcer***

***What is the  
best way to  
consume these  
spices?***



# Add Spice to Your Life (Dals)





# Add Spice to Your Life (Sabji)



# Add Spice to Your Life (Sabji)





# Comparison of Cancer Incidence in USA and India

Cancer	USA		India	
	Cases	Deaths	Cases	Deaths
Breast	660	160	79	41
Prostate	690	130	20	9
Colon/Rectum	530	220	30	18
Lung	660	580	38	37
Head & Neck SCC	140	44	153	103
Liver	41	44	12	13
Pancreas	108	103	8	8
Stomach	81	50	33	30
Melanoma	145	27	1.8	1
Testis	21	1	3	1
Bladder	202	43	15	11
Kidney	115	44	6	4
Brain, Nervous system	65	47	19	14
Thyroid	55	5	12	3
Endometrial Cancers	163	41	132	72
Ovary	76	50	20	12
Multiple myeloma	50	40	6	5
Leukemia	100	70	19	17
Non-Hodgkin lymphoma	180	90	17	15
Hodgkin's disease	20	5	7	4

Showing cases per 1 million persons calculated on the basis of current consensus: Endometrial cancers include Cervix uteri and Corpus uteri.

GLOBOCAN 2000: Cancer Incidence, Mortality and Prevalence Worldwide, Version 1.0. IARC Cancer Base No. 5. Lyon, IARC Press, 2001.



# ***Thank you!***

***Arigato! Teşekkür ederim! Obrigado! Thank you! Namaste! Merci! Gamsa hamnida!  
Terima Kasih! Kiitos! Gracias! Shalom! Shei-shei! Do Jeh! Danke!***

