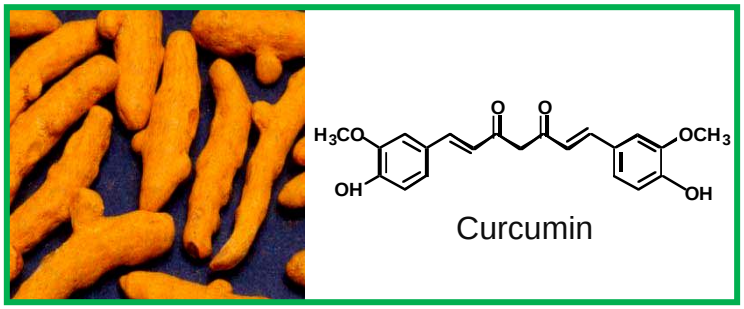


Curcuma longa
Turmeric

Prof Attilio Giacosa

Gastroenterologo

UNIVERSITA' di Pavia

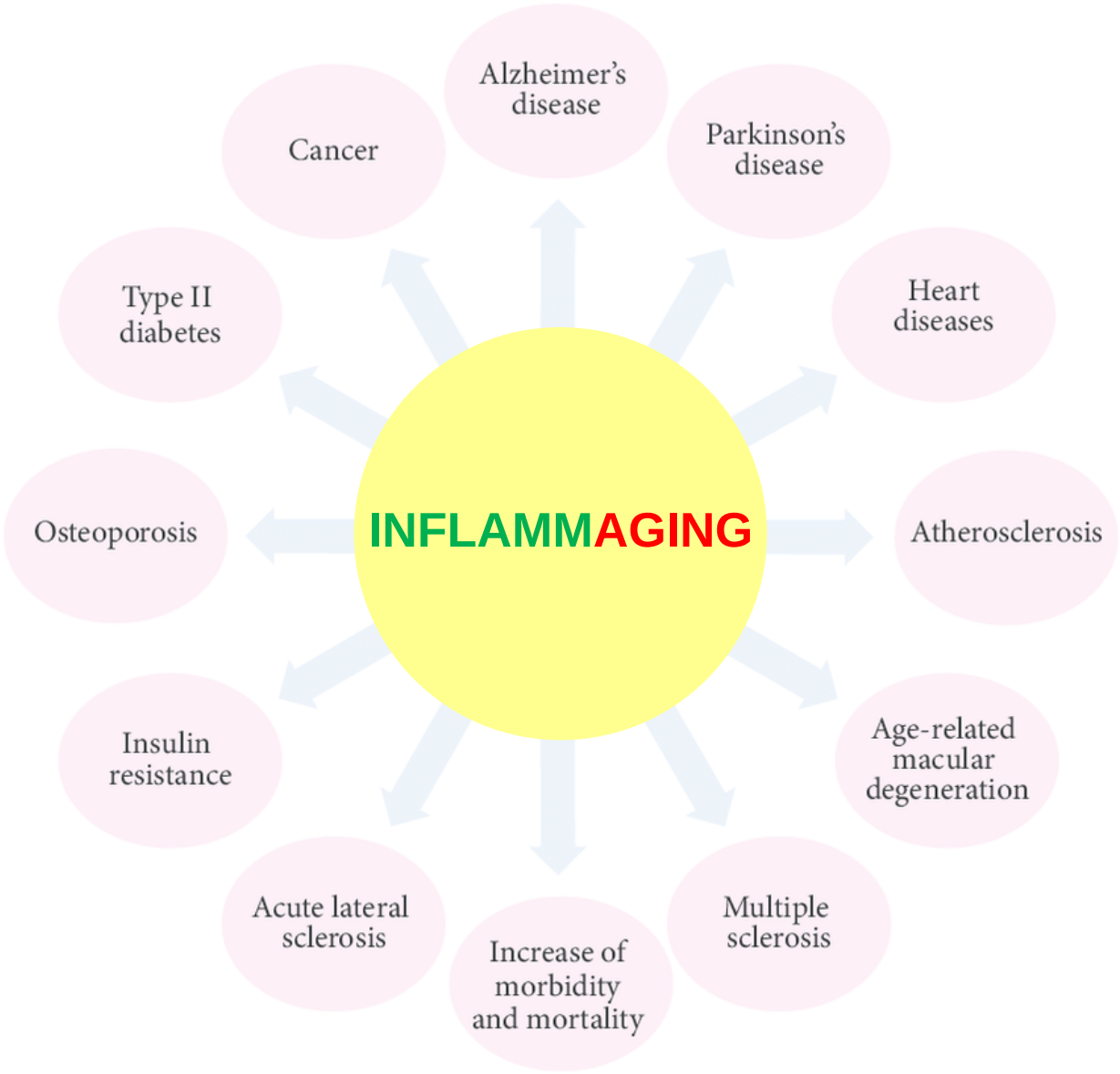
HUMANITAS San Pio X , Milano

INFLAMMAGING

A RAMPANT ISSUE IN
SCIENTIFIC LITERATURE AND DIVULGATIVE PRESS IN THE LAST YEARS

TIME Feb. 23, 2004

INFLAMMAGING:
THE COMMON SOIL OF AGE-RELATED DISORDERS



Curcuma longa L.

(Zingiberacee)

Plants (mostly edible) for an antiinflammatory diet

Spices


Asian ginger)
(*Alpinia galanga*)


Cloves
(*Eugenia caryophyllu*)


Fennel
(*Foeniculum vulgare*)


Fenugreek
(*Trigonella foenum graecum*)


Gamboge
(*Garcinia hanburyi*)


Holy basil
(*Ocimum sanctum*)


Onion
(*Allium cepa*)


Onion seed
(*Nigella sativa*)


Poppy seed
(*Papaver somniferum*)


Pomegranate
(*Punica granatum*)


Red chili
(*Capsicum annum*)


Sesame seed
(*Sesamum indicum*)


Turmeric
(*Curcuma longa*)

Ayurvedic Medicine


Aloe
(*Aloe vera*)


Ashwagandha
(*Withania somnifera*)


Boswellia
(*Boswellia serrata*)


Beauty berry
(*Callicarpa macrophylla*)


Chitrak
(*Plumbago zeylanica*)


False pepper
(*Embelia ribes*)


Guggulu
(*Commiphora mukul*)


Himalayan fir
(*Abies webbiana*)


Indigo
(*Polygonum tinctorium*)


Neem
(*Azadirachta indica*)


Picroliv
(*Picrorhiza kurroa*)


Pinecone ginger
(*Zingiber zerumbet*)


Rohitukine
(*Dysoxylum binectariferum*)


Veldt-grape
(*Cissus quadrangularis*)


Peacock ginger
(*Kaempferia oulchra*)

Fruits & Vegetables


Artichoke
(*Cynara cardunculus*)


Cauliflower
(*Brassica oleracea*)


Grapes
(*Vitis vinifera*)


Mullberry
(*Morus nigra*)


Soybean
(*Glycine max*)

Traditional Chinese Medicine


Evodia
(*Evodia rutaecarpa*)


Goldenseal
(*Hydrastis canadensis*)


God of thunder vine
(*Tripterygium wilfordii*)


Indigo
(*Polygonum tinctorium*)


Lacquer tree
(*Rhus verniciflua*)


Magnolia
(*Magnolia officinalis*)


Smoke tree
(*Cotinus coggygria*)

Song gen
(*Phellinus linteus*)

Others

Cottonseed oil
(*Gossypium*)

Cashew nut
(*Anacardium occidentale*)

Cork bush
(*Mundulea sericea*)

Elephant's foot
(*Elephantopus scaber Linn*)

Fire lily
(*Gloriosa superba*)

Ginger lily
(*Hedychium coronarium*)

Hop
(*Humulus lupulus L.*)

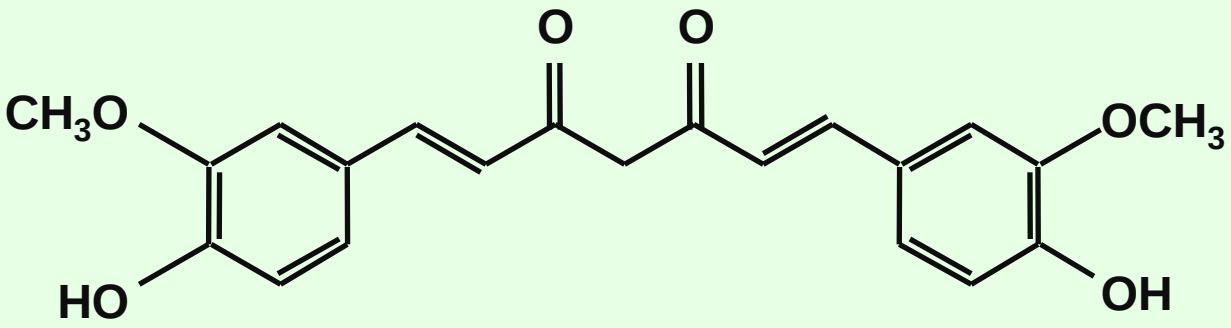
Horse chestnut
(*Aesculus hippocastanum*)

Palm
(*Elaeis guineensis*)

Oleander
(*Nerium oleander*)

Tropical rose mallow
(*Hibiscus vitifolius*)

Structure of Curcumin



Diferuloylmethane

Milobedzka J., von Kostnecki St, and Lampe V.

Zur Kenntnis des curcumins.

Ber Deutsch Chem Ges, 1910, 43, 2163-2170

8

INCREDIBLE HEALTH
BENEFITS OF TURMERIC

Boosts Cognitive Function

Curcumin protects brain cells by binding to and dissolving abnormal proteins.

Supports Joint & Muscle Health

Curcumin promotes a healthy inflammatory response and eases aches and pains.

Fights Body-Wide Inflammation

Curcumin has been proven to significantly lower levels of inflammatory markers.

Boosts Detoxification

Curcumin optimizes function of the liver, the body's primary organ of detoxification.

Supports Cardiovascular Function

Curcumin supports heart health by promoting a healthy inflammatory response.

Promotes Healthy Mood Balance

Curcumin has been shown to be an extremely effective natural mood enhancer.

Promotes Youthful Radiant Skin

Curcumin promotes soft, smooth, glowing skin and fights fine lines and wrinkles.

Supports Natural Weight Loss

Curcumin can enhance weight loss when combined with healthy diet and exercise.

Multi-targeted

Inflammatory cytokines
IL-1, IL-2, IL-5, IL-6, IL-8, IL-12, IL-8, MCP-1, MIP-1, MaIP

Enzymes
ATFase, ATPase, Desaturase, FPTase, GST, GCL, HO-1, iNOS, MMPs, NQO-1, ODC, PhPD, TIMP-3, 5-LOX, Telomerase

Growth factors
TGF β, FGF, HGF, PDGF, TF

Receptors
AR, AHR, CXCR4, DR, EGFR, ER-α, FasR, H2R, IL-8R, ITPR, IR, LD-R

Adhesion molecules
ELAM-1, ICAM-1, VCAM-1

Anti-apototic proteins
Bcl-2, BclxL, IAP-1

Protein Kinases
IKK, AAPK, Ca2+ PK, EGFR, ERK, FAK, IL-1 RAK, JAK, JNK, MAPK, PhK, PK, PKA, PKB, PKC, pp60c-src tK, PTK

Transcriptional factors
AP-1, β-Catenin, CBP, ERG-1, ERE, HIF-1, Notch-1, Nrf-2, NF-κB, PPAR-γ, STAT-1, STAT-3, STAT-4, STAT-5, WTG-1

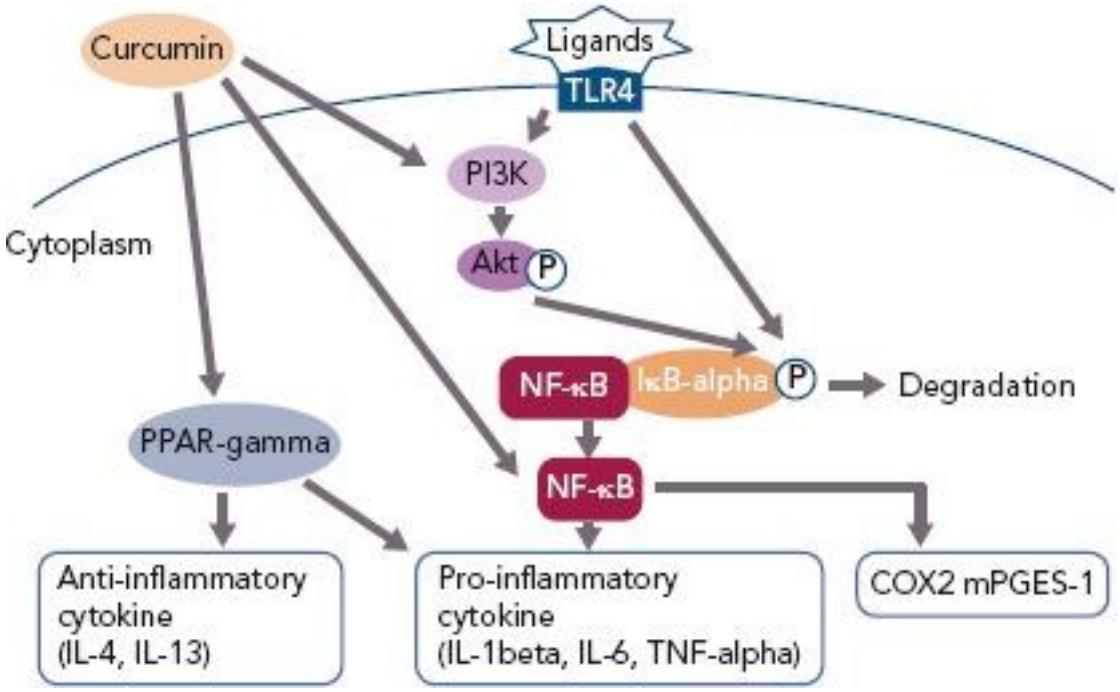
Others
Cyclin D1, Cyclin E, HsP 70, MDR

Curcumin Targets

Mono-targeted

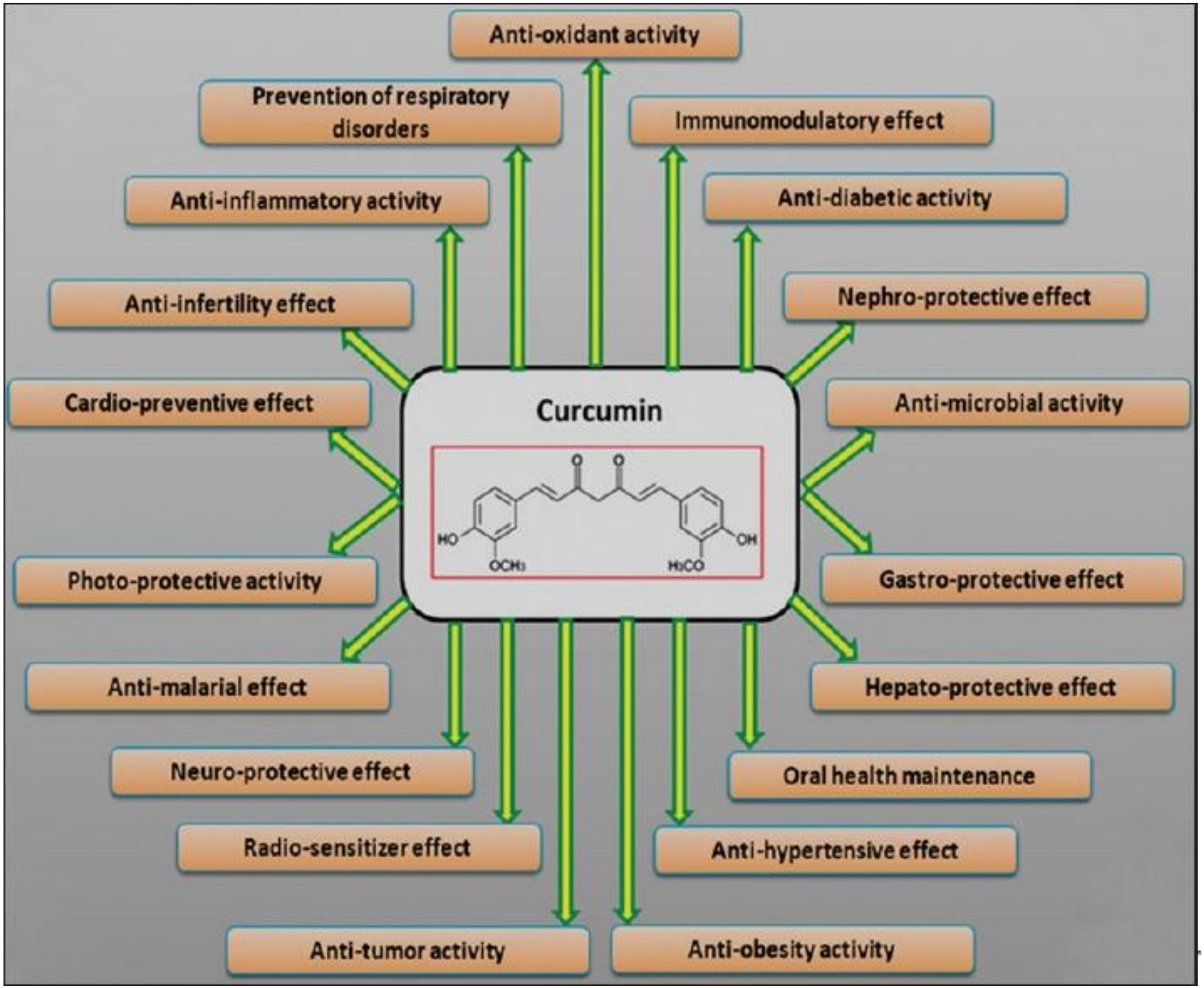
COX-2	Celecoxib
EGFR	Erbitux
TNF	Remicade Humira Enbrel
HER-2	Herceptin
Bcr-Abl	Gleevac
VEGF	Avastin
Tubulin	Paclitaxel
Topoisomerase	Camptothecin

Kunnumakkara et al., Cancer Lett. 269, 199-225 (2008)



The Mechanisms of Curcumin Action on Inflammation

COX2 = cyclooxygenase-2; IκB = inhibitor of kappaB; IL = interleukin; mPGES-1 = microsomal prostaglandin E synthase-1; NF-κB = nuclear factor-kappaB; PI3K = phosphatidylinositol-3 kinase; PPAR-gamma = peroxisome proliferator-activated receptor-gamma; TLR4 = toll-like receptor 4; TNF-alpha = tumour necrosis factor-alpha.


Anti-oxidant activity
Prevention of respiratory disorders
Immunomodulatory effect
Anti-inflammatory activity
Anti-diabetic activity
Anti-infertility effect
Nephro-protective effect
Cardio-preventive effect
Curcumin
Anti-microbial activity
HO
OCH3
OH
H3CO
Photo-protective activity
Gastro-protective effect
Anti-malarial effect
Hepato-protective effect
Neuro-protective effect
Oral health maintenance
Radio-sensitizer effect
Anti-hypertensive effect
Anti-tumor activity
Anti-obesity activity

Altern Ther Health Med. 2013 Mar-Apr;19(2):20-2.

Clinical utility of curcumin extract.

Asher GN[1], Spelman K.
University of North Carolina, Chapel Hill, North Carolina, USA

Preclinical studies point to mechanisms of action that are predominantly anti-inflammatory and antineoplastic,

early human clinical trials suggest beneficial effects for **dyspepsia, peptic ulcer, inflammatory bowel disease, rheumatoid arthritis, osteoarthritis, uveitis, orbital pseudotumor, and pancreatic cancer**.

Curcumin is well-tolerated; the most common side effects are nausea and diarrhea

Mol Nutr Food Res. 2013 Sep;57(9):1510-28. doi: 10.1002/mnfr.201100741. Epub 2012 Aug 13.

Multitargeting by turmeric, the golden spice: From kitchen to clinic.

Gupta SC[1] The University of Texas MD Anderson Cancer Center, Houston

Curcumin, which constitutes 2-5% of turmeric, is perhaps the most-studied component. Although some of the activities of turmeric can be mimicked by curcumin, other activities are curcumin-independent. Cell-based studies have demonstrated the potential of turmeric as **an antimicrobial, insecticidal, larvicidal, antimutagenic, radioprotector, and anticancer agent**. Numerous animal studies have shown the potential of this spice against proinflammatory diseases, cancer, neurodegenerative diseases, depression, diabetes, obesity, and atherosclerosis. At the molecular level, this spice has been shown to modulate numerous cell-signaling pathways.

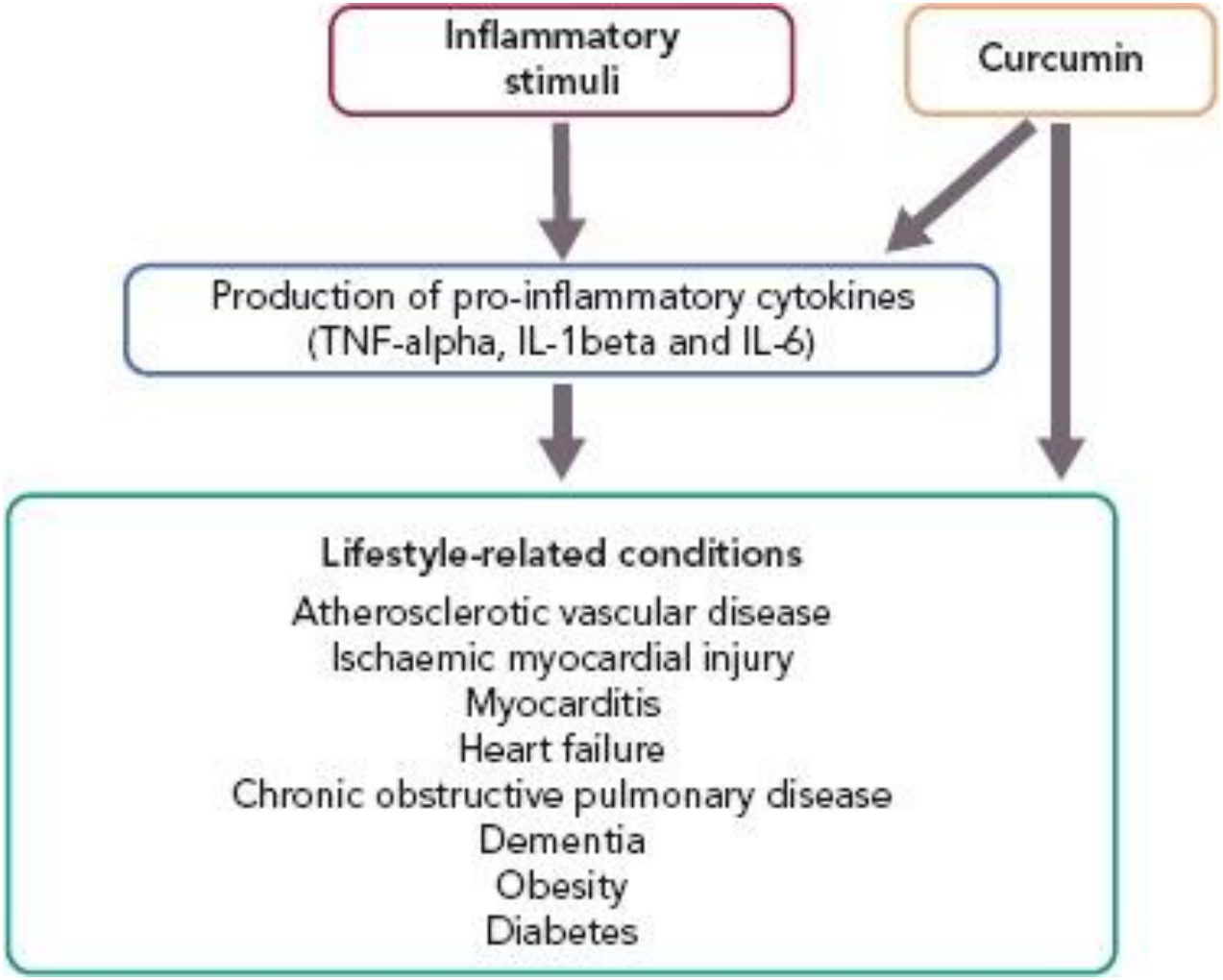
In clinical trials, turmeric has shown efficacy against numerous human ailments including lupus nephritis, cancer, diabetes, irritable bowel syndrome, acne, and fibrosis

Biofactors. 2013 Jan-Feb;39(1):2-13. doi: 10.1002/biof.1079. Epub 2013 Jan 22.
Curcumin, a component of turmeric: from farm to pharmacy.
Gupta SC[1], Kismali G, Aggarwal BB.

Cytokine Research Laboratory, Department of Experimental Therapeutics, The University of Texas MD Anderson Cancer Center, Houston, TX, USA.

To date, more than 65 human clinical trials of curcumin, which included more than 1000 patients, have been completed, and as many as 35 clinical trials are underway.

Curcumin is now used as a supplement in several countries including the United States, India, Japan, Korea, Thailand, China, Turkey, South Africa, Nepal, and Pakistan



Eur Cardiol. 2019 Jul 11;14(2):117-122. doi: 10.15420/ecr.2019.17.2.

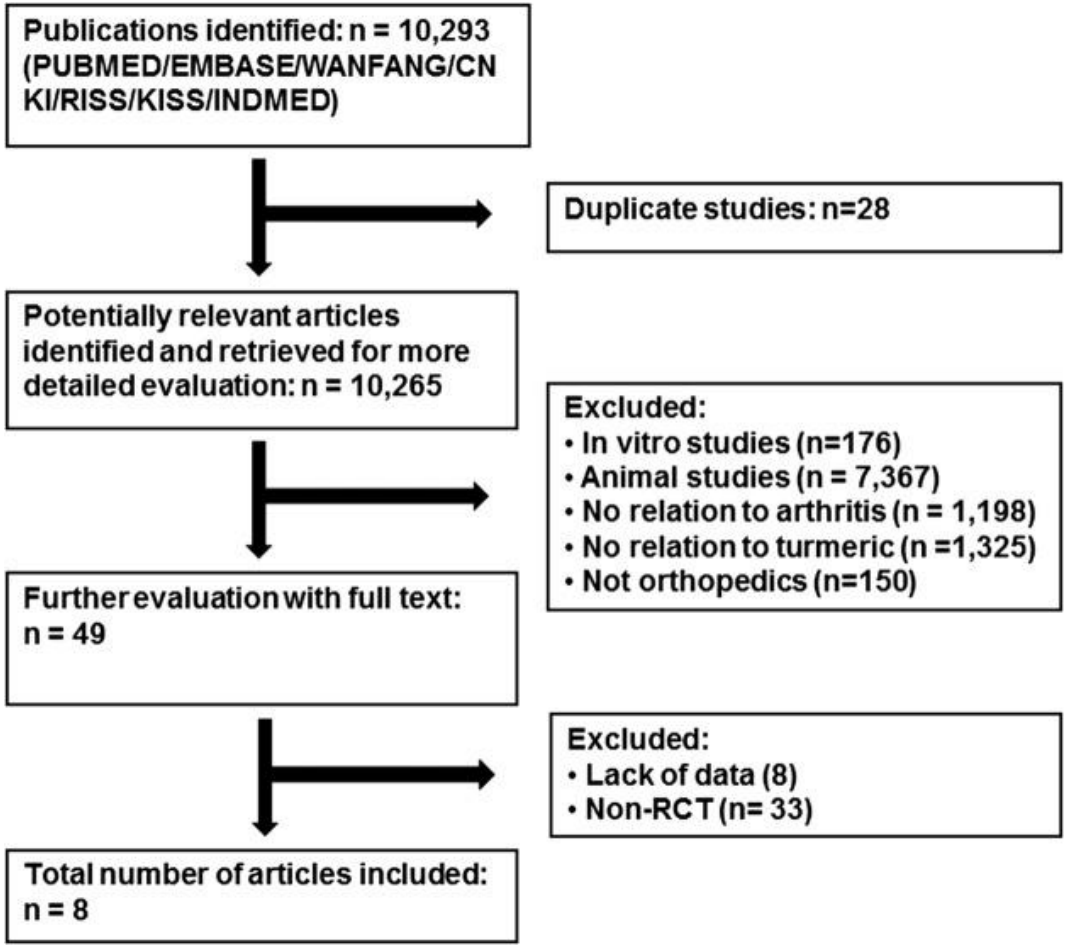
Anti-inflammatory Action of Curcumin and Its Use in the Treatment of Lifestyle-related Diseases.

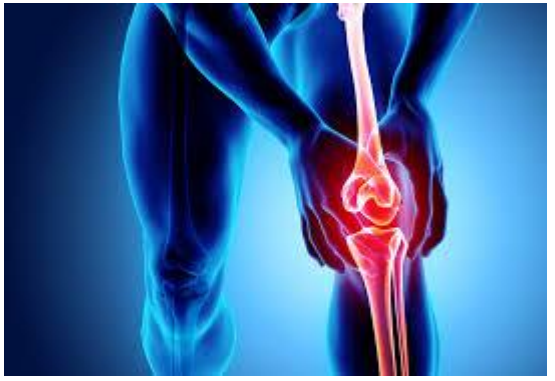
Shimizu K

J Med Food. 2016 Aug;19(8):717-29. doi: 10.1089/jmf.2016.3705.

Efficacy of Turmeric Extracts and Curcumin for Alleviating the Symptoms of Joint Arthritis: A Systematic Review and Meta-Analysis of Randomized Clinical Trials.

Daily JW, Yang M, Park S



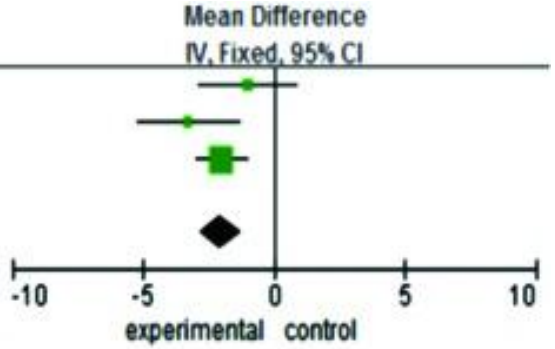


A

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
Madhu et al (22)	2.9	2.675	12	3.917	2.01	12	18.0%	-1.02 [-2.91, 0.88]	2013
Panhi et al (17)	6.1	2.9	19	9.4	3.4	21	16.9%	-3.30 [-5.25, -1.35]	2014
Chandran et al (24)	3.7	1.9	19	5.7	1.2	21	65.0%	-2.00 [-3.00, -1.00]	2014
Total (95% CI)			**50**			**54**	**100.0%**	**-2.04 [-2.85, -1.24]**	

Heterogeneity: $Chi^2 = 2.73$, $df = 2$ ($P = 0.26$); $I^2 = 27\%$

Test for overall effect: $Z = 4.98$ ($P < 0.00001$)

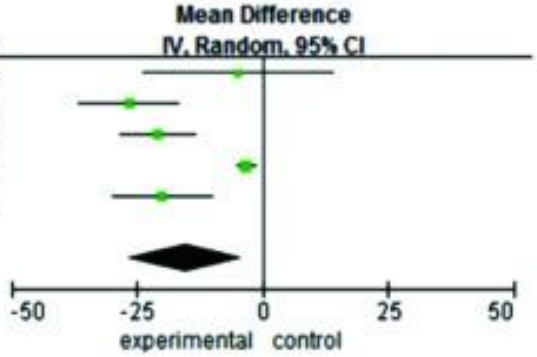


B

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Chandran et al (24)	34.29	26.75	12	39.17	20.1	12	14.5%	-4.88 [-23.81, 14.05]	2012
Madhu et al V (22)	19.48	17.84	29	46.03	20.84	29	20.2%	-26.55 [-36.53, -16.57]	2012
Madhu et al W (22)	27.14	16.13	29	47.9	12.59	29	21.6%	-20.76 [-28.21, -13.31]	2013
Panhi et al W (17)	6.1	2.9	19	9.4	3.4	21	23.6%	-3.30 [-5.25, -1.35]	2014
Panhi et al V (17)	37	19	19	57	12	21	20.2%	-20.00 [-29.97, -10.03]	2014
Total (95% CI)			**108**			**112**	**100.0%**	**-15.36 [-26.94, -3.77]**	

Heterogeneity: $Tau^2 = 147.28$; $Chi^2 = 46.18$, $df = 4$ ($P < 0.00001$); $I^2 = 91\%$

Test for overall effect: $Z = 2.60$ ($P = 0.009$)

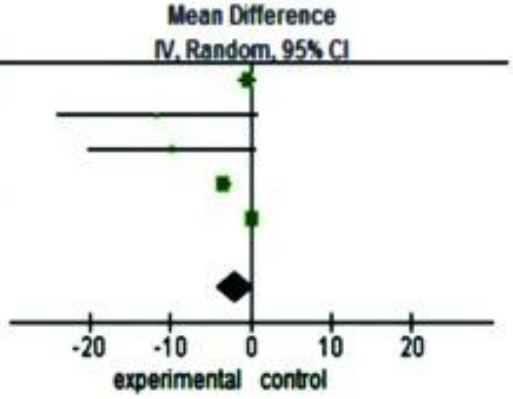


C

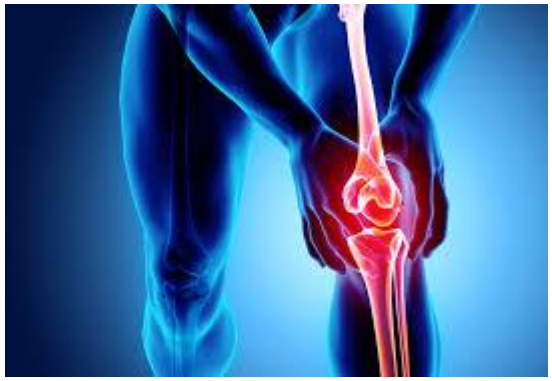
Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Kuptniratsaikul et al (16)	2.7	2.5	45	3.1	2.3	46	30.2%	-0.40 [-1.39, 0.59]	2009
Chandran et al (24)	27.5	9.35	14	39.17	20.1	12	3.0%	-11.67 [-24.05, 0.71]	2012
Madhu et al (22)	19.48	17.84	29	29.29	20.58	24	4.0%	-9.81 [-20.30, 0.68]	2013
Belcaro et al (19)	6.8	2	63	10.2	2.2	61	31.0%	-3.40 [-4.14, -2.66]	2014
Kuptniratsaikul et al (18)	3.25	2.11	171	3.17	1.98	160	31.7%	0.08 [-0.36, 0.52]	2014
Total (95% CI)			**322**			**303**	**100.0%**	**-1.89 [-4.13, 0.35]**	

Heterogeneity: $Tau^2 = 4.07$; $Chi^2 = 69.08$, $df = 4$ ($P < 0.00001$); $I^2 = 94\%$

Test for overall effect: $Z = 1.65$ ($P = 0.10$)



In conclusion, these RCTs provide scientific evidence that supports the efficacy of turmeric extract (about 1000 mg/day of curcumin) in the treatment of arthritis.



J Med Food. 2016 Aug;19(8):717-29.
doi: 10.1089/jmf.2016.3705.

Efficacy of Turmeric Extracts and Curcumin for Alleviating the Symptoms of Joint Arthritis.

Three among the included RCTs reported reduction of PVAS (mean difference: -2.04 [-2.85, -1.24]) with turmeric/curcumin in comparison with placebo ($P < .00001$), whereas meta-analysis of four studies showed a decrease of WOMAC with turmeric/curcumin treatment (mean difference: -15.36 [-26.9, -3.77]; $P = .009$).

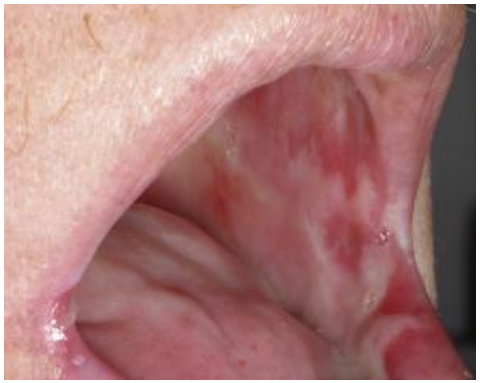
There was **no significant mean difference in PVAS between turmeric/curcumin and pain medicine in meta-analysis of five studies**. Eight RCTs included in the review exhibited low to moderate risk of bias. There was no publication bias in the meta-analysis.

In conclusion, these RCTs provide **scientific evidence that supports the efficacy of turmeric extract (about 1000 mg/day of curcumin) in the treatment of arthritis.** However, the total number of RCTs included in the analysis, the total sample size, and the methodological quality of the primary studies were **not sufficient to draw definitive conclusions**

Phytother Res. 2019 May;33(5):1318-1329. doi: **10.1002/ptr.6326**. Epub 2019 Mar 6.

Effects of turmeric and curcumin on oral mucositis: A systematic review.

Normando AGC, de Menêses AG, de Toledo IP, Borges GÁ, de Lima CL, Dos Reis PED, Guerra ENS



Four randomized and one nonrandomized clinical trials were included in the analysis.

Turmeric/curcumin was applied topically as a gel or as a mouthwash. Patients treated with turmeric/curcumin experienced reduced grade of mucositis, pain, erythema intensity, and ulcerative area.

Current evidence suggests that **topical application of turmeric or curcumin is effective in controlling signs and symptoms of oral mucositis**.

Thus, **further investigation is required** to confirm the promising effect of turmeric and curcumin in oral inflammatory lesions

Diabetes Res Clin Pract. 2017 Sep;131:91-106. doi: 10.1016/j.diabres.2017.05.024.

Effects of medicinal food plants on impaired glucose tolerance: A systematic review of randomized controlled trials.

Demmers A, Korthout H, van Etten-Jamaludin FS, Kortekaas F, Maaskant JM

RESULTS:

This review **included ten trials.**

Most studies were highly biased as data were incomplete or reporting was selective.

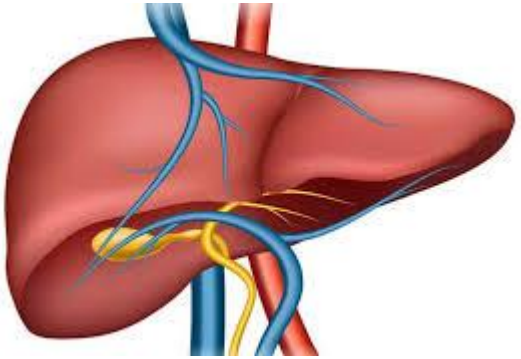
The two-hour fasting plasma glucose after the curcumin extract intervention showed statistical significance after 3, 6 and 9months: **p<0.01.** Also, **glycosylated haemoglobin levels** A1c (HbA1c) values after curcumin extract intervention showed statistical significance after 3, 6 and 9months: **p<0.01.**

Insulin resistance (HOMA-IR) after curcumin extract intervention showed statistical significance after 6months and after 9months: **p<0.05 and p<0.01**.

Ann Hepatol. 2017 November-December,;16(6):835-841. doi: 10.5604/01.3001.0010.5273.
Curcumin in Hepatobiliary Disease: Pharmacotherapeutic Properties and Emerging Potential Clinical Applications.
Hu RW, Carey EJ, Lindor KD, Tabibian JH.

Recent in vitro and in vivo studies have found that curcumin's cytoprotective and other biological activities may play a role in an array of benign and malignant hepatobiliary conditions, including :

- **non-alcoholic fatty liver disease**
- **cholestatic liver disease (e.g. primary sclerosing cholangitis)**
- **cholangiocarcinoma**



indena

Int Ophthalmol. 2019 Mar;39(3):725-734. doi: 10.1007/s10792-018-0845-y.

Therapeutic potential of curcumin in major retinal pathologies.

Peddada KV, Brown A, Verma V, Nebbioso M.

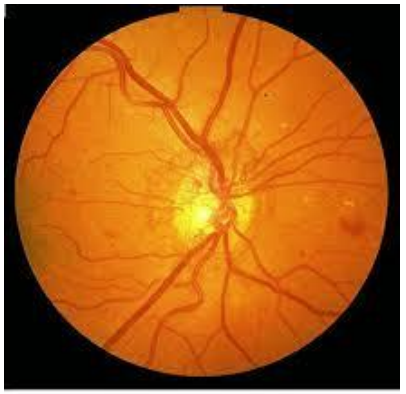


Fig. 25. A view of the fundus of the eye and of the retina in a patient who has advanced diabetic retinopathy.

RESULTS:

Curcumin has found a role in slowing, and in some cases even reversing, **age-related macular degeneration, diabetic retinopathy, retinitis pigmentosa, proliferative vitreoretinopathy, and retinal cancers.**

CONCLUSIONS:

However, studies on curcumin's efficacy have been limited mostly to animal studies. Moreover, the biomedical potential of curcumin is not easy to use, given its **low solubility and oral bioavailability**-more attention therefore has been given **to nanoparticles and liposomes**

Biomed Pharmacother. 2017 Jan;85:102-112. doi: 10.1016/j.biopha.2016.11.098.
Phytosomal curcumin: A review of pharmacokinetic, experimental and clinical studies.
Mirzaei H

Instability at physiological pH, low solubility in water and rapid metabolism results in **a low oral bioavailability of curcumin**. The **phytosomal formulation of curcumin** (**a complex of curcumin with phosphatidylcholine**) has been shown to improve curcumin bioavailability.

The **efficacy and safety of curcumin phytosomes** have been shown against several human diseases including cancer, osteoarthritis, diabetic microangiopathy and retinopathy, and inflammatory diseases.

Curcumin phytosome has an ethnopharmacological rationale. Turmeric is «formulated» in Indian medicine (and cuisine as well)

Turmeric milk

Turmeric eggs

Chicken curry

Curcumin phytosome (Meriva®) is validated in terms of curcuminoid absorption, clinical efficacy…

PK studies: 2 (rodent and human)

Human clinical studies: 31

Main areas covered:

- ✓ **Osteoarthritis and pain**
- ✓ **Sport nutrition**
- ✓ **Eye health**
- ✓ **Diabetes**
- ✓ **Gut health**
- ✓ **Cancer supportive care**

31 POSITIVE CLINICAL STUDIES AVAILABLE

THERAPEUTICAL AREA	N° OF STUDIES
OSTEOARTHRITIS	3
OSTEOPENIA	1
SARCOPENIA	1
EYES DISORDERS	4
SKIN DISORDERS (PSORIASIS)	1
DIABETES	2
LIVER HEALTH (NAFLD)	2
CARDIOVASCULAR HEALTH	1
GASTROINTESTINAL BARRIER	1
AIRWAY inflammation (pediatric)	1
BENIGN PROSTATIC HYPERPLASIA	1
PAIN MANAGEMENT	1
NEUROPATHIES	2
SPORT MEDICINE	2
DIAGNOSTIC (AD)	1

*+ 1 Pharmacokinetic ; + 2 reviews; + **6 CLINICAL STUDIES in the supportive care***

CURCUMIN PHYTOSOME

CLINICAL STUDIES (continues)

PAIN MANAGEMENT

11. Di Pierro F., *et al.* Comparative evaluation of the pain-relieving properties of a lecithinized formulation of curcumin (Meriva®), nimesulide, and acetaminophen. *J. Pain Res.* 2013, 6; 201-205.

NEUROPATHIES

12. Di Pierro F., Settembre R. Safety and efficacy of an add-on therapy with curcumin phytosome and piperine and/or lipoic acid in subjects with a diagnosis of peripheral neuropathy treated with dexibuprofen. *J Pain Res* 2013. 6; 497-503.
13. Pajardi G., *et al.* Clinical usefulness of oral supplementation with alpha-lipoic Acid, curcumin phytosome, and B-group vitamins in patients with carpal tunnel syndrome undergoing surgical treatment. *Evid Based Complement Alternat Med* 2014; 2014: 891310.

DIABETES

14. Appendino G., *et al*. Potential role of curcumin phytosome (Meriva) in controlling the evolution of diabetic microangiopathy. A pilot study. *Panminerva Med* 2011; 53(3 Suppl 1): 43-49.
15. Steigerwalt R., *et al*., Meriva(R), a lecithinized curcumin delivery system, in diabetic microangiopathy and retinopathy. *Panminerva Med* 2012; 54(1 Suppl 4): 11-16.

SPORT NUTRITION

16. Drobnic F., *et al.* Reduction of delayed onset muscle soreness by a novel curcumin delivery system (Meriva®): a randomised, placebo-controlled trial. J Int Soc Sports Nutr 2014; 11: 31.
17. Sciberras J.N., *et al.* The effect of turmeric (Curcumin) supplementation on cytokine and inflammatory marker responses following 2 hours of endurance cycling. *J Int Soc Sports Nutr* 2015; 12(1): 5.

CURCUMIN PHYTOSOME

CLINICAL STUDIES (continues)

SUPPORTIVE CARE

18. Serpe R., *et al.* Curcuma Longa extract is effective in reducing blood levels of reactive oxygen species (ROS) and increasing antioxidant enzyme Glutathione peroxidase (GPx) in patients with cancer-related cachexia and oxidative stress. 6th Cachexia Conference, Milan, Italy, December 8-10, 2011.
19. Belcaro G., *et al.* A controlled study of a lecithinized delivery system of curcumin (Meriva®) to alleviate the adverse effects of cancer treatment. *Phytother Res* 2014; 28(3): 444-450.
20. Panahi Y., *et al*. Adjuvant therapy with bioavailability-boosted curcuminoids suppresses systemic inflammation and improves quality of life in patients with solid tumors: a randomized double-blind placebo-controlled trial. *Phytother Res* 2014; 28(10): 1461-7.
21. Panhai Y., *et al*. Antioxidant effects of bioavailability-enhanced curcuminoids in patients with solid tumors: A randomized double-blind placebo-controlled trial. *J Functional Food* 2014; 6: 615-622.
22. Golombick T., *et al*. The effect of curcumin (as Meriva) on absolute lymphocyte count (ALC), NK cells and T cell populations in patients with stage 0/1 chronic lymphocytic leukemia. *Journal of Cancer Therapy* 2015; 6 (7): 566-571.
23. Soldà C., *et al*. A case of locally advanced pancreatic cancer successfully resected after 14 months therapy with gemcitabine and Meriva®. *IJPPE* Vol 2, 2017.

CURCUMIN PHYTOSOME

CLINICAL STUDIES (continues)

MYELOFIBROSIS

24. Maccio A., Gramignano G., Madeddu C. Surprising results of a supportive integrated therapy in myelofibrosis. *Nutrition*, 2015; 31(1): 239-43.

PSORIASIS

25. Antiga A ., *et al*. Oral Curcumin (Meriva) Is Effective as an Adjuvant Treatment and Is Able to Reduce IL-22 Serum Levels in Patients with Psoriasis Vulgaris. *BioMed Research International*, vol. 2015, Article ID 283634.

SARCOPENIA

26. Franceschi F., *et al.* A novel phospholipid delivery system of curcumin (Meriva®) preserves muscular mass in healthy aging subjects. *Eur Rev Med Pharmacol Sci*. 2016; 20: 762-766.

LIVER HEALTH (NAFLD)

27. Panahi Y., *et al*. Curcumin lowers serum lipids and uric acid in subjects with nonalcoholic fatty liver disease: a randomized controlled trial. *J. Cardiovasc Pharmacol*. 2016; 68: 223-229.
28. Panahi Y., *et al*. Efficacy and Safety of Phytosomal Curcumin in Non-Alcoholic Fatty Liver Disease: A Randomized Controlled Trial. *Drug Res (Stuttg)*. 2017; 67(4): 244-251.

RESPIRATORY HEALTH (PEDIATRIC POPULATION)

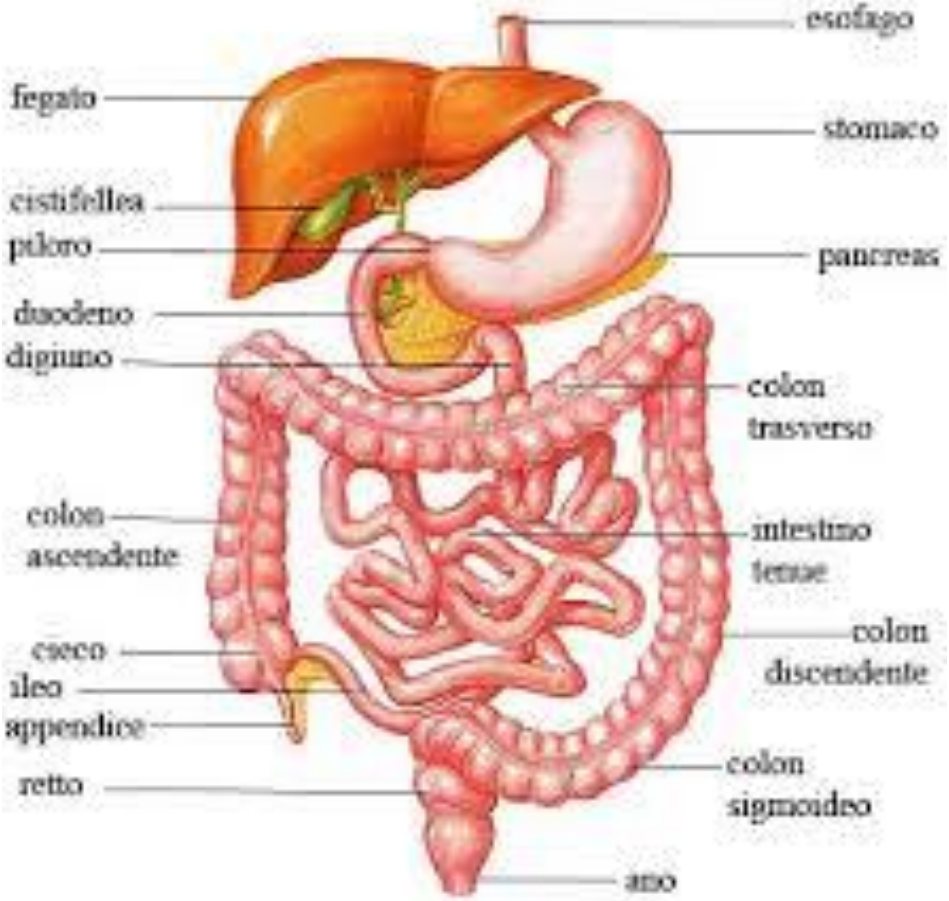
29. Tenero L., *et al*. Antioxidant supplementation and exhaled nitric oxide in children with asthma. *Allergy Asthma Proc*. 2016; 37:e8-e13.

GASTROINTESTINAL HEALTH

30. Szymanski M.C., *et al*. Short term dietary curcumin supplementation reduces gastrointestinal barrier damage and physiological strain responses during exertional heat stress. *J Appl Physiol* 2017. doi: 10.1152/japplphysiol.00515.2017.

CARDIOVASCULAR HEALTH

31. Ferguson J.J.A., *et al.* Curcumin potentiates cholesterol-lowering effects of phytosterols in hypercholesterolaemic individuals. A randomized controlled trial. Metabolism. 2017 Dec 29. pii: S0026-0495(17)30356-6. doi: 10.1016/j.metabol.2017.12.009.

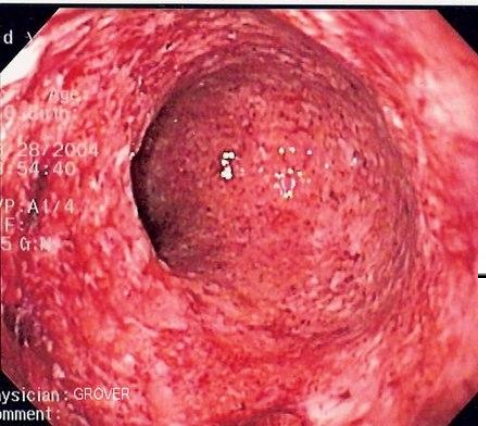

esofago
fegato
stomaco
cistifellea
piloro
pancreas
duodeno
digiuno
colon
trasverso
colon
ascendente
intestino
tenue
ceco
colon
discendente
ileo
appendice
colon
sigmoideo
retto
ano

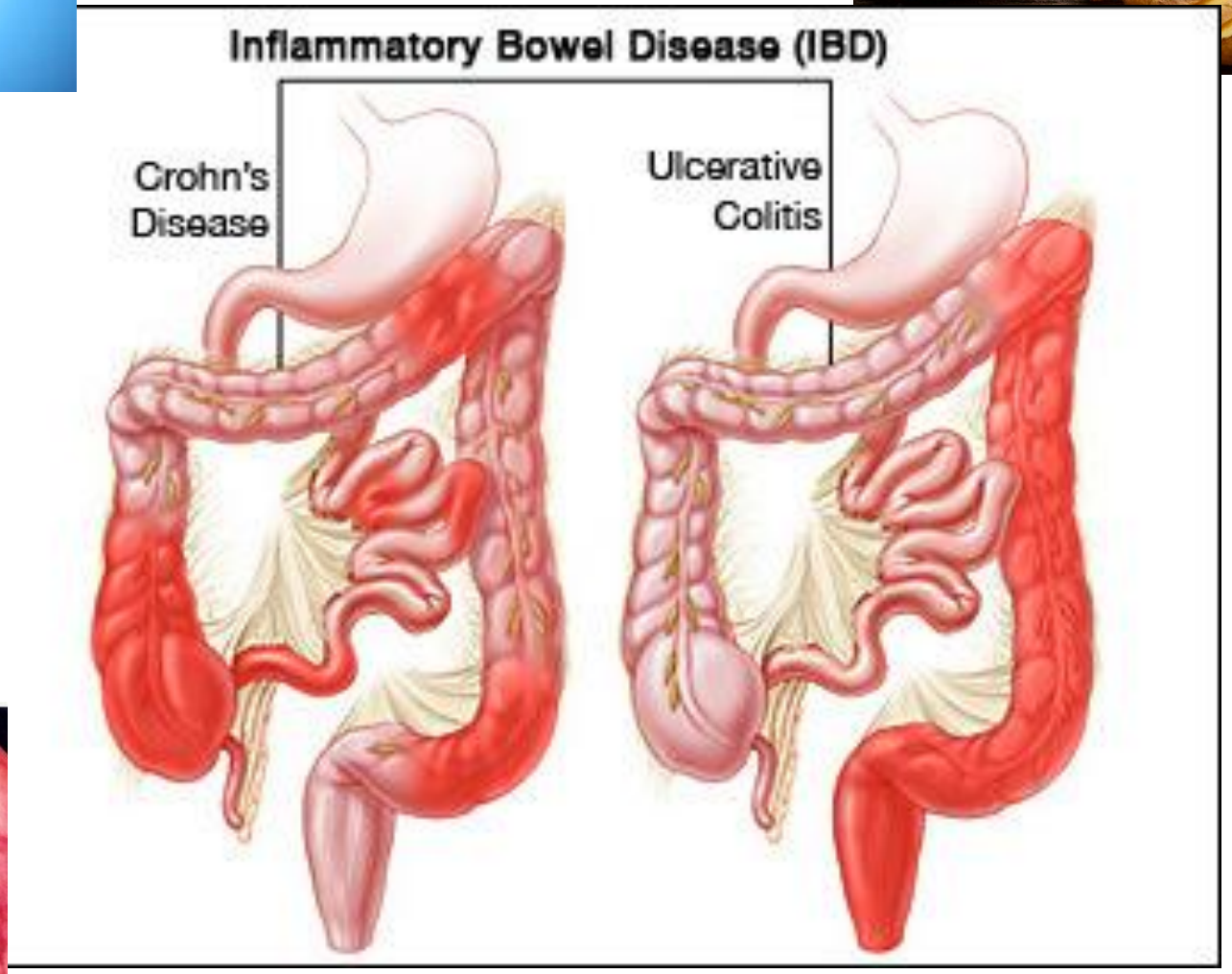
Anti-inflammatory Effect

→ IBD

Several studies have been investigated the role of Curcumin in Inflammatory Bowel Diseases and Irritable Bowel Syndrome

- Curcumin therapy in inflammatory bowel disease: a pilot study. [Holt et al., 2005]
- Curcumin maintenance therapy for ulcerative colitis: randomized, multicenter double-blind, placebo-controlled trial. [Hanai et al., 2006]
- Turmeric exctract may improve irritable bowel syndrome symptomology in otherwise healthy adults [Rafe et a., 2004]
- Therapeutic potential of curcumin in gastrointestinal diseases [Rajaserkaran, 2011]
- Formulation and evaluation of colon specific drug delivery systems for selected anti-inflammatory agent [Hukeri et al., 2012]
- Anti-inflammatory properties of curcumin, a major constituent of curcuma longa. A review of preclinical and clinical research [Jurenka, 2009]
- Curcumin for inflammatory bowel disease: a review of human studies [Taylor et al., 2011]




Inflammatory Bowel Disease (IBD)
Crohn's Disease
Ulcerative Colitis

MI- SPX

Positive clinical studies on curcumin in IBD

1. Holt PR, Katz S, Kirschoff R.
   Curcumin therapy in inflammatory bowel disease: a pilot study.
   Dig Dis Sci 2005;50:2191-2193.

2. Hanai H, Iida T, Takeuchi K *et al*.
   Curcumin maintenance therapy for ulcerative colitis: randomized, multicenter double-blind, placebo-controlled trial.
   Clin Gastroenterol Hepatol 2006;4:1502-1506.

Curcumin Maintenance Therapy for Ulcerative Colitis: Randomized, Multicenter, Double-Blind, Placebo-Controlled Trial

HIROYUKI HANAI,*,‡

Table 4. Recurrence Status at 6 Months

	Curcumin	Placebo	*P* value
No. of patients treated	43	39	
No. of patients with recurrence	2	8	
% with recurrence	4.65	20.51	.040
95% confidence interval	0.56–15.47	9.30–36.46	

Analysis is based on the number of eligible patients who completed the study, excluding the 7 patients who became protocol violators during the study.

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Curcumin Maintenance Therapy for Ulcerative Colitis: Randomized, Multicenter, Double-Blind, Placebo-Controlled Trial

HIROYUKI HANAI,*,‡

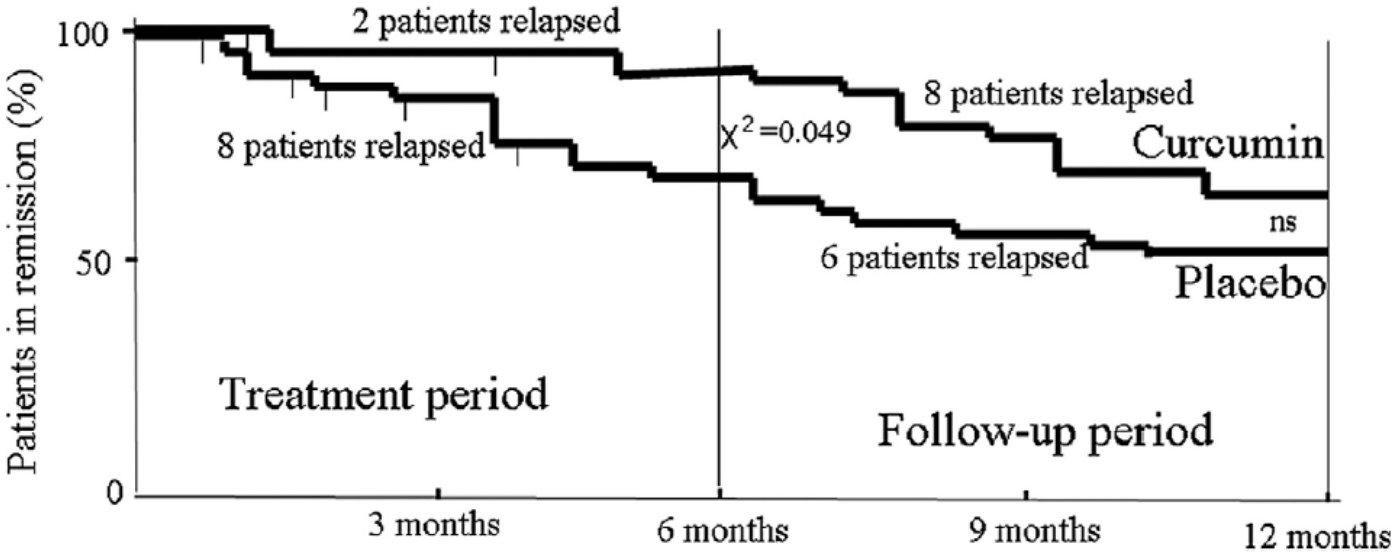

Figure 2. The Kaplan-Meier curves showing the efficacy outcomes during the 6 months of therapy and 6 months of follow-up.

Table 5. Changes in CAI and EI During the 6 Months of Treatment

	Curcumin		Placebo	
	Entry	6 Mo	Entry	6 Mo
CAI	1.3 ± 1.1	1.0 ± 2.0	1.0 ± 1.1	2.2 ± 2.3
P value	.038		.0003	
EI	1.3 ± 0.8	0.8 ± 0.6	1.3 ± 1.0	1.6 ± 1.6
P value	.0001		.0728	

P values by the χ^2 test.

Curcumin & UC

Cochrane Database Syst Rev. 2012 Oct 17;10:CD008424.
Curcumin for maintenance of remission in ulcerative colitis.
Kumar S et al

Curcumin may be a safe and effective therapy for maintenance of remission in quiescent UC when given as adjunctive therapy along with mesalamine or sulfasalazine.

However, further research in the form of a large scale methodologically rigorous randomized controlled trial is needed to confirm any possible benefit of curcumin in quiescent UC.

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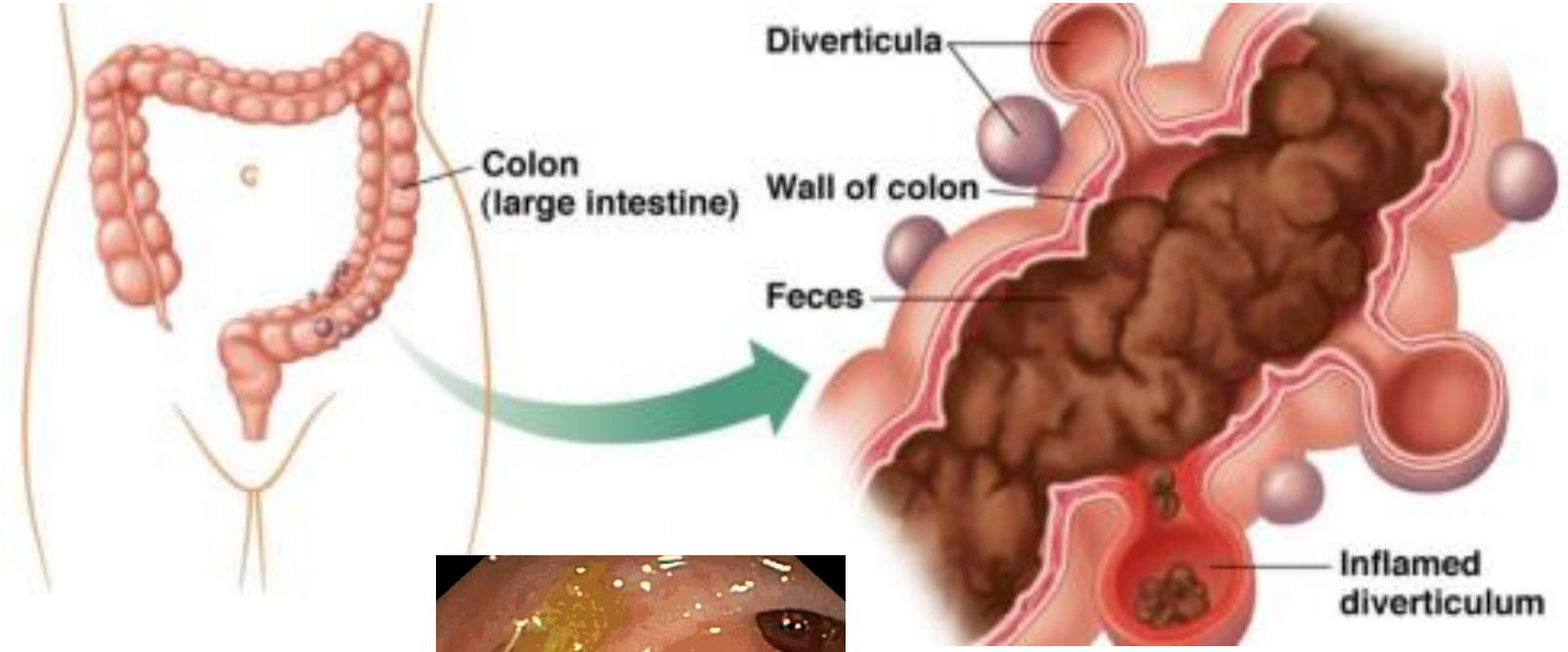
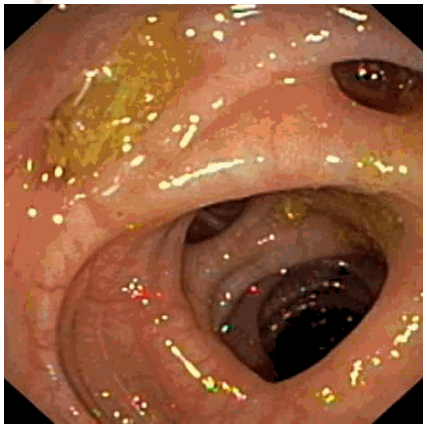
Diverticulosis





MI- SPX

Therap Adv Gastroenterol. 2013 May; 6(3): 205–213.
New strategies for the management of diverticular disease: insights for the clinician
Wen Boynton and Martin Floch

1. **chronic inflammation is present in the colon in patients with diverticulosis without overt diverticulitis. [Floch, 2006].**

2. [Horgan *et al*. 2001] **75% out of 940 surgical specimens from patients with symptomatic uncomplicated diverticular disease had chronic inflammation** in and around diverticula

3. It has been proposed that **the chronic inflammation in diverticular disease is similar to that in inflammatory bowel disease (IBD)** [Di Mario *et al*. 2006]

4. **ongoing low-grade inflammation and upregulation of tachykinins in symptomatic diverticulosis patients may explain their visceral hypersensitivity [Humes *et al*. 2012].**

5. **5-aminosalicylic acid (5-ASA) drugs have been studied in the management of symptomatic uncomplicated diverticular disease and recurrent diverticulitis**.

GiacosaMI-SPX

Rifaximin vs Mesalazine

In a prospective, randomized open trial, Di Mario and colleagues compared the efficacy of cyclic use of rifaximin to mesalazine (mesalamine) in achieving symptom relief in patients with symptomatic uncomplicated colonic diverticular disease
[Di Mario *et al*. 2005].

They found mesalazine was
- as effective as rifaximin for diminishing symptoms
- better than rifaximin for improving the global score in those patients

GiacosaMI
- SPX

Mesalazine and/or Lactobacillus casei & Diverticular Disease

Hepatogastroenterology. 2008 May-Jun;55(84):916-20.

Mesalazine and/or Lactobacillus casei in maintaining long-term remission of symptomatic uncomplicated diverticular disease of the colon.

Tursi A[1], Brandimarte G, Giorgetti GM, Elisei W

Sixty six patients **(88%) were symptom-free after the 24th month of treatment**: 11 of group M1 (on i-t-t: 84% [CI 95%: 55.5-98.8]), 8 of group M2 (on i-t-t: 80% [CI 95%: 44.39-97.48]), 15 of group LM1 (on i-t-t: 93.75% [CI 95%: 69.77-99.84]), 12 of group LM2 (on i-t-t: 92.30% [CI 95%: 63.97-99.81]), 20 in group L (on i-t-t: 86.95% [CI 95%: 66.41-97.22]) (p-ns).

Mesalazine and/or Lactobacillus casei seem to be effective in maintaining remission of DD for long-time. Moreover, we found recurrence of the disease and complications in all patients suspending treatments

GiacosaMI - SPX

Int J Colorectal Dis. 2013 Oct;28(10):1423-31. doi: 10.1007/s00384-013-1722-9. Epub 2013 Jun 12.

Intermittent treatment with mesalazine in the prevention of diverticulitis recurrence: a randomised multicentre pilot double-blind placebo-controlled study of 24-month duration.

Parente F, Bargiggia S, Prada A, Bortoli A, **Giacosa A**, Germanà B, Ferrari A, Casella G, De Pretis G, Miori G; "Gismi Study Group"

92 pts (mean age, 61.5) completed the study, 45 mesalazine, and 47, placebo.

Diverticulitis relapse incidence in mesalazine-treated group was 5/45 (11%) at the 12th month and 6/45 (13%) at the 24th month;
in the placebo-treated group, the correspondent rates were 13% (6/47) and 28% (13/47), respectively.

Mean values of TIQ at 24 months were significantly better in mesalazine-treated group than in placebo-treated group (p = 0.02); in addition, average additional drug consumption was significantly lower (-20.4%, p < 0.03) in mesalazine than in placebo

GiacosaMI - SPX

Role of curcumin and boswellic acids in the treatment of Symptomatic Diverticular disease

Giacosa A, Rondanelli M, Riva A , Allegrini P

(Ongoing study)

Small Intestine Bacterial Overgrowth

GiacosaMI - SPX

la SIBO è una condizione patologica multifattoriale epidemiologicamente sottostimata

Risk factors for SIBO:

Low stomach acid (PPI treatment)
Irritable bowel syndrome
Celiac disease (long-standing)
Crohn's disease
Prior bowel surgery
Diabetes mellitus (type I and type II)
Multiple courses of antibiotics
Organ system dysfunction, such as liver cirrhosis, chronic pancreatitis, or renal failure

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SIBO: terapia

la terapia della SIBO è costituita dalla somministrazione di antibiotici per 0s (Rifaximina, metronidazolo, ciprofloxacina)

la eradicazione della SIBO con antibiotici non costituisce una terapia definitiva dato l'elevato indice di recidiva

Intestinal Barrier
Bactericidal effects

Am J Physiol Cell Physiol. 2017 Apr 1;312(4)
Curcumin improves intestinal barrier function: modulation of intracellular signaling, and organization of tight junctions.
Wang J et al

Antibacterial effects of curcumin
Hayati Gunes, Dumrul Gulen
P. aeruginosa, *B. subtilis*, MSSA, MRSA, E. *coli*, *E. faecalis* and *K. Pneumonia*

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Curcumin & IBS

- Antinflammatory effects
- Bactericidal effects
- Regulation of Intestinal motility disfunction (Pari et al ,2008, Kumar et al 2010))
- Brain-Gut axis regulation (Xu et al , Brain Res, 2007, Yu et al , Metab Bran Dis , 2015)
- Antidepressant activity (Lulkami, 2008)

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Bundy *et al*, J Altern Complement Med. 2004

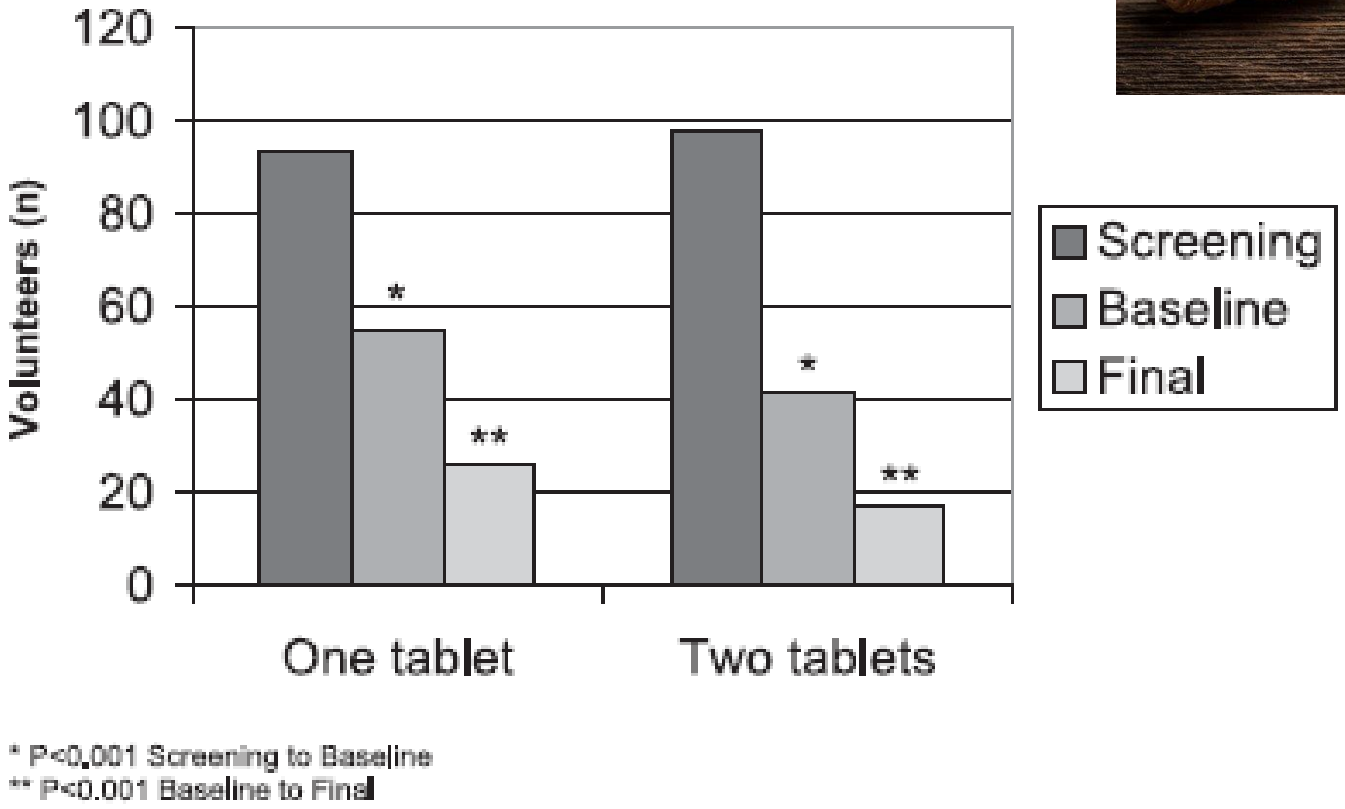


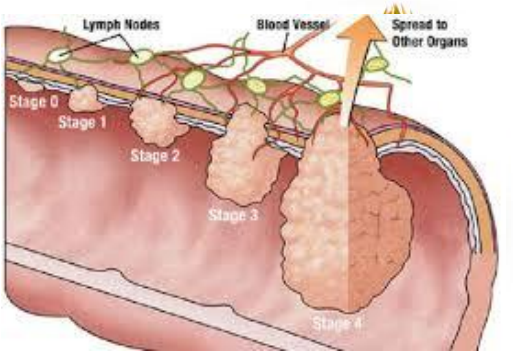
FIG. 2. Prevalence of irritable bowel syndrome (IBS) at screening, baseline, and after 8 weeks of treatment with turmeric (*Circuma longa*) extract, in two doses, given to volunteers who have IBS.

GiacosaMI - SPX

Cancer Lett. 2007 Oct 8;255(2):170-81. Epub 2007 Apr 19.

Curcumin for chemoprevention of colon cancer.

Johnson JJ[1], Mukhtar H.



The **robust activity of curcumin in colorectal cancer** has led to five phase I clinical trials being completed showing the safety and tolerability

The success of these trials has led to the **development of phase II and III trials** that are currently enrolling patients. Overwhelming in vitro evidence and completed clinical trials suggests that **curcumin may prove to be useful for the chemoprevention of colon cancer in humans**. interact with multiple molecular targets affecting the multistep process of carcinogenesis.

- **arrests the cell cycle,**
- **inhibits the inflammatory response and the oxidative stress**
- **induces apoptosis in cancer cells**
- **potentiates the growth inhibitory effect of cyclo-oxygenase (COX)-2 inhibitors and traditional chemotherapy agents**

(Villegas I., *et al*., 2008; Sehzad D., *et al.* 2010)

GiacosaMI - SPX

The New York Times

y Dawn MacKeen
Published Oct. 16, 2019

Turmeric, native to South Asia, is one of the fastest-growing dietary supplements. In **2018 products racked up an estimated $328 million in sales in the United States**, a more than sevenfold increase from a decade earlier, according to a report from Nutrition Business Journal

According to **Natural Medicines**, a database that provides monographs for dietary supplements, herbal medicines, and complementary and integrative therapies, while some clinical evidence shows that **curcumin might be beneficial for depression, hay fever, hyperlipidemia, ulcerative colitis, osteoarthritis and nonalcoholic fatty liver disease, it's still too early to recommend the compound for any of these conditions.**


WHEN YOU REALIZE..
MORE RESEARCH IS NEEDED
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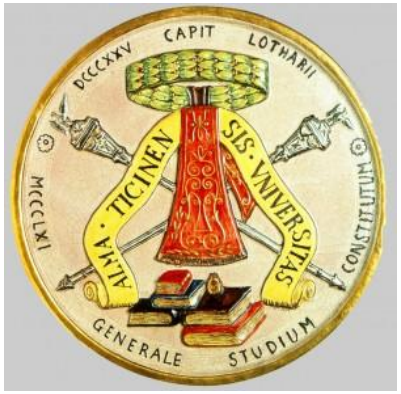
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Grazie per l'attenzione

attilio.giacosa@gmail.com

Nutrients **2019**, *11*(10), 2376; https://doi.org/10.3390/nu11102376
Review
Curcumin and Cancer
A. Giordano, G. Tommonaro

Curcumin exhibits anticancer ability by targeting different cell signaling pathways including growth factors, cytokines, transcription factors, and genes modulating cellular proliferation and apoptosis

However, curcumin is not immune from side effects, such as nausea, diarrhea, headache, and yellow stool.

Moreover, it showed poor bioavailability due to the fact of low absorption, rapid metabolism, and systemic elimination that limit its efficacy in diseases treatment.

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Turmeric

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- Turmeric Coffee
- Turmeric Tea
- Golden Milk
- Turmeric Fat Bombs
- Turmeric Healing Paste
- Turmeric Lemonade
- Turmeric Supplements
- Turmeric Soups
- Turmeric in Stir Fry's
- Turmeric Water

- Anti-Allergy
- Anti-Cancer
- Anti-Fungal
- Anti-Inflammatory
- Anti-Viral
- Heals Wounds Fast
- Helps Control Blood Sugar
- Immunity Booster
- Improves Digestion
- Improves Memory
- Prevents Tooth Decay
- Prevents Alzheimer's Disease
- Reduces Arthritis Symptoms
- Reduces Risk of Heart Disease
- Reduces symptoms of Depression
- Helps with aging
- Promotes a Longer Lifespan
- Natural Painkiller
- Protects Lungs

Recipes + More at : www.HealthyHappySmart.com

Journal of Ethnopharmacology
Volume 38, Issues 2–3, March 1993,
Pages 105-112

Mechanism of antiinflammatory actions of curcumine and boswellic acids

H.P.T. Ammon, H.Safayh, T.Mack J.Sabieraj

Curcumine from *Curcuma longa* inhibites the 5-lipoxygenase activity in rat peritoneal neutrophils
as well as the 12-lipoxygenase and the cyclooxygenase activities in human platelets.

In a cell free peroxidation system curcumine exerted strong antioxidative activity.

Thus, its effects on the dioxygenases are probably due to its reducing capacity

GiacosaMI - SPX