CURCUMIN C3 COMPLEX®

True Benefits of Science & Marketing

THE MOST CLINICALLY STUDIED CURCUMIN BRAND

THE MOST SAFETY DATA

THE MOST STABLE SUPPLY CHAIN

WE WROTE THE BOOK(S)

NO ONE KNOWS CURCUMIN LIKE WE DO

THE STUDY LIST

YOUR BODY: OUR C3 COMPLEX

CURCUMIN C3 COMPLEX®

curcuminoids.com

JULY 2020

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THE MOST CLINICALLY STUDIED CURCUMIN BRAND

The following contain a few facts for your understanding and to differentiate our Curcumin C3 Complex® from other generic and modified curcumin extracts.

More than 100 scientific publications, including clinical trials, have been published using Curcumin C3 Complex. Curcumin C3 Complex is 100% natural and is independently verified using C^{14} testing by University of Georgia and 3rd party independent labs.

Curcumin C3 Complex is the preferred curcumin brand with the NIH (National Institutes of Health) and other top Universities including University of Texas – MD Anderson Cancer Center, Tufts, Rutger's, and the University of California.

NBJ® Scientific Achievement Award 2007

NBJ® Product Merit Award 2008

* Panahi Y, Khalili N, Hosseini MS, Abbasinazari M, Sahebkar A. Lipid-modifying effects of adjunctive therapy with curcumioids-piperine combination in patients with metabolic syndrome: Results of a randomized controlled trial. *Complement Ther Med*. 2014; 22(5): 851-57.

THE MOST SAFETY DATA

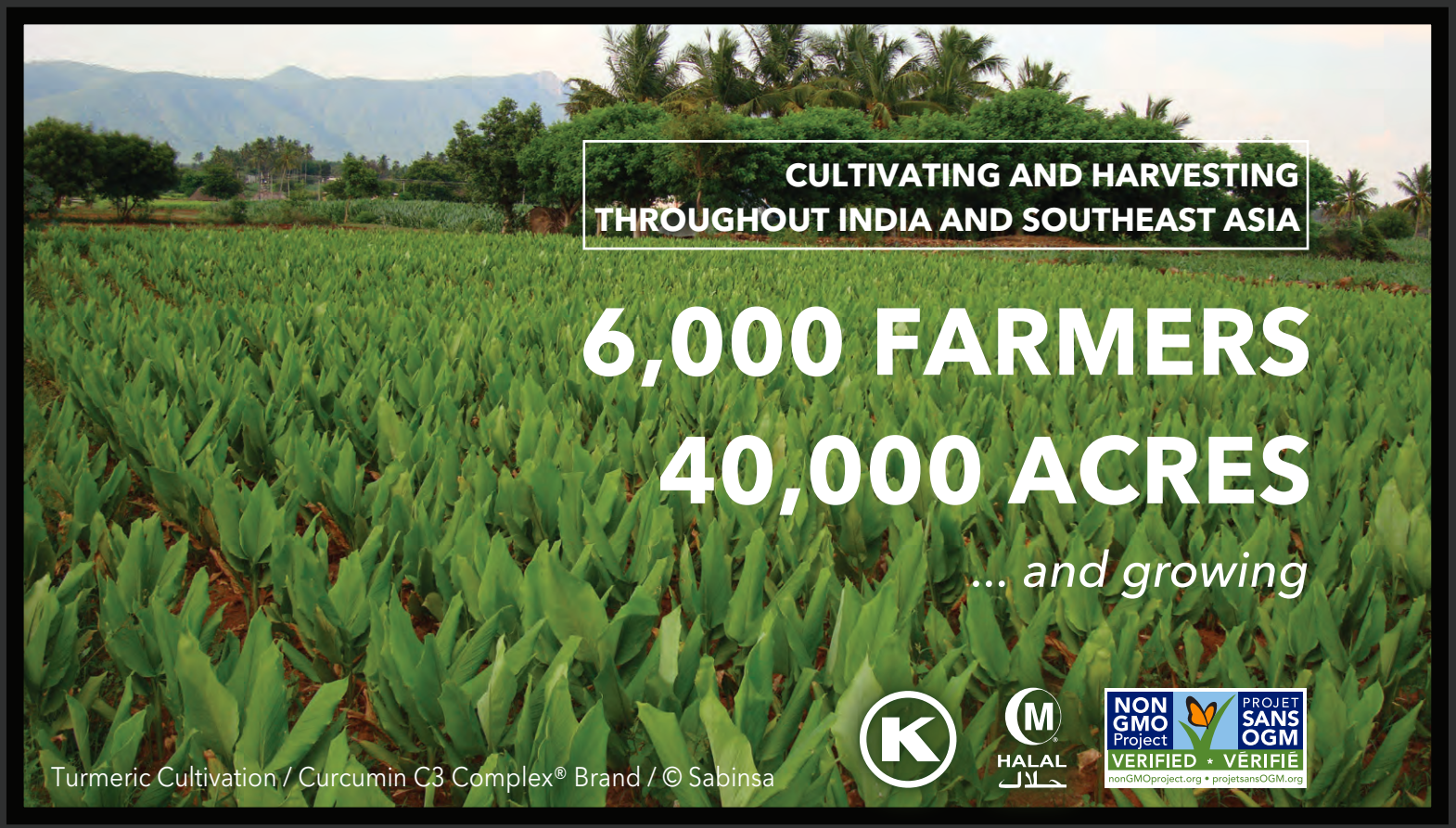
Sabinsa's Curcumin C3 Complex, standardized for 95% curcuminoids, is designated Generally Recognized As Safe (GRAS) and listed in US FDA's GRAS Notice, a status predicated on rigorous safety assessments. Because our brand's manufacturing process is unique, the collection of data backing it applies to no other curcumin ingredient. Considering its health and safety competencies, the C3 Complex brand is unparalleled.

VALIDATED TESTING FOR ASSAY AND CARBON DATING WITH EACH BATCH OF CURCUMIN C3 COMPLEX

THE MOST STABLE SUPPLY CHAIN

Sabinsa's cultivation programs ensure a stable supply, providing our farmer partners with technical support and advice, financial help, and incentives to motivate the farmers to grow crops in a sustainable manner using modern technology. In the past years while there was shortage of turmeric in the market, Sabinsa was able to provide an uninterrupted supply of genuine Curcumin C3 Complex to our loyal customer base at competitive prices. Our technical support to farmers also produces a higher quality raw material, so the superiority of Curcumin C3 Complex begins literally at the ground level.

GLUTEN FREE | GMO FREE | NANOPARTICLE FREE | SYNTHETIC FREE



Turmeric Cultivation / Curcumin C3 Complex® Brand / © Sabinsa

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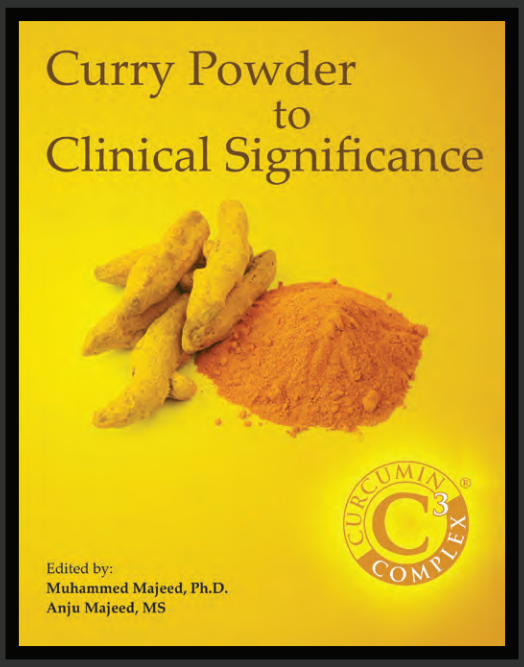
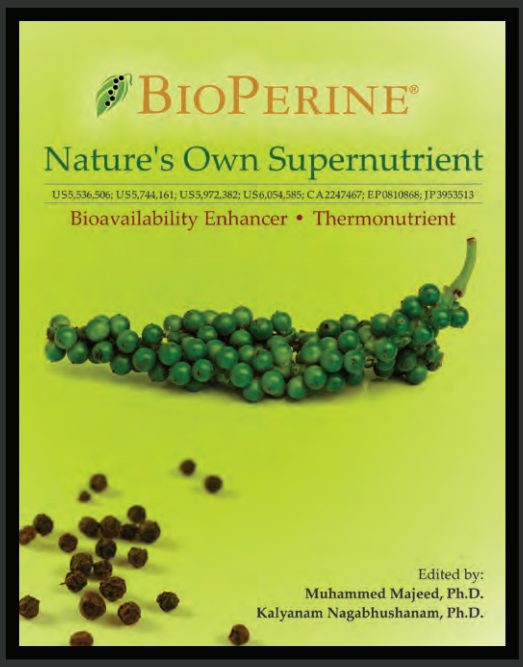


CURRY POWDER TO CLINICAL SIGNIFICANCE, 2015

A culmination of studies on Sabinsa's branded curcumin ingredient. Discover the start of this industry leading ingredient and the studies that captured the attention of marketers, media and consumers everywhere.



NATURE'S OWN SUPERNUTRIENT, 2017

The making of BioPerine®, from it's mechanism of action, to its bio-availability enhancement, to its various health benefits, it's metabolism and long-term safety, everything we know is captured here for you.

DR. MUHAMMED MAJEED

Founder and Chairman, Sami-Sabinsa Group Limited

Dr. Majeed has over 45 years of experience in the pharmaceutical, nutritional and cosmetic industries. After obtaining his Masters from Long Island University (New York, USA) and his PhD from St. John's University (New York, USA), he founded Sabinsa Corporation in New Jersey, USA in 1988 as the first phase of his vision to build upon traditional Ayurvedic knowledge utilizing modern scientific methods. In 1991, he established Sami Labs Ltd, a cutting-edge research and manufacturing facility in Bengaluru, India. Today, the Sami-Sabinsa Group is a pioneer and global leader in health science and a leading producer of nutraceuticals, cosmeceuticals, standardized herbal extracts, fine chemicals, specialty chemicals and probiotics.

NO ONE KNOWS CURCUMIN LIKE WE DO



Turmeric: Whole plant *Curcuma longa*
Curcumin: Single entity present in turmeric
Curcuminoids: Three major common constituents found in turmeric, of which curcumin is abundant

Sabinsa assisted the United States Pharmacopeial Convention (USP) in preparing published monographs on turmeric and curcuminoids, and in developing validated analytical methods. Additionally, Sabinsa supplied reference standards for the individual curcuminoids to the USP. These monographs are published in the Pharmacopeial Forum 33(6), Nov-Dec 2007. This elicited a note of appreciation from USP.

Sabinsa has not only invested in research in making the product successful but also initiated, supported and invested in several clinical trials on Curcumin C3 Complex to increase the knowledge on its health benefits.

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Curcumin C3 Complex® is a registered trademark of Sabinsa

CLINICAL STUDIES

1. **Influence of piperine on the pharmacokinetics of curcumin in animals and human volunteers.** Shoba G, Joseph T, Majeed M, Rajendran R and Srinivas PSSR. *Planta Med.* 1998;353-56.

   Curcumin C3 Complex® + BioPerine® (2000 mg + 20 mg/day).
   Piperine enhances the serum concentration and bioavailability of curcumin in both rats and human. Relative bioavailability of curcumin when combined with BioPerine® is 2000%.

2. **Phase I clinical trial of oral curcumin: Biomarkers of systemic activity and compliance.** Sharma RA, Euden SA, Platton SL, Cooke DN, Shafayat A, Hewitt HR, Marczylo TH, Morgan B, Hemingway D, Plummer SM, Pirmohamed M, Gescher AJ and Steward WP. *Clin Can Res.* 2004; 10:6847-54.

   Curcumin C3 Complex® (450 mg and 3600 mg/day), 4 months.
   Curcumin and its glucuronide and sulfate metabolites were detected in plasma in the 10 nmol/L range and in urine. A daily dose of 3.6 g curcumin engendered 62% and 57% decreases in inducible PGE2 production in blood samples taken 1 hour after dose on days 1 and 29, respectively.

3. **Detection of curcumin and its metabolites in hepatic tissue and portal blood of patients following oral administration.** Garcea G, Jones DJL, Dennison AR, Farmer FB, Sharma RA, Steward WP, Gescher AJ and Berry DP. *Br J Cancer* 2004; 90(5):1011–15.

   Curcumin C3 Complex® (450 mg and 3600 mg/day), 1 week.
   Following oral administration trace levels of curcumin along with its metabolites in the liver and portal circulation were detected.

4. **Consumption of the putative chemo preventive agent curcumin by cancer patients: Assessment of curcumin levels in the colorectum and their pharmacodynamic consequences.** Garcea G, Berry DP, Jones DJL, Singh R, Dennison AR, Farmer PB, Sharma RA, Steward WP and Gescher AJ. *Cancer Epidemiol Biomarkers Prev*. 2005; 14(1):120-25.

   Curcumin C3 Complex® (3,600, 1,800, or 450 mg daily).
   Curcumin achieves pharmacologically efficacious levels in the colorectum.

5. **Dose escalation of a curcuminoid formulation.** Lao CD, Ruffin MT, Normolle D, Health DD, Myrray SI, Bailey JM, Boggs ME, Crowell J, Rock CL and Brenner DE. *BMC Complementary and Alternative Medicine* 2006; 6(10): 1-4.

   Curcumin C3 Complex® (500, 1000, 2000, 4000, 6000, 8000, 10000 and 12000 mg).
   Tolerance of curcumin in high single oral doses appears to be excellent. Only minimal toxicity was reported even at higher doses.

6. **Combination treatment with curcumin and quercetin of adenomas in familial adenomatous polyposis.** Cruz-correa M, Shoskes DA, Sanchez P, Zhao R, Hylind LM, Wexner SD and Giardiello FM. *Clinical Gastroenterology and Hepatology* 2006; 4: 1035-38.

   Curcumin C3 Complex® (480 mg), Quercetin (20 mg), 3 times
   Supplementation of curcumin and quercetin appears to reduce the number and size of ileal and rectal adenomas in patients with FAP without appreciable toxicity.

CLINICAL STUDIES

7. **A randomized, placebo-controlled, double-blind clinical trial of curcuminoids in oral lichen planus.** Chainani-Wu N, Silverman S, Reingold A, Bostrom A, Mc Culloch C, Lozada-Nur F and Weintraub J. *Phytomedicine*. 2007; 14(7-8):437-46. *Epub* 2007 Jul 2.

   Curcumin C3 Complex® (2000 mg).
   Curcumin was found to be well tolerated at the dosage of 2000 mg/day with no significant adverse effects arising from Curcumin supplementation.

8. **Curcumin downregulates NF-κB and related genes in patients with multiple myeloma: Results of a Phase I/II study.** Vadhan-Raj S, Weber DM, Wang M, Giralt SA, Thomas SK, Alexanian R, Zhou X, Patel P, Bueso-Ramos CE, Newman RA and Aggarwal BB. *Blood* 2007; 110: Abstract 1177.

   Curcumin C3 Complex® + BioPerine® (up to 12 g + 10 mg/day).
   Exerted anti-inflammatory effects by down-regulating NF-κB, STAT3 and COX-2 expression.

9. **Pharmacokinetics of curcumin conjugate metabolites in healthy human subjects.** Vareed SK, Kakarala M, Ruffin MT, Crowell JA, Normolle DP, Djuric Z, Brenner DE. *Cancer Epidemiol Biomarkers Prev*. 2008; 17(6):1411-17.

   Curcumin C3 Complex® (250 mg capsules; 10 and 12 g).
   Curcumin is absorbed after oral dosing in humans and can be detected as glucuronide and sulfate conjugates in plasma.

10. **Phase II trial of curcumin in patients with advanced pancreatic cancer.** Dhillon N, Aggarwal BB, Newman RA, Wolf RA, Kunnumakkara AB, Abbruzzese JL, Ng CS, Badmaev V and Kurzrock R. *Clin Cancer Res*. 2008; 14(14):4491-99.

    Curcumin C3 Complex® (8000 mg), 2 months.
    Curcumin down-regulated expression of NF-kB, cyclooxygenase-2, and phosphorylated signal transducer and activator of transcription 3 in peripheral blood mononuclear cells from patients. Thus was well tolerated and has biological activity in some patients with pancreatic cancer.

11. **Oral curcumin in the treatment of moderate to severe Psoriasis vulgaris: A prospective clinical trial.** Kurd SK, Smitha N, VanVoorhees A, Troxel AB, Badmaev V, Seykpra JT and Gelfand JM. *J am Acad Dermatol*. 2008; 58:625-31.

    Curcumin C3 Complex® (4500 mg).
    The intention-to-treat analysis response rate was 16.7% and both responders achieved a Psoriasis Area and Severity Index 75 score.

12. **The potential role of curcumin in patients with monoclonal gammopathy of undefined significance--its effect on paraproteinemia and the urinary N-telopeptide of type I collagen bone turnover marker.** Golombick T, Diamond TH, Badmaev V, Manoharan A and Ramakrishna R. *Clin Cancer Res*. 2009; 15(18):5917-22.

    Curcumin C3 Complex® (4000 mg).
    Curcumin was able to decrease paraprotein load as well as decrease in urinary N-telopeptide of type I collagen in patients with monoclonal gammopathy.

CLINICAL STUDIES

13. **Curcumin and Gemcitabine in patients with advanced pancreatic cancer.** Epelbaum R, Schaffer M, Vizel B, Badmaev V and Bar-Sela G. *Nutri Cancer* 2010;62(8): 1137-1141.

    Curcumin C3 Complex® (8000 mg); Gemcitabine (1,000 mg/m^2 iv) weekly for 3 of 4 weeks. Low compliance for curcumin at a dose of 8,000 mg/day, when taken together with systemic gemcitabine, may prevent the use of high doses of oral curcumin needed to achieve systemic effect.

14. **Phase I dose escalation trial of docetaxel plus curcumin in patients with advanced and metastatic breast cancer.** Bayet-Robert M, Kwiatkowski F, Leheurteur M, Gachon F, Planchat E, Abrial C, Mouret-Reynier M, Durando X, Barthomeuf C and Chollet P. *Cancer Biology & Therapy* 2010; 9(1): 8-14.

    Curcumin C3 Complex® (500 to 8000 mg).
    The recommended dose of curcumin is 6,000 mg/d for seven consecutive days in combination with a standard dose of docetaxel. Also demonstrated the feasibility, the safety and the tolerability of the combination of curcumin and docetaxel therapy.

15. **Possible action mechanism for curcumin in pre-cancerous lesions based on serum and salivary markers of oxidative stress.** Rai B, Kaur J, Jacobs R and Singh J. *J Oral Sci*. 2010; 52(2): 251-56.

    Curcumin C3 Complex® (1000 mg).
    In oral leukoplakia, submucous fibrosis and lichen planus, the levels of serum and salivary vitamins C and E increased significantly, while MDA and 8-OHdG levels decreased after 131, 211 and 191 days respectively. Hence, curcumin mediates its anti-pre-cancer activities by increasing levels of vitamins C and E, preventing lipid peroxidation and DNA damage.

16. **Phase IIa clinical trial of curcumin for the prevention of colorectal neoplasia.** Carroll RE, Benya RV, Turgeon DK, Vareed S, Neuman M, Rodriguez L, Kakarala M, Carpenter PM, McLaren C, Meyskens FL and Brenner DE. *Cancer Prev Res*. 2011; 4(3): 354-64.

    Curcumin C3 Complex® (2000 or 4000 mg), 30 days.
    Curcumin was well tolerated at both 2 g and 4 g. The data suggest that curcumin can decrease ACF number.

17. **Curcumin and EGCG suppress apurinic/apyrimidinic endonuclease 1 and induce complete remission in B-cell non-hodgkin's lymphoma patients.** Bassiouny AR, Atteya MA, El-Rashidy FH and Neenaa HM. *Functional Foods in Health and Disease*. 2011; 1(12):525-44.

    Curcumin C3 Complex® (0.9 to 5.4 g), Green tea extract (9 g).
    Combination of curcumin with EGCG resulted in a synergistic antitumor activity and that with CHOP agents in additivity or sub-additivity, down-regulated the expression of all NF-κB regulated gene products, leading to the suppression of angiogenesis, metastasis and entering in complete remission as indicated by β2-microglobulin and lactate dehydrogenase (LDH) levels.

CLINICAL STUDIES

18. **A phase I/II study of gemcitabine-based chemotherapy plus curcumin for patients with gemcitabine-resistant pancreatic cancer.** Kanai M, Yoshimura K, Asada M, Imaizumi A, Suzuki C, Matsumoto S, Nishimura T, Mori Y, Masui T, Kawaguchi Y, Yanagihara K, Yazumi S, Chiba T, Guha S and Aggarwal BB. *Cancer Chemother Pharmacol*. 2011; 68(1):157-64.

    Curcumin C3 Complex® (8 g).
    Combination therapy using 8 g oral curcumin daily with gemcitabine-based chemotherapy was found to be safe and feasible in patients with pancreatic cancer.

19. **Oral curcumin supplementation in patients with atopic asthma.** Kim DH, Phillips JF and Lockey RF. *Allergy Rhinol (Providence)*. 2011; 2(2):e51-3.

    Curcumin C3 Complex® (2 g), 6 months.
    No differential response was seen in the treatment and placebo groups regarding the primary end point, postbronchodilator forced expiratory volume in 1 second (FEV(1)).

20. **Improvement of sulphur mustard – induced chronic pruritus, quality of life and antioxidant status by curcumin: Results of a randomized double blind, placeo controlled trial.** Panahi Y, Sahebkar A, Amiri M, Davoudi SM, Beiraghdar F, Hoseininejad SL and Kolivand M. *Br J Nutr*. 2012; 108(7):1272-79.

    Curcumin C3 Complex® + BioPerine® (1000 mg + 10 mg/day).
    Supplementation significantly increased the activity of antioxidant enzymes, which helps to fight the oxidative stress. Oxidative stress plays an important role in pathogenesis of sulphur mustard complications.

21. **A randomized controlled trial on the anti-inflammatory effects of curcumin patients with chronic sulphur mustard induced cutaneous complications.** Panahi Y, Sahebkar A, Parvin S and Saadat A. *Ann Clin Biochem*. 2012; 49:580-88.

    Curcumin C3 Complex® + BioPerine® (1000 mg + 10 mg/day), 4 weeks.
    Supplementation significantly reduced the serum interleukin-8 levels as well as hs-CRP levels. It also helped to reduce the pruritus score as seen from a marked declined in pruritus score.

22. **To assess the efficacy and safety of NILIN® SR tablets in the management of osteoarthritis of knee.** Natarajan S and Majeed M. *Int J Pharm & Life Sci*. (IJPLS), 2012; 3(2): 1413-23.

    Curcumin C3 Complex® + Boswellin® + Gingerols (500 mg + 544 mg + 200 mg/twice a day).
    Showed significant decrease in WOMAC score and increase in six-minute walk distance. Thus safe and effective for osteoarthritis.

23. **High-dose curcuminoids are efficacious in the reduction in symptoms and signs of oral lichen planus.** Chainani-Wu N, Madden E, Lozada-Nur and Silverman S. *J Am Acad Dermatol*. 2012; 66(5): 752-60.

    Curcumin C3 Complex® (6000 mg), 2 weeks.
    Curcuminoids was well tolerated and may prove efficacious in controlling signs and symptoms of oral lichen planus.

CLINICAL STUDIES

24. **Use of curcuminods in a cohort of patients with oral lichen planus, an autoimmune disease.** Chainani-Wu N, Collins K and Silverman S. *Phytomedicine*. 2012; 19(5): 418-23.

    Curcumin C3 Complex® (2000 mg/day).
    Majority of patients reported reduction of symptoms with Curcuminoids, which validated curcumin's long term benefit on oral lichen planus conditions and paved way for the use of curcuminoids in the management of oral lichen planus.

25. **Proof of concept of randomized controlled study of Curcumin C3 Complex® as an adjunct treatment in schizophrenia: effects on negative and depressive symptoms.** Woodbury-Farina M, Cernovsky Z, Chiu S, Bureau Y, Campbell R, Houicin J, Terpstra K, Raheb H, Husni M and Badmaev V. *Cultivating Natural Bioactives: International Conference,* Canada. July 9 to 11, 2012. S2-3.

    Curcumin C3 Complex® (4 g & 1 g) and BioPerine® (5 mg per 1g of Curcumin), 12 weeks.
    Both 1 and 4 g supplementation improved in their negative symptoms of schizophrenia over 12 weeks.

26. **Oral curcumin for Alzheimer's disease: Tolerability and efficacy in a 24-week randomized, double blind, placebo-controlled study.** Ringman JM, Frautschy SA, Teng E, Begum AN, Bardens J, Beigi M, Gylys KH, Badmaev V, Heath DD, Apostolova LG, Porter V, Vanek Z, Marshall GA, Hellemann G, Sugar C, Masterman DL, Montine TJ, Cummings JL and Cole GM. *Alzheimers Res Ther*. 2012; 4:43.

    Curcumin C3 Complex® (2 g and 4 g), 24 weeks.
    Supplementation of curcumin in geriatric subjects at the dosage of 2g and 4 g was well tolerated and further studies to be carried out for the use of curcumin in the management of Alzheimer's disease.

27. **Monoclonal gammopathy of undetermined significance, smoldering multiple myeloma, and curcumin: A randomized, double-blind placebo controlled cross-over 4g study and an open-label 8g extension study.** Golombick T, Diamond TH, Manoharan A and Ramakrishna R. *Am J Hematol*. 2012; 87: 455-60.

    Curcumin C3 Complex® (4 and 8 g).
    Curcumin therapy decreased the free light-chain ratio (rFLC), reduced the difference between clonal and nonclonal light-chain (dFLC) and involved free light-chain (iFLC). The supplementation suggest that curcumin might have the potential to slow the disease process in patients with MGUS and SMM.

28. **Long term use of curcumin in two smoldering multiple myeloma patients.** Golombick T, Diamond TH, Manoharan A, Ramakrishna R. *Journal of Hematological Malignancies*. 2013; 3(1): 18-23.

    Curcumin C3 Complex® (4 and 8 g), 9 months.
    Curcumin has the potential to slow the disease progression as shown by decrease in free light chain (rFLC) ratio and can be used to plan intervention strategies in patients with MGUS and SMM.

CLINICAL STUDIES

29. **Topical curcumin for the prevention of oral mucositis in pediatric patients: case series.** Elad S, Meidan I, Sellam G, Simaan S, Zeevi I, Waldman E, Weintraub M and Revel-Vilk S. *Altern Ther Health Med*. 2013; 19(3): 21-24.

    Curcumin C3 Complex® mouth wash.
    Curcumin mouthwash was safe and well-tolerated.

30. **Curcumin for radiation dermatitis: A randomized, double-blind, placebo-controlled clinical trial of thirty breast cancer patients.** Ryan JL, Heckler CE, Ling M, Katz A, Williams JP, Pentland AP, Morrow GR. *Radiat Res*. 2013; 180(1):34-43.

    Curcumin C3 Complex® (6 g), 1 week.
    Supplementation reduces the severity of radiation dermatitis in breast cancer patients.

31. **A pilot double-blind, randomized, placebo-controlled trial of curcumin/BioPerine® for lung cancer chemoprevention in patients with chronic obstructive pulmonary disease.** Sharafkhaneh A, Lee JJ, Liu D, Katz R, Caraway N, Acosta C, Wistuba II, Aggarwal B, Dickey B, Moghaddam SJ, Hanania N, Newman R, Abdel-Monem H, Nguyen NB, Farhangfar CJ, Hong WK and Kurie JM. *Advances in Lung Cancer*. 2013; 2(3):62-69.

    Curcumin C3 Complex® + BioPerine® (1g + 5 mg) for a month, 1.5 g + 5 mg for another month, and 2 g +5 mg for an additional month.
    Reversed the cytological parameter abnormalities in patients with chronic obstructive pulmonary disease.

32. **Effect of a herbal extract containing curcumin and piperine on midazolam, flurbiprofen and paracetamol (acetaminophen) pharmacokinetics in healthy volunteers.** Volak LP, Hanley MJ, Masse G, Hazarika S, Harmatz JS, Badmaev V, Majeed M, Greenblatt DJ and Court MH. *Br J Clin Pharmacol*. 2013; 75(2):450-62.

    Curcumin C3 Complex® + BioPerine® (4 g and 24 mg).
    Piperine-enhanced curcuminoid preparation is unlikely to result in a clinically significant interaction involving CYP3A, CYP2C9 or the paracetamol conjugation enzymes.

33. **Curcuminoids modulate pro-oxidant-antioxidant balance, but not the immune response to heat shock protein 27 and oxidized LDL in obese individuals.** Sahebkar A, Mohammadi A, Atabati A, Rahiman S, Tavallaie S, Iranshahi M, Akhlaghi S, Ferns GA and Ghayour-Mobarhan M. *Phytother Res*. 2013; 27(12):1883-88.

    Curcumin C3 Complex® + BioPerine® (1000 mg + 10 mg/day).
    Supplementation mitigates oxidative stress in obese individuals.

34. **Prolonged biologically active colonic tissue levels of curcumin achieved after oral administration - A clinical pilot study including assessment of patient acceptability.** Irving GRB, Howells LM, Sale S, Kralj-Hans I, Atkin WS, Clark SK, Britton RB, Jones DJL, Scott EN, Berry DP, Hemingway D, Miller AS, Brown K, Gescher AJ and Steward WP. *Cancer Prev Res (Phila)*. 2013; 6(2): 119-28.

    Curcumin C3 Complex® (2.35 g).
    Pharmacologically active levels of curcumin were recovered from colonic mucosa. The regimen used here appears safe, and patients support its use in long-term trials.

CLINICAL STUDIES

35. **Effects of supplementation with curcuminoids on dyslipidemia in obese patients: A randomized crossover trial.** Mohammadi A, Sahebkar A, Iranshahi M, Amini M, Khojasteh R, Ghayour-Mobarhan M and Ferns GA. *Phytother Res*. 2013; 27(3):374-79.

Curcuminoids + BioPerine® (1000 mg + 10 mg/day).
Reduced the lipid profile parameters including serum triglycerides.

36. **Curcuminoid treatment for knee osteoarthritis: A randomized double-blind placebo-controlled trial.** Panahi Y, Rahimnia AR, Sharafi M, Alishiri G, Saburi A and Sahebkar A. *Phytother Res*. 2014; 28(11):1625-31.

Curcumin C3 Complex® + BioPerine® (1500 mg+15 mg/day).
Supplementation showed significant decrease in pain, physical function and stiffness, the LPFI and VAS scores also showed a significant reduction. Also there was 84% decrease in pain in the subjects who took naproxen along with curcuminoids.

37. **Investigation of the effect of short-term supplementation with curcuminoids on circulating small dense low-density lipoprotein concentrations in obese dyslipidemic subjects: A randomized double-blind placebo-controlled cross-over trial.** Moohebati M, Yazdandoust S, Sahebkar A, Mazidi M, Sharghi-Shahri Z, Ferns G, Ghayour-Mobarhan M. *ARYA Atheroscler*. 2014; 10(5):280-86.

Curcumin C3 Complex® + BioPerine® (1000 mg + 5 mg/day), 4 weeks.
Curcuminoids was not associated with any significant alteration in circulating small density LDL concentrations.

38. **Investigation of the effects of curcumin on serum cytokines in obese individuals: A randomized controlled trial.** Ganjali S, Sahebkar A, Mahdipour E, Jamialahmadi K, Torabi S, Akhlaghi S, Ferns G, Parizadeh SM and Ghayour-Mobarhan M. *Sci World J*. 2014.

Curcumin C3 Complex® + BioPerine® (1000 mg + 10 mg/day).
Curcumin was able to modulate the inflammatory response in obese subjects. Supplementation significantly reduced the serum concentrations of interleukin 1β, vascular endothelial growth factor and interleukin-4.

39. **Lipid modifying effects of adjunctive therapy with curcuminoids-piperine combination in patients with metabolic syndrome: Results of a randomized controlled trial.** Panahi Y, Khalili N, Hosseini MS, Abbasinazari M and Sahebkar A. *Complement Ther Med*. 2014; 22(5):851-57.

Curcumin C3 Complex® + BioPerine® (1000 mg + 10 mg/day).
Combination resulted in greater reduction of serum triglycerides, total cholesterol, serum low density lipoprotein-cholesterol, non-high density lipoprotein-cholesterol, Lipoprotein and increase in high density lipoprotein-cholesterol concentration.

40. **Antioxidant and anti-inflammatory effects of curcuminoid - piperine combination in subjects with metabolic syndrome: A randomized controlled trial and an updated meta-analysis.** Panahi Y, Hosseini MS, Khalili N, Naimi E, Majeed M and Sahebkar A. *Clin Nutr*. 2015; 34(6):1101-08.

Curcumin C3 Complex® + BioPerine® (1000 mg + 10 mg/day).
Supplementation significantly reduced the serum hs-CRP concentrations and improved the biomarkers of inflammation and oxidative stress.

CLINICAL STUDIES

41. **Impact of supplementation with curcuminoids on systemic inflammation in patients with knee osteoarthritis: Findings from a Randomized double-blind placebo-controlled trial.** Rahimnia AR, Panahi Y, Alishiri G, Sharafi M, Sahebkar A. *Drug Res (Stuttg).* 2015; 65(10):521-25.

    Curcumin C3 Complex® + BioPerine® (1500 mg + 15 mg/day), 6 weeks.
    Significant improvement in clinical symptoms of osteoarthritis in curcumin-treated subjects because of a local anti-inflammatory effect in osteo-cartilagenous tissue.

42. **Short-term curcuminoid supplementation for chronic pulmonary complications due to sulfur mustard intoxication: Positive results of a randomized double-blind placebo-controlled trial.** Panahi Y, Ghanei M, Bashiri S, Hajihashemi A, Sahebkar A. *Drug Res (Stuttg).* 2015; 65(11):567-73.

    Curcumin C3 Complex® + BioPerine® (1500 mg + 15 mg/day), 4 weeks.
    Short-term adjunctive therapy with curcuminoids can suppress systemic inflammation in patients suffering from SM-induced chronic pulmonary complications.

43. **Investigation of the efficacy of adjunctive therapy with bioavailability-boosted curcuminoids in major depressive disorder.** Panahi Y, Badeli R, Karami GR and Sahebkar A. *Phytother Res*. 2015; 29(1):17-21.

    Curcumin C3 Complex® + BioPerine® (1000 mg + 10 mg/day).
    Supplementation may be used as a safe and effective add-on to standard antidepressants in patients with major depressive disorder (MDD).

44. **Enhanced systemic bioavailability of curcumin through transmucosal administration of a novel micrograniular formulation.** Latimer B, Ekshyyan O, Nathan N, Moore-Medlin T, Rong X, Ma X, Khandelwal A, Christy HT, Abreo F, McClure G, Vanchiere JA, Caldito G, Dugas T, McMartin K, Lian T, Mehta V, Nathan CA. *Anticancer Res*. 2015; 35(12):6411-18.

    Curcumin C3 Complex® (4 g).
    Transmucosal administration of micrograniular curcumin leads to enhanced curcumin bioavailability that is associated with significant biological effects.

45. **An investigation of the effects of curcumin on anxiety and depression in obese individuals: A randomized controlled trial.** Esmaily H, Sahebkar A, Iranshahi M, Ganjali S, Mohammadi A, Ferns G and Ghayour-Mobarhan M. *Chin J Integr Med*. 2015; 21(5):332-38.

    Curcumin C3 Complex® + BioPerine® (1000 mg + 10 mg/day), 4 weeks.
    Supplementation showed a significant reduction in the mean Beck Anxiety Inventory score and was able to show significant antianxiety effect. Also the bioavailability of curcuminoids had the advantage by the addition of BioPerine®.

CLINICAL STUDIES

46. **The effect of curcumin on some of traditional and non-traditional cardiovascular risk factors: A pilot randomized, double-blind, placebo-controlled trial.** Mirzabeigi P, Mohammadpour AH, Salarifar M, Gholami K, Mojtahedzadeh M and Javadi MR. *Iran J Pharm Res*. 2015 Spring; 14(2): 479–86.

    Curcumin C3 Complex® (2 g/day).
    A significant improvement was observed in individual taking Curcumin in comparison to baseline values, wherein a reduction in serum values of triglyceride, low density lipoprotein and very low density low lipoprotein were recorded. This has paved way for further extensive studies on the use of Curcuminoids in cardiovascular disorder.

47. **Curcumin inhibits cancer stem cell phenotypes in *ex vivo* models of colorectal liver metastases, and is clinically safe and tolerable in combination with FOLFOX chemotherapy.** James MI, Iwuji C, Irving G, Karmokar A, Higgins JA, Griffin-Teal N, Thomas A, Greaves P, Cai H, Patel SR, Morgan B, Dennison A, Metcalfe M, Garcea G, Lloyd DM, Berry DP, Steward WP, Howells LM and Karen Brown. *Cancer Lett* 2015; 364(2): 135-41.

    Curcumin C3 Complex® (0.5, 1 or 2 g).
    The phase I dose escalation study revealed curcumin to be a safe and tolerable adjunct to FOLFOX chemotherapy in patients with colorectal liver metastases at doses up to 2 grams daily.
    Curcumin may provide added benefit in subsets of patients when administered with FOLFOX, and is a well-tolerated chemotherapy adjunct.

48. **Combining curcumin (C3-complex, Sabinsa) with standard care FOLFOX chemotherapy in patients with inoperable colorectal cancer (CUFOX): Study protocol for a randomised control trial.** Irving GRB, Iwuji COO, Morgan B, Berry DP, Steward WP, Thomas A, Brown K and Howells LM. *Trials* 2015; 16.

    Curcumin C3 Complex® (0.5, 1.0 and 2.0g)
    This study is the first to combine daily oral curcumin with standard care FOLFOX-based (5-fluorouracil, folinic acid and oxaliplatin) chemotherapy in colorectal cancer patients with inoperable liver metastases. CUFOX is first randomized trial of its kind and results of this trial can provide early evidence of clinical efficacy of Curcumin within the chemotherapeutic setting.

49. **Effects of curcuminoids-piperine combination on systemic oxidative stress, clinical symptoms and quality of life in subjects with chronic pulmonary complications due to sulphur mustard: A randomized controlled trial.** Panahi Y, Ghanei M, Hajhashemi A and Sahebkar A. *J Diet Suppl*. 2014; 13(1):93-105.

    Curcumin C3 Complex® + BioPerine® (1500 mg + 15mg/day).
    Supplementation mitigated the oxidative stress as indicated by a decrease in MDA levels and increased health related quality of life in patients having sulphur mustard-induced pulmonary complications and suggested curcuminoids as “safe adjuvants”.

50. **Mitigation of systemic oxidative stress by curcuminoids in osteoarthritis: Results of a randomized controlled trial.** Panahi Y, Alishiri GH, Parvin S and Sahebkar A. *J Diet Suppl*. 2016; 13(2):209-20.

    Curcumin C3 Complex® + BioPerine® (1500 mg+15 mg/ day).
    Reduced oxidative stress with increase in serum levels of superoxide dismutase and glutathione, and decrease in the malondialdehyde concentration.

CLINICAL STUDIES

51. **Adjunctive therapy with curcumin for peptic ulcer: A randomized controlled trial.** Khonche A, Biglarian O, Panahi Y, Valizadegan G, Soflaei SS, Ghamarchehreh ME, Majeed M and Sahebkar A. *Drug Res (Stuttg)*. 2016; 66(8):444-48.

    Curcumin C3 Complex® + BioPerine® (500 mg + 5 mg/day).
    Adjunctive therapy with curcumin showed greater improvement of dyspepsia symptoms.

52. **Effects of curcumin on serum cytokine concentrations in subjects with metabolic syndrome: A post-hoc analysis of a randomized controlled trial.** Panahi Y, Hosseini MS, Khalili N, Naimi E, Simental-Mendía LE, Majeed M and Sahebkar A. *Biomed Pharmacother*. 2016; 82:578–82.

    Curcumin C3 Complex® + BioPerine® (1000 mg + 10 mg/day).
    Reduced serum concentrations of pro-inflammatory cytokines.

53. **The new combination docetaxel, prednisone and curcumin in patients with castration-resistant prostate cancer: A pilot Phase II study.** Mahammedi H, Planchat E, Pouget M, Durando X, Curé H, Guy L, Van-Praagh I, Savareux L, Atger M, Bayet-Robert M, Gadea E, Abrial C, Thivat E, Chollet P, Eymard JC. *Oncology*. 2016; 90(2):69-78.

    Curcumin C3 Complex® (500 mg x 12 tablets), 1 week.
    This combination study produced additional data on curcumin as a treatment for cancer, with a high response rate, good tolerability and patient acceptability.

54. **Effects of supplementation with curcumin on serum adipokine concentrations: A randomized controlled trial.** Panahi Y, Hosseini MS, Khalili N, Naimi E, Soflaei SS, Majeed M and Sahebkar A. *Nutrition*. 2016; 32(10):1116-22.

    Curcumin C3 Complex® + BioPerine® (1 g + 10 mg/day).
    Elevated serum adiponectin and reduced leptin concentrations.

55. **Evaluation of the efficacy of curcumin in the treatment of oral lichen planus: A randomized controlled trial.** Amirchaghmaghi M, Pakfetrat A, Delavarian Z, Ghalavani H2, Ghazi A. *J Clin Diagn Res*. 2016; 10(5): 134-37.

    Curcumin C3 Complex® 500 mg tablets two times a day.
    No detectable effect was observed in Oral Lichen Planus with low dose curcumin treatment. It is suggested that curcumin can be effective only at higher doses.

56. **Effect of Nilitis® SR on knee pain in japanese adults: A double-blind, randomized, placebo controlled study.** Majeed M, Vaidyanathan P, Natarajan S, Majeed S, Kiran Kumar Vuppala KK. *Int J Innovat Res Med Sci* (IJIRMS) 2016; 01 (06): 2455-8737.

    NiLitis® SR is a dietary supplement containing Boswellin® Super, Curcumin C3 Complex® and ginger extract.
    Intake of NiLitis® SR relieves knee pain and may control hyaluronic acid outflow into the bloodstream.

CLINICAL STUDIES

57. **Curcuminoids plus piperine modulate adipokines in type 2 diabetes mellitus.** Panahi Y, Khalili N, Sahebi E, Namazi S, Atkin SL, Majeed M and Sahebkar A. *Curr Clin Pharmacol*. 2017; 12(4):253-58.

    Curcumin C3 Complex® + BioPerine® (1 g + 10 mg/day).
    Combination reduced the serum levels of leptin. Improved leptin:adiponectin ratio.

58. **Curcumin and piperine supplementation and recovery following exercise induced muscle damage: A randomized controlled trial.** Delecroix B, Abaïdia AE, Leduc C, Dawson B and Dupont G. *J Sports Sci Med*. 2017; 16(1):147-53.

    Curcumin C3 Complex® + BioPerine® (2000 mg + 20 mg, 3 times a day).
    Supplementation before and after exercise can attenuate muscle damage.

59. **Randomized pharmacokinetic cross-over study comparing two curcumin preparations in plasma and rectal tissue of healthy human volunteers.** Asher GN, Xie Y, Moaddel R, Sanghvi M, Dossou KS, Kashuba AD, Sandler RS, Hawke RL. *J Clin Pharmacol*. 2017; 57(2):185-93.

    Curcumin C3 Complex® (4000 mg).
    Once-daily dosing is sufficient to maintain detectable curcuminoids at steady-state in both plasma and rectal tissues.

60. **Curcuminoids modify lipid profile in type 2 diabetes mellitus: A randomized controlled trial.** Panahi Y, Khalili N, Sahebi E, Namazi S, Reiner Ž, Majeed M and Sahebkar A. *Complement Ther Med*. 2017; 33:1-5.

    Curcumin C3 Complex® + BioPerine® (1000 mg + 10 mg/day).
    Significantly reduced total cholesterol, non-HDL-C and elevated serum HDL-C levels. It also reduces the risk for cardiovascular events in Type 2 Diabetes.

61. **Long-term stabilisation of myeloma with curcumin.** Zaidi A, Lai M and Cavenagh J. *BMJ Case Rep*. 2017.

    Curcumin C3 Complex® + BioPerine® (8 g + 5 mg/day), 60 months.
    Blocks the progression of myeloma with normal range of blood cell counts. Also maintained a good quality of life throughout the study.

62. **Antioxidant effects of curcuminoids in patients with type 2 diabetes mellitus: A randomized controlled trial.** Panahi Y, Khalili N, Sahebi E, Namazi S, Karimian MS, Majeed M and Sahebkar A. *Inflammopharmacol*. 2017; 25(1):25-31.

    Curcumin C3 Complex® + BioPerine® (1000 mg + 10 mg/day).
    Elevate total antioxidant capacity, while reducing lipid peroxidation.

63. **Phase I dose-escalation trial of intravaginal curcumin in women for cervical dysplasia.** Leda Gattoc, Paula M Frew, Shontell N Thomas, Kirk A Easley, Laura Ward, H-H Sherry Chow, Chiemi A Ura, and Lisa Flowers. *J Clin Trials*. 2017; 9: 1–10.

    Curcumin C3 Complex® (500 mg, 1000 mg, 1500 mg and 2000 mg) for 14 days.
    No dose-limiting toxicities (0/13) were experienced. Intravaginal curcumin was well tolerated by all subjects and safe.

CLINICAL STUDIES

64. **Translating curcumin into clinical practice for treatment of metastatic colorectal cancer: the CUFOX trial.** Iwuji, COO. Doctoral (PhD) Thesis. University of Leicester, UK. Degree Awarded date: April 26, 2017.

Curcumin at a daily dose of 2 g was given to metastatic colorectal patients who received standard FOLFOX chemotherapy.
No notable safety concerns were reported.

65. **Effects of curcuminoids plus piperine on glycemic, hepatic and inflammatory biomarkers in patients with type 2 diabetes mellitus: A randomized double-blind placebo-controlled trial.** Panahi Y, Khalili N, Sahebi E, Namazi S, Simental-Mendía LE, Majeed M and Sahebkar A. *Drug Res (Stuttg)*. 2018; 68 (7) 403-09.

Curcumin C3 Complex® + BioPerine® (500 mg + 5 mg/day).
Supplementation reduced the serum glucose and improved liver health enzymes in Type 2 Diabetes mellitus.

66. **Effects of turmeric and curcumin dietary supplementation on human gut microbiota: A double-blind, randomized, placebo-controlled pilot study.** Peterson CT, Vaughn AR, Sharma V, Chopra D, Mills PJ, Peterson SN, Sivamani RK. *J Evid Based Integr Med*. 2018;23:1-8.

Group A: Turmeric powder (1000 mg) + BioPerine® (1.25 mg) (n=6)
Group B: Curcumin C3 Complex® (1000 mg) + BioPerine® (1.25 mg) (n=5)
Group C: Placebo (1000 mg) (n=3). 2 Months.
The study found that both turmeric and curcuminoids have similar qualitative effects on the intestinal bacterial population. However, curcuminoids has a far larger quantitative effect indicating that curcumunoliods in turmeric are the decisive components in influencing the bacterial population. Thus, curcuminoids have an unique role and effect on the gut microbiome.

67. **A phase II study of curcumin and vitamin d in previously untreated patients with early stage chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).** William BM, Brillhart K, Afable M, Bakalarz K, Cooper B, Lazarus HM, Gerson SL, MD , Creger R, Nagabhushanam K, Grote J, Fu P, Kunati S, Yang S, Xu Y, Woost P, Jacobberger J, de Lima M, Caimi P. *Blood*. 2018; 132(Suppl.): 1875/ASH Annual Meeting 2018, Abstract 1875.

Curcumin 8 g and 10,000 IU of vitamin D3 daily.
Curcumin and high-dose vitamin D combination is safe and well tolerated in patients with early stage CLL.

68. **Safety and efficacy of nanocurcumin as add-on therapy to Riluzole in patients with amyotrophic lateral sclerosis: A pilot randomized clinical trial.** Ahmadi M, Agah E, Nafissi S, Jaafari MR, Harirchian MH, Sarraf P, Faghihi-Kashani S, Hosseini SJ, GhoreishiA6, Aghamollaii V, Hosseini M, Tafakhori A. *Neurotherapeutics*. 2018;15(2):430-438. (SinaCurcumin - a certified curcuminoid product in Iran comprises curcumin, desmethoxycurcumin, and bisdemethoxy-Curcumin-C3 complex).

Curcumin C3 Complex® (nano form) 80 mg daily.
Curcumin treatment was safe and might improve the probability of survival as an add-on treatment in patients with ALS

CLINICAL STUDIES

69. **Curcumin combined with FOLFOX chemotherapy is safe and tolerable in patients with metastatic colorectal cancer in a randomized Phase IIa trial.** Howells LM, Iwuji COO, Irving GRB, Barber S, Walter H, Sidat Z, Griffin-Teall N, Singh R, Foreman N, Patel SR, Morgan B, Steward WP, Gescher A, Thomas AL, Brown K. *J Nutr*. 2019; 149(7):1133-39.

    FOLFOX ± Bevacizumab; FOLFOX ± Bevacizumab + 2 g Curcumin C3 Complex®/d.
    The first randomized controlled trial for curcumin in combination with FOLFOX chemotherapy for patients with metastatic colorectal cancer.
    Combination of curcumin with FOLFOX chemotherapy represents a safe and tolerable treatment with potential to provide patient benefit.

70. **The effects of curcumin on the prevention of atrial and ventricular arrhythmias and heart failure in patients with unstable angina: A randomized clinical trial.** Mostafa Dastani, Leila Bigdelu, Mahsa Hoseinzadeh, Hamid Reza Rahimi, Asieh Karimani, Amir Hooshang Mohammadpour, Masoumeh Salari. *Avicenna J Phytomed*. 2019 Jan-Feb; 9(1): 1–9.

    Curcumin C3 Complex® (80 mg/day for 5days) and placebo (80 mg/day for 5days).
    Nanocurcumin administered at the dose of 80 mg/day for five days had no effect in the incidence of cardiovascular complications in patients with unstable angina.

71. **Oral administration of nanomicelle curcumin in the prevention of radiotherapy-induced mucositis in head and neck cancers.** Delavarian Z, Pakfetrat A, Ghazi A, Jaafari MR, Homaei Shandiz F, Dalirsani Z, Mohammadpour AH, Rahimi HR. *Spec care in dentist.* 2019; 39(2), 166-72.

    80 mg/day nanocurcumin (1 soft gel capsule of SinaCurcumin® 80 per day) during the radiotherapy, 6 weeks.
    The control-group patients, developed Oral Mucositis (OM) in the 2nd week of radiotherapy, only 32% of the case group developed OM with no obvious oral or systemic side effects. Data shows nanocurcumin is an effective agent in the prevention of OM or reducing its severity.

72. **Pharmacokinetics, pharmacodynamics, and PKPD modelling of curcumin in regulating antioxidant and epigenetic gene expression in healthy human volunteers.** Cheng D, Li W, Wang L, Lin T, Poiani G, Wassef A, Hudlikar R, Ondar P, Brunetti L, Kong AN. *Mol Pharm*. 2019; 16(5):1881-89.

    Curcumin C3 Complex® + BioPerine® (4 g+ 20 mg).
    Oral administration of curcumin resulted in detectable levels of its metabolite, curcumin glucuronide, but more importantly, it increased the gene expression of antioxidant genes NRF2, HO-1, and NQO1 and suppressed epigenetic genes HDAC1, HDAC2, HDAC3, and HDAC4.

73. **Pharmacokinetics of liposomal curcumin (Lipocurc™) infusion: Effect of co-medication in cancer patients and comparison with healthy individuals.** Bolger GT, Licollari A, Tan A, Greil R, Vcelar B, Greil-Ressler S, Weiss L, Schönlieb C, Magnes T, Radl B, Majeed M, Sordillo PP. *Cancer Chemother. Pharmacol*. 2019; 83(2):265-75.

    The co-medications and health status, either or both, impact the pharmacokinetics of curcumin in the cancer patients.

CLINICAL STUDIES

74. **Curcuminoids plus piperine improve nonalcoholic fatty liver disease: A clinical trial.** Panahi Y, Valizadegan G, Ahamdi N, Ganjali S, Majeed M, Sahebkar A. *J Cell Biochem*. 2019; 120(9):15989-96.

Curcumin C3 Complex® + BioPerine® (500 mg + 5 mg), 12 weeks.
Supplementation with curcuminoids plus piperine significantly improved NAFLD severity and reduced the

- hematocrit
- erythrocyte sedimentation rate
- alanine aminotransferase
- aspartate aminotransferase
- alkaline phosphatase
- cholesterol
- low-density lipoprotein cholesterol
- iron
- hemoglobin
- increased total iron binding capacity

75. **Exploratory study of curcumin isolated from turmeric *Curcuma longa*, the putative histone deacetylase inhibitor, as added-on strategy to antipsychotics in treating negative symptoms and neuro-cognitive deficits in schizophrenia.** Chiu S, Farina MW, Terpstra K, Badmaev V, Cernovsky Z, Bureau Y, Raheb H, Husni M, Copen J, Shad M, Jirui H, Campbell R, Khazaeipool Z, Carriere A. *Adv Res J Multidisciplinary Discov*. 2019; 40(2): 6-15.

Supercurcumin™ (Curcumin C3 Complex® + BioPerine®; 1 g + 5 mg).
Supercurcumin™ (Curcumin C3 Complex® + BioPerine®; 4 g + 20 mg), 16 weeks.
The Curcumin was safe and benefitted when combined with piperine in schizophrenia.
Supercurcumin™ was well tolerated with no serious adverse events.

76. **The synergistic effects of nano-curcumin and coenzyme Q_{10} supplementation in migraine prophylaxis: a randomized, placebo-controlled, double-blind trial.** Parohan M, Sarraf P, Javanbakht MH, Foroushani AR, Ranji-Burachaloo S, Djalali M. (2019): *Nutr Neurosci.* 2019. 1-10. (SinaCurcumin - a certified curcuminoid product in Iran comprises curcumin, desmethoxycurcumin, and bisdemethoxy-Curcumin-C3 complex®).

Curcumin C3 Complex® (nano form) 80 mg plus coenzyme Q_{10} (CoQ_{10}) 300 mg daily.
A possible synergistic effect of nano-curcumin and CoQ_{10} on clinical features of migraine.

77. **Effects of supplementation with curcuminoids on serum adipokines in critically ill patients: A randomized double-blind placebo-controlled trial.** Shadnoush M, Zahedi H, Norouzy A, Sahebkar A, Sadeghi O, Najafi A, Hosseini S, Qorbani M, Ahmadi A, Hossein S, Mohammad A, Hosseinzadeh-Attar J. *Phytother Res*. 2020.

Group A: Curcumin C3 Complex® (500 mg) + BioPerine® (5 mg) (n=31)
Group B: Placebo (500 mg) (n=31). 7 days
Supplementation with curcuminoids significantly reduced serum levels of leptin but had no significant effect on adiponectin levels in critically ill patients with traumatic brain injury (TBI).

CLINICAL STUDIES

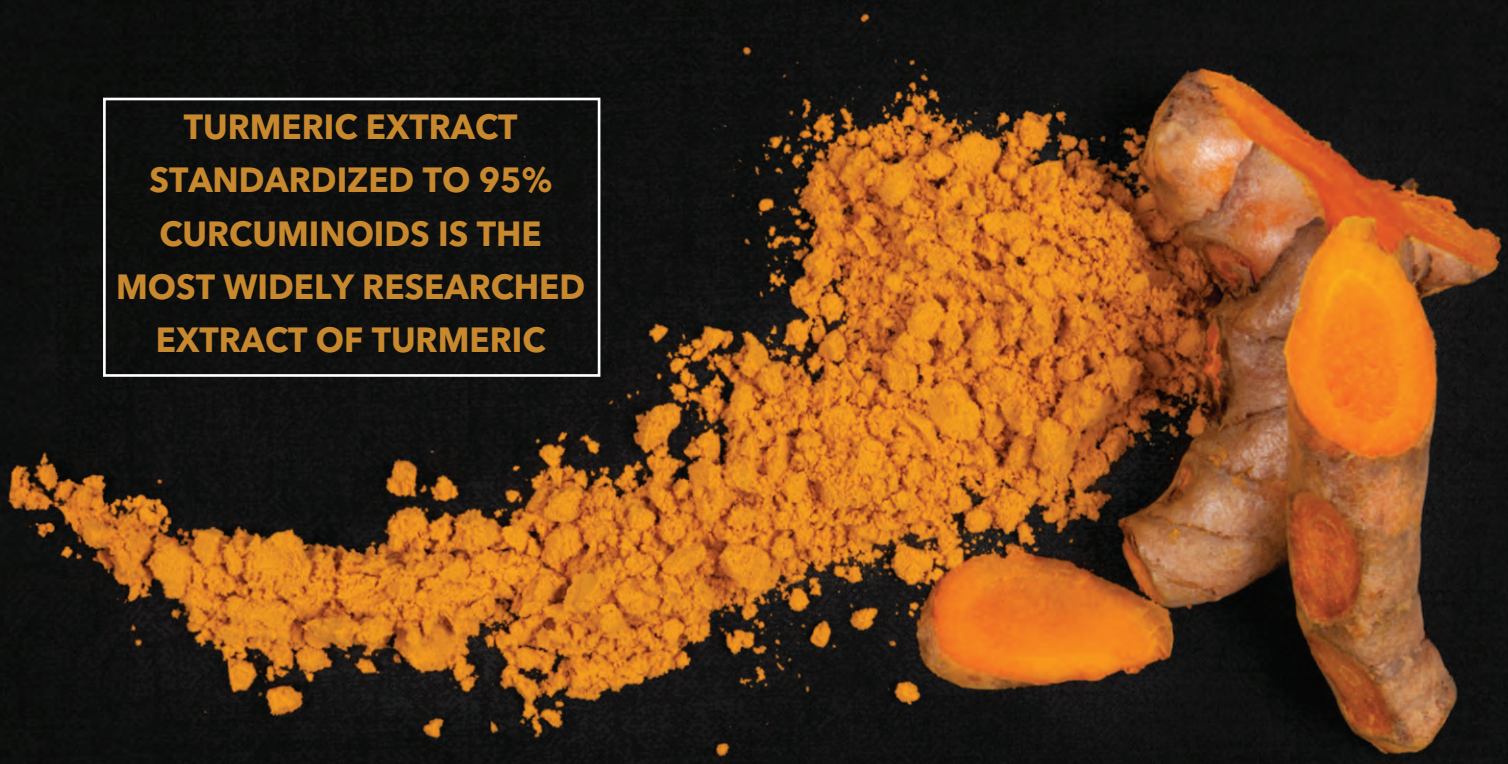
78. **Effects of curcuminoids on inflammatory status in patients with non-alcoholic fatty liver disease: A randomized controlled trial.** Saberi-Karimian M, Keshvari M, Ghayour-Mobarhan M, Salehizadeh L, Rahmani S, Behnam B, Jamialahmadi T, Asgary S, Sahebkar A. *Complement Ther Med*. 2020:102322.

One capsule containing 500 mg C3 Complex® plus 5 mg BioPerine® daily.
Curcumin supplementation can improve serum levels of inflammatory cytokines in subjects with NAFLD and this might be at least partly responsible for the anti-steatotic effects of curcuminoids.

79. **Use of curcumin in multiple myeloma patients intolerant of steroid therapy.** Ramakrishna R, Diamond TH, Alexander W, Manoharan A, Golombick T. *Clin Case Rep*. 2020; 8(4): 739-44.

Curcumin C3 Complex® combined with either an immunomodulatory drug (IMiD) or PI (ie, bortezomib, carfilzomib, or ixazomib) in the treatment of older (>55 years) Multiple Myeloma (MM) patients intolerant of Dexamethasone.

Curcumin possess the potential to impede myeloma activity and improve the quality of life in MM patients.



Curcumin C3 Complex is...

the original 95% patented extract

PRECLINICAL STUDIES

80. **Curcumin inhibits formation of amyloid beta oligomers and fibrils, binds plaques, and reduces amyloid *in vivo*.** Yang F, Lim GP, Begum AN, Ubeda OJ, Simmons MR, Ambegaokar SS, Chen PP, Kayed R, Glabe CG, Frautschy SA and Cole GM. *J Biol Chem*. 2005 Feb 18; 280(7):5892-901.

Curcumin at low dose decreased amyloid formation in aged animals, thus providing a rationale for clinical trials for Curcumin in the prevention or even treatment of AD.

81. **Curcumin suppresses the paclitaxel-induced nuclear factor-kappaB pathway in breast cancer cells and inhibits lung metastasis of human breast cancer in nude mice.** Aggarwal BB, Shishodia S, Takada Y, Banerjee S, Newman RA, Bueso-Ramos CE and Price JE. *Clin Cancer Res*. 2005 Oct 15; 11(20):7490-98.

Curcumin showed therapeutic potential alone as well as in combination with paclitaxel in preventing breast cancer metastasis possibly through suppression of NF-κB and NF-κB-regulated gene products.

82. **Dietary curcumin significantly improves obesity-associated inflammation and diabetes in mouse models of diabesity.** Weisberg SP, Leibel R and Tortoriello DV. *Endocrinology*. 2008 Jul; 149(7):3549-58.

Curcumin was effective in reversing many of the inflammatory and metabolic derangements associated with obesity and improved glycemic control in mouse models of type 2 diabetes.

83. **Curcumin sensitizes human colorectal cancer xenografts in nude mice to gamma-radiation by targeting nuclear factor-kappaB-regulated gene products.** Kunnumakkara AB, Diagaradjane P, Guha S, Deorukhkar A, Shentu S, Aggarwal BB and Krishnan S. *Clin Cancer Res*. 2008 Apr 1; 14(7):2128-36.

Antitumor effects of radiation therapy in colorectal cancer were enhanced by Curcumin by inhibiting NF-κB and NF-κB-regulated gene products.

84. **Enhancing anti-inflammation activity of curcumin through O/W nanoemulsions.** Wang X, Jiang Y, Wang YW, Huang MT, Ho CT, Huang Q. *Food Chem*. 2008;108(2):419-24.

The enhanced anti-inflammation activity of curcumin encapsulated in oil-in-water (O/W) emulsions is evidenced by the mouse ear inflammation model. There is a 43% or 85% inhibition effect of 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced edema of mouse ear for 618.6 nm and 79.5 nm 1% curcumin O/W emulsions, respectively.

85. **Curcumin circumvents chemoresistance *in vitro* and potentiates the effect of Thalidomide and Bortezomib against human multiple myeloma in nude mice model.** Sung B, Kunnumakkara AB, Sethi G, Anand P, Guha S and Aggarwal BB. *Mol Cancer Ther*. 2009 Apr; 8(4):959-70.

Curcumin potentiated the effects of bortezomib and thalidomide, and overcame chemoresistance as well as sensitized multiple myeloma cells by down-regulating NF-κB and NF-κB-regulated gene products.

PRECLINICAL STUDIES

86. **Curcumin sensitizes human colorectal cancer to capecitabine by modulation of cyclin D1, COX-2, MMP-9, VEGF and CXCR4 expression in an orthotopic mouse model.** Kunnumakkara AB, Diagaradjane P, Anand P, Harikumar KB, Deorukhkar A, Gelovani J, Guha S, Krishnan S and Aggarwal BB. *Int J Cancer*. 2009 Nov 1; 125(9):2187-97.

Curcumin was found to be potentiating the antitumor and antimetastatic effects of capecitabine by suppressing NF-κB cell signalling pathway, thus could be an effective adjunctive in the management of colorectal cancer.

87. **Inhibitory effect of curcuminoids on acetylcholinesterase activity and attenuation of scopolamine-induced amnesia may explain medicinal use of turmeric in Alzheimer's disease.** Ahmed T and Gilani AH. *Pharmacol Biochem Behav*. 2009 Feb; 91(4):554-59.

Curcuminoids mixture was found to be exhibiting a wide range of pharmacological activities beneficial for AD.

88. **Attenuation of proteolysis and muscle wasting by Curcumin C3 Complex® in MAC16 colon tumour-bearing mice.** Siddiqui RA, Hassan S, Harvey KA, Rasool T, Das T, Mukerji P and DeMichele S. *Br J Nutr*. 2009 Oct; 102(7):967-75.

Curcumin treatment resulted in the prevention and reversal of cachexia in cachectic animals bearing MAC16 tumours, thus possess an effective adjuvant therapy potential against cachexia.

89. **Curcuminoids enhance memory in an amyloid-infused rat model of Alzheimer's disease.** Ahmed T, Enam SA and Gilani AH. *Neuroscience*. 2010 Sep 1; 169(3):1296-306.

At varied time and dose of curcuminoid mixture, as well as individual components, showed a beneficial effect on the expression levels of genes involved in synaptic plasticity. Thus, suggesting that potential effects of Curcuminoids involve multiple target sites in spatial memory enhancing and disease modifying in AD.

90. **Curcumin improves sclerosing cholangitis in *Mdr2*$^{-/-}$ mice by inhibition of cholangiocyte inflammatory response and portal myofibroblast proliferation.** Baghdasaryan A, Claudel T, Kosters A, Gumhold J, Silbert D, Thüringer A, Leski K, Fickert P, Karpen SJ and Trauner M. *Gut*. 2010 Apr; 59(4):521-30.

Curcumin reduces liver damage, cholangitis and biliary fibrosis by acting on multiple targets: inhibiting the inflammatory phenotype of bile duct epithelial cells through PPARγ activation and blocking proliferation/ activation of portal myofibroblasts (MFBs) through inhibition of ERK1/2 signalling.

91. **Curcumin inhibits carcinogen and nicotine-induced mammalian target of rapamycin pathway activation in head and neck squamous cell carcinoma.** Clark CA, McEachern MD, Shah SH, Rong Y, Rong X, Smelley CL, Caldito GC, Abreo FW and Nathan CO. *Cancer Prev Res (Phila)*. 2010 Dec; 3(12):1586-95.

Curcumin effectively inhibited the adverse effects of nicotine by blocking nicotine-induced activation of the AKT/MTOR pathway in HNSCC, in turn retarding cell migration, suggesting that Curcumin may be useful as an oral chemopreventive agent.

PRECLINICAL STUDIES

92. **Curcumin activates the p38MPAK-HSP25 pathway *in vitro* but fails to attenuate diabetic nephropathy in DBA2J mice despite urinary clearance documented by HPLC.** Ma J, Phillips L, Wang Y, Dai T, LaPage J, Natarajan R, Adler SG. *BMC Complement Altern Med*. 2010; 10:67.

In curcumin-treated DBA2J mice with STZ-diabetes, HPLC measurements confirmed the presence of urinary curcuminoid. It has been suggested that timed urine collections may be useful for monitoring curcumin dosing and renal pharmacodynamic effects.

93. **Curcuminoids rescue long-term potentiation impaired by amyloid peptide in rat hippocampal slices.** Ahmed T, Gilani AH, Hosseinmardi N, Semnanian S, Enam SA and Fathollahi Y. *Synapse*. 2011 Jul; 65(7):572-82.

Curcuminoid mixture successfully restored the susceptibility for plastic changes in hippocampal region, which was impaired by Aβ peptide. Hence, it can be useful in providing a pharmacological basis for the medicinal use of Curcuminoids in AD.

94. **A comparative study of curcuminoids to measure their effect on inflammatory and apoptotic gene expression in an Aβ plus ibotenic acid-infused rat model of Alzheimer's disease.** Ahmed T and Gilani AH. *Brain Res*. 2011 Jul 11; 1400:1-18.

Curcuminoids, along with each constituent in the mixture played a significant role, via different pathways, in the attenuation of Aβ-induced apoptosis and inflammatory features, which clearly indicated their potential beneficial role in treating AD.

95. **Curcumin inhibits skin squamous cell carcinoma tumor growth *in vivo*.** Phillips JM, Clark C, Herman-Ferdinandez L, Moore-Medlin T, Rong X, Gill JR, Clifford JL, Abreo F and Nathan CO. *Otolaryngol Head Neck Surg*. 2011 Jul; 145(1):58-63.

Tumor volume increased 2.3 times faster in control mice compared with the group receiving 15 mg of curcumin. Curcumin inhibited S6 phosphorylation, suggesting inhibition of the MTOR pathway.

96. **Curcumin induces the differentiation of myeloid-derived suppressor cells and inhibits their interaction with cancer cells and related tumor growth.** Tu SP, Jin H, Shi JD, Zhu LM, Suo Y, Lu G, Liu A, Wang TC, Yang CS. *Cancer Prev Res (Phila)*. 2012 Feb; 5(2):205-15.

Curcumin significantly inhibited the activation of Myeloid-derived suppressor cells (MDSCs), induced the differentiation of MDSCs and suppressed tumour growth. Hence, anti-tumerigenic activity of curcumin may be a promising strategy for cancer prevention and therapy.

97. **Topical curcumin-based cream is equivalent to dietary curcumin in a skin cancer model.** Sonavane K, Phillips J, Ekshyyan O, Moore-Medlin T, Roberts Gill J, Rong X, Lakshmaiah RR, Abreo F, Boudreaux D, Clifford JL and Nathan CA. *J Skin Cancer*. 2012; 2012:147863.

Curcumin slowed progression of aggressive skin SCC by inhibiting several signalling pathways; hence it can be explored as a chemopreventive and therapeutic agent for skin cancer treatment.

PRECLINICAL STUDIES

98. **Curcumin: A novel Stat3 pathway inhibitor for chemoprevention of lung cancer.** Alexandrow MG, Song LJ, Altiok S, Gray J, Haura EB and Kumar NB. *Eur J Cancer Prev*. 2012 Sep; 21(5):407-12.

    Curcumin effectively inhibited the Stat3 pathway, along with a reduction in cell proliferation, thus can be an effective chemopreventive agent in high risk populations, such as former smokers.

99. **Improving the oral bioavailability of curcumin using novel organogel-based nanoemulsions.** Yu H, Huang Q. *J Agric Food Chem.* 2012;60(21):5373-79.

    In vivo pharmacokinetics analysis of organogel-based nanoemulsions on mice confirmed that the oral bioavailability of curcumin in the nanoemulsion was increased by 9-fold compared with unformulated curcumin.

100. **Curcumin inhibits prostate cancer metastasis *in vivo* by targeting the inflammatory cytokines CXCL1 and -2.** Killian PH, Kronski E, Michalik KM, Barbieri O, Astigiano S, Sommerhoff CP, Pfeffer U, Nerlich AG, Bachmeier BE. *Carcinogenesis*. 2012;33(12):2507-19.

    Chronic inflammation can induce a metastasis prone phenotype in prostate cancer cells by maintaining a positive pro-inflammatory and pro-metastatic feed-back loop between NF- B and the proinflammatory cytokine CXCL1/-2. Curcumin disrupts this feed-back loop by the inhibition of NF-κB signaling leading to reduced metastasis formation *in vivo*.

101. **Controlled-release systemic delivery - a new concept in cancer chemoprevention.** Gupta RC, Bansal SS, Aqil F, Jeyabalan J, Cao P, Kausar H, Russell GK, Munagala R, Ravoori S, Vadhanam MV. *Carcinogenesis*. 2012;33(8):1608-15.

    Polymeric implants of curcumin inhibit benzo[a]pyrene induced lung DNA adducts in female Sprague–Dawley rats. This approach provides continuous delivery for long durations and lowers the total required dose, eliciting both chemopreventive/ chemotherapeutic activities

102. **Controlled systemic delivery by polymeric implants enhances tissue and plasma curcumin levels compared with oral administration.** Bansal SS, Kausar H, Vadhanam MV, Ravoori S, Gupta RC. *Eur J Pharm Biopharm*. 2012;80(3):571-77.

    Curcumin implants provided much higher plasma and tissue concentrations and are a viable alternative for delivery of curcumin to various organs like brain.

103. **Curcumin inhibits UV radiation-induced skin cancer in SKH-1 mice.** Phillips J, Moore-Medlin T, Sonavane K, Ekshyyan O, McLarty J and Nathan CA. *Otolaryngol Head Neck Surg*. 2013 May; 148(5):797-803.

    Curcumin appears to inhibit skin cancer formation and prolong time to tumor onset when administered by either an oral or topical route. These data suggest that curcumin may have chemopreventive potential against skin cancer.

PRECLINICAL STUDIES

104. **Liposomal-formulated curcumin [Lipocurc™] targeting HDAC (Histone Deacetylase) prevents apoptosis and improves motor deficits in Park 7 (DJ-1)-knockout rat model of Parkinson's disease: implications for epigenetics-based nanotechnology-driven drug platform.** Chiu S, Terpstra KJ, Bureau Y, Hou J, Raheb H, Cernvosky Z, Badmeav V, Copen J, Husni M, Woodbury-Farina M. *J Complement Integr Med*. 2013.

    For the first time Lipocurc™'s anti-apoptotic and neurotrophic effects in the DJ-1- KO rat model of Parkinson's disease was demonstrated.

105. **Curcumin implants, not curcumin diet, inhibit estrogen-induced mammary carcinogenesis in ACI rats.** Bansal SS, Kausar H, Vadhanam MV, Ravoori S, Pan J, Rai SN, Gupta RC. *Cancer Prev Res (Phila).* 2014;7(4):456-65.

    HPLC analysis of plasma and liver samples showed substantially higher curcumin levels via implants versus the dietary route despite substantially higher dose was administered.

106. **Photopreventive effect and mechanism of AZD4547 and Curcumin C3 Complex® on UVB-induced epidermal hyperplasia.** Khandelwal AR, Rong X, Moore-Medlin T, Ekshyyan O, Abreo F, Gu X2, Nathan CA. *Cancer Prev Res (Phila).* 2016 Apr; 9(4):296-304.

    Curcumin C3 Complex® inhibited both mTOR and FGFR2 signaling, which can be considered as a new therapeutic strategy for advanced cancer with dual pathway dysregulations.

107. **Effect of combination of low doses of epa and curcumin on muscle wasting in mac16 colon tumor-bearing mice.** Luo M, Mirza KA, Pereira SL, Tisdale MJ, Das T. *FASEB J*. 2016; 30(1) Suppl. lb 312.

    Combination of a low dose of curcumin with a low dose of EPA may be more effective than EPA or curcumin alone in preventing muscle wasting in cancer cachexia in the MAC16 model.

108. **Mechanisms of colitis-accelerated colon carcinogenesis and its prevention with the combination of aspirin and curcumin: Transcriptomic analysis using RNA-seq.** Guo Y, Su ZY, Zhang C, Gaspar JM, Wang R, Hart RP, Verzi MP and Kong AN. *Biochem Pharmacol*. 2017 Jul 1; 135:22-34.

    Co-administration of low-dose combination of aspirin and curcumin produced chemopreventive effects against CAC. Furthermore, the transcriptional profile obtained in this study may be helpful in identifying underlying mechanism of the carcinogenesis process of inflammatory CRC as well as the chemopreventive effects and potential molecular targets of aspirin and curcumin.

109. **Distribution and metabolism of Lipocurc™ (Liposomal Curcumin) in dog and human blood cells: Species selectivity and pharmacokinetic relevance.** Bolger GT, Licollari A, Tan A, Greil R, Vcelar B, Majeed M, Helson L. *Anticancer Res*. 2017 Jul; 37(7):3483-92.

    There were species dependence and an excellent correlation between the *in vitro* disposition of curcumin and THC following incubation with red blood cells and *in vivo* plasma levels of curcumin and THC in dog and human following intravenous infusion.

PRECLINICAL STUDIES

110. **Disposition, metabolism and histone deacetylase and acetyltransferase inhibition activity of tetrahydrocurcumin and other curcuminoids.** Novaes JT, Lillico R, Sayre CL, Nagabushnam K, Majeed M, Chen Y, Ho EA, Oliveira ALP, Martinez SE, Alrushaid S, Davies NM, Lakowski TM. *Pharmaceutics*. 2017 Oct 12; 9(4). pii: E45.

Curcumin and calebin-A has anticancer potential by direct inhibition of HDAC1 and HAT PCAF mechanisms, while the THC has different anticancer mechanism maybe by virtue of its anti-inflammatory and antioxidant potentials. There was an excellent correlation between the *in vitro* disposition of curcumin and THC following incubation with red blood cells and *in vivo* plasma levels of curcumin and THC in dog and human following intravenous infusion.

111. **Curcumin and salsalate suppresses colonic inflammation and procarcinogenic signaling in high-fat-fed, azoxymethane-treated mice.** Wu X, Pfalzer AC, Koh GY, Tang S, Crott JW, Thomas MJ, Meydani M, Mason JB. *J Agric Food Chem.* 2017;65(33):7200-09.

Curcumin a dietary polyphenol and salsalate reduces the concentration of pro-inflammatory cytokines and diminishes activation of Akt and NF-κB more effectively than curcumin alone, providing a scientific basis for examining whether this combination mitigates the risk of CRC in obese individuals.

112. **Exosomes for the enhanced tissue bioavailability and efficacy of curcumin.** Aqil F, Munagala R, Jeyabalan J, Agrawal AK, Gupta R. *AAPS J.* 2017;19(6):1691-702.

Exosomal curcumin showed significant inhibition of cervical tumor xenograft, and thus can be developed as potential nano carriers for delivering curcumin.

113. **The role of nitric oxide in anticonvulsant effect of nanocurcumine on pentylenetetrazole-induced seizure in mice.** Aminirad A, Mousavi SE, Fakhraei N, Mousavi SM, Rezayata SM. *Neurosci Lett.* 2017;651:226-31.

Nanocurcumin showed anticonvulsant effect and this effect was reversed following l-arginine as an external NO precursor. However, both the non-selective NOS inhibitor and selective iNOS inhibitor increased the thresholds. It is evident that nanocurcumin may influence the seizure thresholds at least in part through a decrease in NO.

114. **Curcumin and piperine supplementation of obese mice under caloric restriction modulates body fat and interleukin-1β.** Miyazawa T, Nakagawa K, Kim SH, Thomas MJ, Paul L, Zingg JM, Dolnikowski GG, Roberts SB, Kimura F, Miyazawa T, Azzi A and Meydani M. *Nutri Metab.* 2018; 15:12.

Supplementing the high fat diet of caloric restriction mice with Curcumin + Piperine may increase loss of body fat and suppresses HFD induced inflammation. Combination of Curcumin and Piperine has potential to enhance caloric restriction effects for the prevention of metabolic syndrome.

PRECLINICAL STUDIES

115. **Local and systemic Curcumin C3 complex inhibits 4NQO-induced oral tumorigenesis via modulating FGF-2/FGFR-2 activation.** Khandelwal AR, Moore-Medlin T, Ekshyyan O, Gu X, Abreo F, Nathan CAO. *Am J Cancer Res*. 2018;8(12):2538-47.

    A combination of local and systemic C3 complex could effectively target proliferation and inhibit 4NQO-induced tumorigenesis via modulation of the FGF-2/FGFR-2 axis as a mechanism for its efficacy.

116. **Curcumin as treatment for bladder cancer: A preclinical study of cyclodextrin-curcumin complex and bcg as intravesical treatment in an orthotopic bladder cancer rat model.** Falke J, Parkkinen J, Vaahtera L, Hulsbergen-van de Kaa CA, Oosterwijk E, Witjes JA. *Biomed Res Int*. 2018;2018:9634902.

    Cyclodextrin-curcumin complex showed an antiproliferative effect on human and rat urothelial carcinoma cell lines *in vitro*. In the aggressive orthotopic bladder cancer rat model, a promising effect of Cyclodextrin-curcumin complex treatment alone and in combination with Bacillus Calmettte Guerin was observed.

117. **Curcumin C3 Complex®/BioPerine® has antineoplastic activity in mesothelioma: an *in vitro* and *in vivo* analysis.** Di Meo F, Filosa S, Madonna M, Giello G, Di Pardo A, Maglione V, Baldi A, CrispiS. *J Exp Clin Cancer Res*. 2019;38(1):360.

    Curcumin C3 Complex®/BioPerine® treatment strongly reduces *in vitro* tumorigenic properties of mesothelioma cells by impairing cellular self-renewal ability, proliferative cell rate and cell migration and delays tumor growth in xenograft mouse model by reducing angiogenesis and increasing apoptosis.

118. **Pharmacokinetics and pharmacodynamics of three oral formulations of curcumin in rats.** Wang L, Li W, Cheng D, Guo Y, Wu R, Yin R, Li S, Kuo HC, Hudlikar R, Yang H, Buckley B, Kong AN. *J Pharmacokinet Phar*. 2020; 47:131–44.

    The three oral curcumin formulations tested induced Nrf2-mediated antioxidant genes, suggesting the potential of oral curcumin in contributing to the overall health beneficial effects.

IN-VITRO STUDIES

119. **Activation of transcription factor NF-κB is suppressed by curcumin (diferuloylmethane).** Singh S and Aggarwal BB. *J Biol Chem*. 1995; Oct 20; 270(42):24995-25000.

Curcumin is a pharmacologically safe and potent agent useful in modulating expression of genes regulated by NF-κB and thus effective in a targeting a wide variety of pathological conditions.

120. **Curcuminoids enhance amyloid-beta uptake by macrophages of Alzheimer's disease patients.** Zhang L, Fiala M, Cashman J, Sayre J, Espinosa A, Mahanian M, Zaghi J, Badmaev V, Graves MC, Bernard G and Rosenthal M. *J Alzheimers Dis*. 2006 Sep; 10(1):1-7.

Curcuminoids could be used for immune modulation of the innate immune system, which might be helpful for assessing the ability of patients to respond to immunomodulatory therapy.

121. **Evidence that curcumin suppresses the growth of malignant gliomas *in vitro* and *in vivo* through induction of autophagy: Role of Akt and extracellular signal-regulated kinase signaling pathways.** Aoki H, Takada Y, Kondo S, Sawaya R, Aggarwal BB and Kondo Y. *Mol Pharmacol*. 2007 Jul; 72(1):29-39.

It was concluded from the study results that curcumin can be a new anticancer agent for malignant glioma because of its prominent effect and its new anticancer mechanism of inducing autophagy.

122. **Curcumin inhibits tumor growth and angiogenesis in ovarian carcinoma by targeting the nuclear factor-kappaB pathway.** Lin YG, Kunnumakkara AB, Nair A, Merritt WM, Han LY, Armaiz-Pena GN, Kamat AA, Spannuth WA, Gershenson DM, Lutgendorf SK, Aggarwal BB, Sood AK. *Clin Cancer Res*. 2007 Jun 1;13(11):3423-30.

Curcumin inhibited inducible NF-kappaB activation and suppressed proliferation. It reduced signal transducers and activators of transcription-3 activation and angiogenic cytokine expression. Based on these it was concluded that curcumin based therapies may be beneficial in patients with ovarian carcinoma with less side effects.

123. **Curcumin potentiates the apoptotic effects of chemotherapeutic agents and cytokines through down-regulation of nuclear factor-kappaB and nuclear factor-kappaB-regulated gene products in IFN-alpha-sensitive and IFN-alpha-resistant human bladder cancer cells.** Kamat AM, Sethi G and Aggarwal BB. *Mol Cancer Ther*. 2007 Mar; 6(3):1022-30.

Curcumin has a role in the prevention and/or treatment of bladder cancer and hence, can be useful either alone or in combination with existing therapy. Antitumor effects of radiation therapy in colorectal cancer were enhanced by Curcumin by inhibiting NF-κB and NF-κB-regulated gene products.

124. **Curcumin potentiates antitumor activity of gemcitabine in an orthotopic model of pancreatic cancer through suppression of proliferation, angiogenesis, and inhibition of nuclear factor-kappaB-regulated gene products.** Kunnumakkara AB, Guha S, Krishnan S, Diagaradjane P, Gelovani J and Aggarwal BB. *Cancer Res*. 2007 Apr 15; 67(8):3853-61.

Curcumin potentiated the apoptotic effects of gemcitabine in pancreatic cancer cells *in vitro* and significantly enhanced the antitumor effects of gemcitabine in orthotopic pancreatic tumors by downregulating NF-κB–regulated gene products and suppression of angiogenesis.

IN-VITRO STUDIES

125. **Curcumin, demethoxycurcumin, bisdemethoxycurcumin, tetrahydrocurcumin and turmerones differentially regulate anti-inflammatory and anti-proliferative responses through a ROS-independent mechanism.** Sandur SK, Pandey MK, Sung B, Ahn KS, Murakami A, Sethi G, Limtrakul P, Badmaev V and Aggarwal BB. *Carcinogenesis*. 2007 Aug; 28(8):1765-73.

    Curcumin mixture showed good results when compared to individual analogs as the best anticancer agent. Among them, curcumin displayed the best results followed by bisdemethoxycurcumin and tetrahydrocurcumin, respectively.

126. ***In vitro* antioxidant activity of selected antiasthmatic herbal constituents.** Nilani P, Kasthuribai N, Duraisamy B, Dhamodaran P, Ravichandran S, Ilango K and Suresh B. *Anc Sci Life*. 2009 Apr-Jun; 28(4): 3–6.

    A better antioxidant activity was exhibited by Forskolin, Piperine and Vasicinone when combined with Curcumin C3 Complex® compared to each phytonutrient alone.

127. **Curcumin activates AMPK and suppresses gluconeogenic gene expression in hepatoma cells.** Kim T, Davis J, Zhang AJ, He X and Mathews ST. *Biochem Biophys Res Commun*. 2009 Oct 16; 388(2):377-82.

    Results suggest that AMPK mediated suppression of hepatic gluconeogenesis may be a potential mechanism mediating glucose-lowering effects of curcuminoids.

128. **Targeting breast stem cells with the cancer preventive compounds curcumin and piperine.** Kakarala M, Brenner DE, Korkaya H, Cheng C, Tazi K, Ginestier C, Liu S, Dontu G and Wicha MS. *Breast Cancer Res Treat*. 2010 Aug; 122(3):777-85.

    Curcumin and Piperine separately, and in combination, inhibited breast stem cell self-renewal but with no toxicity to differentiated cells. Hence, these compounds could be potential cancer preventive agents.

129. **Antibacterial activity of subtilosin alone and combined with curcumin, poly-lysine and zinc lactate against *Listeria monocytogenes* strains.** Amrouche T, Sutyak Noll K, Wang Y, Huang Q, Chikindas ML. Probiotics *Antimicrob Proteins*. 2010 Dec; 2(4):250-57.

    The combination of subtilosin with curcumin, poly-lysine, or zinc lactate, a lower effective dose can be used to control *L. monocytogenes* infection. The findings suggest that subtilosin could be used as alternative bacteriocin to nisin, providing an opportunity to use a novel natural and efficacious biopreservative against *L. mono*cytogenes in food preservation.

130. **Investigation of the absorption mechanism of solubilized curcumin using caco-2 cell monolayers.** Yu H and Huang Q. *J Agric Food Chem*. 2011 Sep 14; 59(17):9120-126.

    Solubilization agents play an important role in the permeation of solubilized curcumin. Stronger binding between the solubilization agents and curcumin may decrease the permeation rate. Lipid-based formulations, which solubilize curcumin in mixed micelles after lipid digestion, are promising vehicles for curcumin oral delivery.

IN-VITRO STUDIES

131. **Curcumin suppresses proliferation and induces apoptosis in human biliary cancer cells through modulation of multiple cell signaling pathways.** Prakobwong S, Gupta SC, Kim JH, Sung B, Pinlaor P, Hiraku Y, Wongkham S, Sripa B, Pinlaor S and Aggarwal BB. *Carcinogenesis*. 2011 Sep; 32(9):1372-80.

    Results indicated that the antiproliferative and apoptotic effects of curcumin were through activation of multiple cell signaling pathways.

132. **Curcumin induces the differentiation of myeloid-derived suppressor cells and inhibits their interaction with cancer cells and related tumor growth.** Tu SP, Jin H, Shi JD, Zhu LM, Suo Y, Lu G, Liu A, Wang TC and Yang CS. *Cancer Prev Res (Phila)*. 2012 Feb; 5(2):205-15.

    Curcumin significantly inhibited the activation of myeloid-derided suppressor cells (MDSCs), induced the differentiation of MDSCs and suppressed tumor growth. Hence, antitumerigenic activity of Curcumin may be a promising strategy for cancer prevention and therapy.

133. **Standardized curcuminoid extract (*Curcuma longa* L.) decreases gene expression related to inflammation and interacts with associated microRNAs in human umbilical vein endothelial cells (HUVEC).** Angel-Morales G, Noratto G and Mertens-Talcott SU. *Food Funct*. 2012 Dec; 3(12):1286-93.

    Curcuminoids are confirmed to have anti-inflammatory properties in HUVEC; however, neither miRNA-146a nor miRNA-126 seem to be involved in the SCE-induced down-regulation of the NF-κB-target genes IRAK-1, TRAF-6, and VCAM-1.

134. **Curcuminoids promote neurite outgrowth in PC12 cells through MAPK/ERK- and PKC-dependent pathways.** Kuo-Kai Liao, Ming-Jiuan Wu, Pei-Yi Chen, Szu-Wei Huang, Shu-Jun Chiu, Chi-Tang Ho, Jui-Hung Yen. *J Agric Food Chem*. 2012;60(1):433-43.

    Both curcumin and DMC, but not BDMC, induced phosphorylation of cAMP response element- binding protein and CRE-reporter gene activity significantly, and thus plays a role in inducing neuroprotective effects.

135. **Metabolomics reveals metabolic targets and biphasic responses in breast cancer cells treated by curcumin alone and in association with docetaxel.** Bayet-Robert M and Morvan D. *PLoS One*. 2013; 8(3):e57971.

    It was concluded that ^{1}H-NMR spectroscopy-based metabolomics revealed important targets of curcumin. Additionally, metabolomics also showed metabolic biphasic responses related to curcumin that likely accounts for its apparently paradoxical effects used at different doses, in various therapeutic combinations and cell types, including oxidative and inflammatory status.

136. **Iron overload causes oxidative stress and impaired insulin signaling in AML-12 hepatocytes.** Messner DJ, Rhieu BH and Kowdley KV. *Dig Dis Sci*. 2013 Jul; 58(7):1899-908.

    The antioxidant curcumin reduced effects of iron on insulin signaling, ROS, and oxidative stress. Curcumin was similarly effective in cells treated with both stearic acid and iron.

IN-VITRO STUDIES

137. **Curcumin enhances the cytotoxic and chemo-sensitising effects of lenalidomide in human multiple myeloma cells.** Rose Wong, Terry Golombick, Terrence H. Diamond, Arumugam Manoharan and Rajeev Ramakrishna. *Journal of Hematological Malignancie*, 2013; 3(2): 1-7.

    Curcumin produced a cytotoxic effect additive to that of lenalidomide on H929 myeloma cells as well as enhanced the chemo-sensitizing effects of lenalidomide.

138. **The drug resistance suppression induced by curcuminoids in colon cancer SW-480 cells is mediated by reactive oxygen species-induced disruption of the microRNA-27a-ZBTB10-Sp axis.** Noratto GD, Jutooru I, Safe S, Angel-Morales G, and Mertens-Talcott SU. *Mol Nutr Food Res*. 2013 Sep; 57(9):1638-48.

    Curcuminoids resulted in inhibition of Sp transcription factors (Sp1, Sp3, and Sp4), which play a major role in the growth and metastasis of many tumour types, and Sp-regulated genes in SW-480 cells.

139. **Curcumin: a double hit on malignant mesothelioma.** Miller JM, Thompson JK, MacPherson MB, Beuschel SL, Westbom CM, Sayan M and Shukla A. *Cancer Prev Res (Phila)*. 2014 Mar; 7(3):330-40.

    Curcumin has a double effect on malignant mesothelioma cells through induction of pyroptosis while subsequently protecting against inflammation.

140. **Combination effects of quercetin, resveratrol and curcumin on *in vitro* intestinal absorption.** *J Restorative Med*. 2014;3(1):112-20.

    Combination of quercetin, resveratrol and curcumin may improve intestinal absorption of resveratrol and curcumin without affecting quercetin absorption.

141. **Synthesis and evaluation of the antioxidant capacity of curcumin glucuronides, the major curcumin metabolites.** Ambar K Choudhury, Suganya Raja, Sanjata Mahapatra, Kalyanam Nagabhushanam, Muhammed Majeed. *Antioxidants (Basel).* 2015;4(4):750-67.

    Curcumin monoglucuronide exhibits 10 fold less anti-oxidant activity while the anti-oxidant capacity of curcumin diglucuronide is highly attenuated, when compared to the anti-oxidant activity of curcumin.

142. ***In vitro* assessment of the combined effect of eicosapentaenoic acid, green tea extract and curcumin C3 on protein loss in C2C12 myotubes.** Mirza KA, Luo M, Pereira S, Voss A, Das T and Tisdale MJ. *In Vitro Cell Dev Biol Anim*. 2016 Sep; 52(8):838-45.

    Curcumin or green tea extract or the combination could enhance the anti-catabolic effect of EPA on lean body mass.

143. **Curcumin and turmeric modulate the tumor-promoting effects of iron *in vitro*.** Donald J Messner, Todd Robinson, Kris V Kowdley. *Nutr Cancer.* 2017;69(3):481-89.

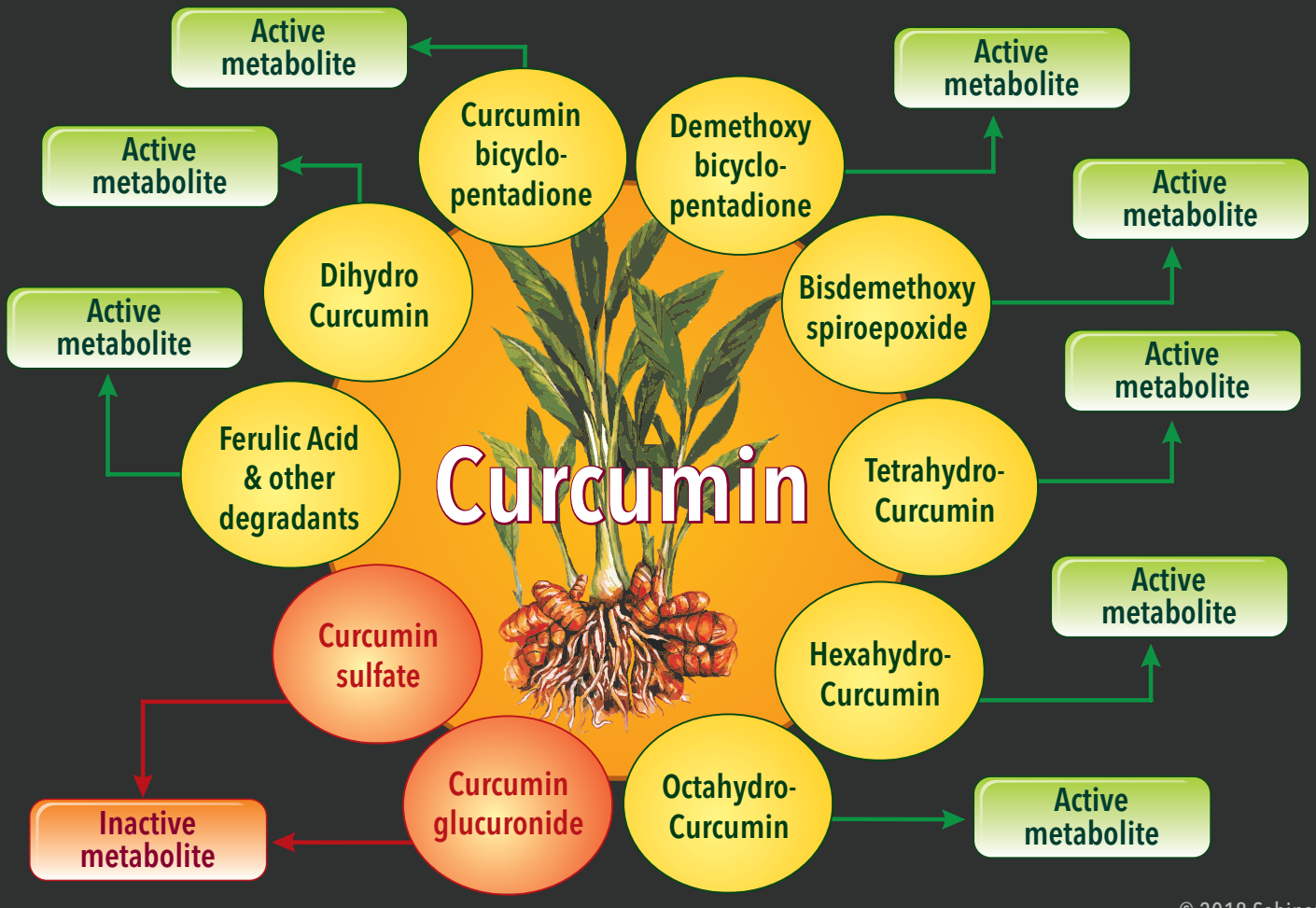
    Curcuminoids can inhibit tumor promotion caused by iron in non-neoplastic rat liver epithelial cells. Curcuminoids delivered as a standardized turmeric extract were taken up better by cells, had a longer half-life, and appeared to be more effective in blocking tumor promotion, suggesting enhanced curcuminoid delivery to cells in culture.

IN-VITRO STUDIES

144. **Effects of different extracts of curcumin on TPC1 papillary thyroid cancer cell line.** Perna A, De Luca A, Adelfi L, Pasquale T, Varriale B, Esposito T. *BMC Complement Altern Med.* 2018; 18(1):63.

Treatment with the three different curcumin extracts displays anti-inflammatory, antioxidant properties, and modulate cell cycle with slightly different effects upon the extracts. The presence of essential oil in the extract diminished the curcuminoids activity.

Metabolism of Curcumin



Curcumin is metabolized by both conjugation and reduction pathways in the body resulting in formation of several metabolites as shown above.

REVIEW ARTICLES

145. **Effect of curcuminoids on oxidative stress: A systematic review and meta-analysis of randomized controlled trials.** Sahebkar A, Serban M, Ursoniu S, Banach M. *Journal of Functional Foods*. 2015; 18:898–909.

The aim of the meta-analysis was to evaluate the efficacy of purified curcuminoids supplementation on plasma activities of superoxide dismutase (SOD), catalase and glutathione (GSH) and lipid peroxides as parameters of oxidative stress. Seven randomized controlled trials were finally selected for the meta-analysis. This meta-analysis showed a significant effect of curcuminoids in elevating serum SOD and catalase activities, GSH concentrations, and reduction of serum lipid peroxides.

146. **Curcumin and endothelial function: Evidence and mechanisms of protective effects.** Karimian MS, Pirro M, Johnston TP, Majeed M, Sahebkar A. *Curr Pharm Des*. 2017; 23(17):2462-73.

The endothelium is a large paracrine organ regulating cell growth, vascular tone and thrombogenicity as well as platelet and leukocyte interactions. Curcumin exerts several positive pharmacological effects; these include anti-inflammatory, antioxidant, anti-hypertensive, anti-cancer, antiviral, anti-infective and wound-healing properties. Specifically, curcumin's anti-inflammatory effects are thought to be caused by reducing trans-endothelial monocyte migration by reduction of mRNA and protein expression of intercellular adhesion molecule-1, vascular cell adhesion molecule-1 and P-selectin and by modulating NFκB, JNK, p38 and STAT-3 in endothelial cells. Hence, it was concluded that curcumin appears to improve endothelial function.

147. **Curcumin and lung cancer: The role of microRNAs.** Diana Lelli D, Pedone C, Majeed M, Sahebkar A. *Curr Pharm Des*. 2017; 23(23):3440-44.

Lung cancer is one of the most common types of cancer worldwide and is characterized by a poor prognosis, related to both late diagnosis and lack of effective treatments. The anti-cancer properties of curcumin against lung cancer have been shown in both cellular and experimental models and are mediated by modulation of several molecular targets, especially by the downregulation of oncogenic miR-21 and upregulation of oncosuppressive miR-192-5p and miR-215.

148. **Curcumin: A naturally occurring modulator of adipokines in diabetes.** Hajavi J, Momtazi AA, Johnston TP, Banach M, Majeed M, Sahebkar A. *J Cell Biochem*. 2017; 118(12):4170-82.

Curcumin has been shown to exert pleiotropic effects by modulating different signalling molecules, including transcription factors, chemokines, cytokines, and adipokines. Disturbed regulation of adipokines, which include adiponectin, leptin, resistin, and visfatin, are implicated in the development of insulin resistance and Type 2 diabetes.

149. **Effects of curcumin on HDL functionality.** Ganjali S, Blesso CN, Banach M, Pirro M, Majeed M and Sahebkar A. *Pharmacol Res*. 2017; 119:208-18.

In this review, the authors concluded that curcumin may modulate markers of HDL function, such as apo-AI, CETP, LCAT, PON1, MPO activities and levels. Curcumin may subsequently improve conditions in which HDL is dysfunctional and may have potential as a therapeutic drug in future.

REVIEW ARTICLES

150. **Curcumin as a natural regulator of monocyte chemoattractant protein-1.** Karimian MS, Pirro M, Majeed M, Sahebkar A. *Cytokine Growth Factor Rev*. 2017;33:55-63.

This meta-analysis of five randomized clinical trials (n = 686) showed a significant increase in plasma levels of adiponectin following curcuminoids therapy.

151. **Impact of curcumin on the regulation of microRNAs in colorectal cancer.** Simental-Mendía LE, Caraglia M, Majeed M, Sahebkar A. *Expert Rev Gastroenterol Hepatol*. 2017; 11(2):99-101.

Curcumin can reverse epithelial-mesenchymal transition which is itself a key promoter of colorectal cancer stem cells formation and tumor invasion and mitigate chemoresistance via modulating the miRNA profile (mainly miR-200 family) in colorectal cancer.

152. **Curcumin as an adjunct therapy and microRNA modulator in breast cancer.** Norouzi S, Majeed M, Pirro M, Generali D, Sahebkar A. *Curr Pharm Des*. 2018; 24(2):171-77.

Pathogenesis of breast cancer is paralleled by distinct alterations in the expression profile of several microRNAs (miRNAs). Recent studies have shown that miRNAs can serve as diagnostic and prognostic markers, and also as therapeutic targets in breast cancer.

The putative anti-tumor properties of curcumin are mediated by diverse mechanisms including inhibition of cell proliferation, metastasis, migration, invasion and angiogenesis, and induction of G2/M cell cycle arrest, apoptosis and paraptosis. Recent evidence implies that curcumin can interact with several oncogenic and tumor-suppressive miRNAs involved in different stages of breast cancer. In this context, up-regulation of miR181b, miR-34a, miR-16, miR-15a and miR-146b-5p, and down-regulation of miR-19a and miR-19b have been shown following the treatment of several breast cancer cell lines with curcumin. Thus, it was concluded that curcumin appears as an important miRNA modulator in breast cancer.

153. **Curcumin: A natural pan-HDAC inhibitor in cancer.** Soflaei SS, Momtazi AA, Majeed M, Derosa G, Maffioli P and Sahebkar A. *Curr Pharm Des*. 2018; 24(2):123-29.

Histone deacetylases (HDACs) are a group of histone modification enzymes with pivotal role in disease pathogenesis especially in cancer development. Increased activity of certain types of HDACs and positive effects of HDAC inhibition has been shown in several types of cancers. HDACs have emerged as novel targets of curcumin that their modulation may contribute to the putative anti-cancer effects of curcumin. Curcumin inhibits HDAC activity, and down-regulates the expression of HDAC types 1, 2, 3, 4, 5, 6, 8 and 11 in different cancer cell lines and mice, while the activity and expression of HDAC2 have been reported to be up-regulated by curcumin in COPD and heart failure models. The available *in vitro* and *in vivo* data are in favour of the HDAC inhibitory activity of curcumin.

REVIEW ARTICLES

154. **Turmeric (*Curcuma longa*) and its major constituent (curcumin) as nontoxic and safe substances: Review.** Soleimani V, Sahebkar, Hosseinzadeh H. *Phytother Res*. 2018; 32(6):985-95.

Oral use of turmeric and curcumin did not have reproductive toxicity in animals at certain doses. Studies on human did not show toxic effects, and curcumin was safe at the dose of 6 g/day orally for 4-7 weeks. In addition, curcumin is known as a generally recognized as safe substance. This review discusses the safety and toxicity of turmeric and curcumin in medicine. Turmeric and curcumin are nontoxic for human especially in oral administration. Turmeric and curcumin are also safe in animals. They are nonmutagenic and are safe in pregnancy in animals.

155. **The versatile role of curcumin in cancer prevention and treatment: A focus on PI3K/AKT pathway.** Hamzehzadeh L, Atkin SL, Majeed M, Butler AE, Sahebkar A. *J Cell Physiol*. 2018;233(10):6530-37.

This review summarizes a key anti-inflammatory pathway for curcumin targeting of PI3K/AKT in different malignancies to inhibit cancer development and prevent further progression.

156. **Anti-cancer and radio-sensitizing effects of curcumin in nasopharyngeal carcinoma.** Momtazi-Borojeni AA, Ghasemi F, Hesari A, Majeed M, Caraglia M, Sahebkar A. *Curr Pharm Des*. 2018;24(19):2121-28.

Curcumin can sensitize nasopharyngeal cancer cells to radiation by the modulation of ROS generation, Jab1/CSN5 and non-coding RNAs. As curcumin is safe and lacks systemic toxic effects in humans, it may be considered as a potential candidate to enhance the therapeutic effects of radiation and potentiate the efficacy of chemotherapy in the context of combination regimens.

157. **Effects of curcumin on hypoxia-inducible factor as a new therapeutic target.** Bahrami A, Atkin SL, Majeed M, Sahebkar A. *Pharmacol Res*. 2018;137:159-69.

A growing body of evidence indicates that curcumin significantly targets hypoxia inducible factor-1 subunits, which regulates cancer growth and angiogenesis. This review summarized the knowledge about the pharmacological effects of curcumin on HIF-1 and the related molecular mechanisms that may be effective candidates for the development of multi-targeted therapy for several human diseases.

158. **Potential therapeutic effects of curcumin in gastric cancer.** Barati N, Momtazi-Borojeni AA, Majeed M, Sahebkar A. *J Cell Physiol*. 2019;234(3):2317-28.

This report summarizes the *in vitro* and *in vivo* findings on the chemosensitizing and anticancer effects of curcumin against the gastric cancer cells. Curcumin has been found to have efficient chemosensitizing effect and also inhibits viability, proliferation, and migration of gastric cancer cells mainly via cell cycle arrest and induction of apoptosis.

REVIEW ARTICLES

159. **Immune modulation by curcumin: The role of interleukin-10.** Mollazadeh H, Cicero AFG, Blesso CN, Pirro M, Majeed M and Sahebkar A. *Crit Rev Food Sci Nutri.* 2019; 59(1): 89-101.

Interleukin-10 (IL-10) is known to be a pleiotropic and potent anti-inflammatory and immunosuppressive cytokine that is produced by both innate and adaptive immunity cells. IL-10 deregulation plays a role in the development of a large number of inflammatory diseases such as neuropathic pain, Parkinson's disease, Alzheimer's disease, osteoarthritis, rheumatoid arthritis, psoriasis, systemic lupus erythematosus, type 1 diabetes, inflammatory bowel disease, and allergy.

Curcumin is a natural anti-inflammatory compound able to induce the expression and production of IL-10 and enhancing its action.

160. **Vascular endothelial growth factor: An important molecular target of curcumin.** Saberi-Karimian M, Katsiki N, Caraglia M, Boccellino M, Majeed M and Sahebkar A. *Crit Rev Food Sci Nutr*. 2019; 59(2):299-312.

Vascular Endothelial Growth Factor (VEGF) is a key modulator of angiogenesis. In this review, the authors elaborated the effect of curcumin on VEGF and angiogenesis and its therapeutic applications.

161. **Lipid-modifying activity of curcuminoids: A systematic review and meta-analysis of randomized controlled trials.** Simental-Mendía LE, Pirro M, Gotto Jr AM, Banach M, Atkin SL, Majeed M and Sahebkar A. *Crit Rev Food Sci Nutr*. 2019; 59(7):1178-87.

In this meta-analysis of 20 Randomized controlled trials (RCTs), with 1427 participants suggested a significant decrease in plasma concentrations of triglycerides (WMD: -21.36 mg/dL, 95% CI: -32.18, -10.53, $p < 0.001$), and an elevation in plasma HDL-C levels (WMD: 1.42 mg/dL, 95% CI: 0.03, 2.81, $p = 0.046$). This meta-analysis has shown that curcuminoid therapy significantly reduces plasma triglycerides and increases HDL-C levels.

162. **A systematic review and meta-analysis of the effect of curcuminoids on adiponectin levels.** Simental-Mendía LE, Cicero AFG, Atkin SL, Majeed M, Sahebkar A. *Obes Res Clin Pract*. 2019;13(4):340-44.

This meta-analysis showed a significant increase in plasma levels of adiponectin following curcuminoids therapy, which may be one of the mechanisms of anti-inflammatory activity of curcumin.

163. **Current evidence and future perspectives for curcumin and its analogues as promising adjuncts to oxaliplatin: state-of-the-art.** Zangui M, Atkin SL, Majeed M Sahebkar A. *Pharmacol Res.* 2019;141:343-56.

This review provides a summary of the studies investigating the effects of curcumin and its analogues, as adjuvants to oxaliplatin treatment in malignant cell lines and in experimental tumor models. Addition of curcumin as an adjunct to oxaliplatin enhances oxaliplatin's toxicity in malignant cells, which potentially allows an oxaliplatin dose reduction and decreasing the adverse effects of chemotherapy. Curcumin also has been shown to exert cytoprotective properties against oxaliplatin's off-target toxicities.

REVIEW ARTICLES

164. **Evidence of curcumin and curcumin analogue effects in skin diseases: A narrative review.** Panahi Y, Fazlolahzadeh O, Atkin SL, Majeed M, Butler AE, Johnston TP, Sahebkar A. *J Cell Physiol*. 2019;234(2):1165-78.

This review is focused on recent studies concerning the use of curcumin for the treatment of skin diseases, as well as offering new and efficient strategies to optimize its pharmacokinetic profile and increase its bioavailability.

165. **Curcumin: a potent agent to reverse epithelial-to-mesenchymal transition.** Bahrami A, Majeed M, Sahebkar A. *Cell Oncol (Dordr)*. 2019;42(4):405-21.

The aim of this review is on how curcumin can mitigate chemoresistance through Epithelial-to-mesenchymal transition (EMT) and promote antiproliferative effects of conventional chemotherapeutics. Curcumin has the potential to be used as a novel adjunctive agent to prevent tumor metastasis, which may at least partly be attributed to its hampering of the EMT process in several human cancer types.

166. **Curcumin as a therapeutic agent in leukemia.** Kouhpeikar H, Butler AE(2), Bamian F, Barreto GE, Majeed M, Sahebkar A. *J Cell Physiol*. 2019;234(8):12404-14.

This review summarizes the effects of curcumin on various types of leukemia, whilst considering its mechanisms of action. Many cellular and experimental studies have reported the benefits of curcumin in treating leukemia.

167. **The effect of curcumin on the differentiation of mesenchymal stem cells into mesodermal lineage.** Gorabi AM, Kiaie N, Hajighasemi S, Jamialahmadi T, Majeed M, Sahebkar A. *Molecules*. 2019;24(22):4029.

In this review, a descriptive mechanism of how curcumin affects the outcome of the differentiation of mesenchymal stem cells (MSCs) into adipocyte, osteocyte, and chondrocytes. The effect of different curcumin doses and its structural modifications on the MSCs differentiation is also discussed.

168. **Modulatory effects of curcumin on heat shock proteins in cancer: A promising therapeutic approach.** Forouzanfar F, Barreto G, Majeed M, Sahebkar A. *Biofactors*. 2019;45(5):631-40.

Curcumin is a potent anti-inflammatory, antioxidant, antimicrobial, and antitumor agent and has been shown to regulate different members of HSPs including HSP27, HSP40, HSP60, HSP70, and HSP90 in cancer. In this review findings suggesting that curcumin may act as a potential therapeutic agent for the treatment of cancer through its regulation of HSPs is discussed.

169. **Effects of curcumin on neurological diseases: Focus on astrocytes.** Eghbaliferiz S, Farhadi F, Barreto GE, Majeed M, Sahebkar A. *Pharmacol Rep*. 2020 May 27.

Astrocytes are the most abundant glial cells in the central nervous system and are important players in both brain injury and neurodegenerative disease. This review discusses the role of astrocytes as essential players in neurodegenerative diseases and suggests that curcumin is capable of inhibiting astrocyte activity in several neurodegenerative diseases.

REVIEW ARTICLES

170. **Potential effects of curcumin in the treatment of COVID-19 infection.** Zahedipour F, Hosseini SA, Sathyapalan T, Majeed M, Jamialahmadi T, Al-Rasadi K, Banach M, Sahebkar A. *Phytother Res*. 2020 May 19:10.1002/ptr.6738.

Curcumin could be a potential treatment option for patients with coronavirus disease. In review some of the potential effects of curcumin in inhibiting the entry of virus into the cell, inhibiting encapsulation of the virus and viral protease, as well as modulating various cellular signaling pathways are discussed. This review provides a basis for the clinical applications of curcumin for the treatment of newly emerged SARS-CoV-2.

171. **Curcumin: an inflammasome silencer.** Hassanzadeh S, Read MI, Bland AR, Majeed M, Jamialahmadi T, Sahebkar A. *Pharmacol Res*. 2020 May 25.

The review outlines various mechanisms of curcumin as an inflammasome modulator in inflammatory-related diseases. Curcumin can exert its anti-inflammatory effect especially through the down regulation of NLRP3 inflammasomes.

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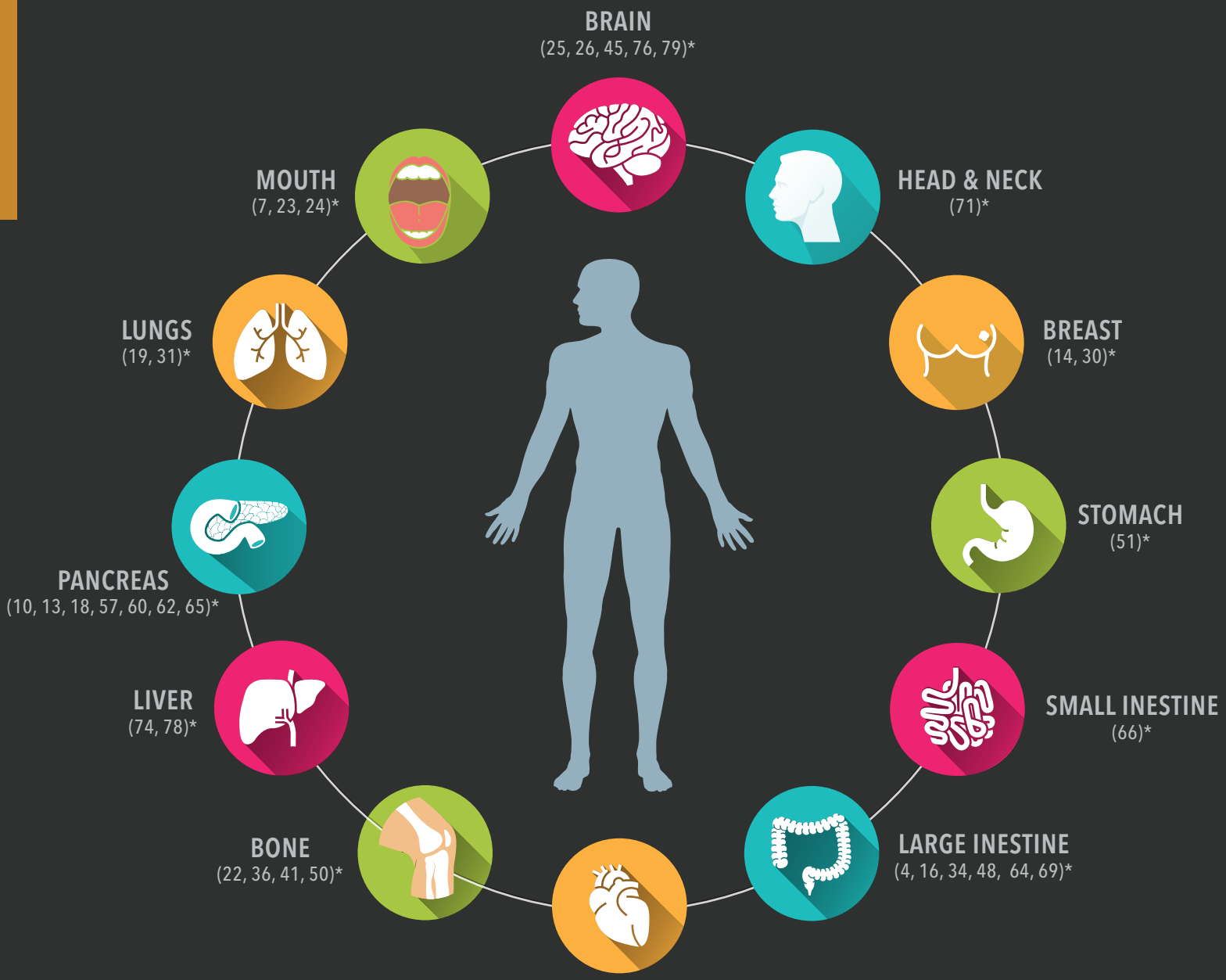

* Clinical Study References

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