Formulations

Curcumin 50 — €49,90*

Item number: 08165516 | **Contents:** 10 ml | **Base price:** € 390.00 / 100 ml | **Available only in pharmacies**
Dosage form: Concentrate for infusion for intravenous use after dilution exclusively in 100 ml of 0.9% NaCl.
Ingredients: Curcumin 50 mg, Hydroxypropyl-beta-Cyclodextrin q.s., PEG 400 q.s., Water
Note: Store away from light at 15–25°C | **Shelf life:** 6 months

Curcumin 250 — €169,90*

Item number: 08165488 | **Contents:** 50 ml | **Base price:** € 298.00 / 100 ml | **Available only in pharmacies**
Dosage form: Concentrate for infusion for intravenous use after dilution exclusively in 100 ml of 0.9% NaCl.
Ingredients: Curcumin 250 mg, Hydroxypropyl-beta-Cyclodextrin q.s., PEG 400 q.s., Water
Note: Store away from light at 15–25°C | **Shelf life:** 6 months

Curcumin-HSA 300 — €299.00*

Item number: 08165613 | **Contents:** 150 ml | **Base price:** € 199.33 / 100 ml | **Prescription-only**
Dosage form: Concentrate for infusion for intravenous use after dilution exclusively in the enclosed carrier solution
Ingredients: Curcumin 300 mg, Hydroxypropyl-beta-Cyclodextrin q.s., PEG 400 q.s., HSA solution
Note: Store away from light at 2–8°C | **Shelf life:** 6 months

Curcumin/Resveratrol 100/50 — €129,90*

Item number: 08165544 | **Contents:** 20 ml | **Base price:** € 549.50 / 100 ml | **Available only in pharmacies**
Dosage form: Concentrate for infusion for intravenous use after dilution exclusively in 500 ml of 0.9% NaCl.
Ingredients: Curcumin 100 mg, Resveratrol 50 mg, Hydroxypropyl-beta-Cyclodextrin q.s., PEG 400 q.s., Water
Note: Store away from light at 15–25°C | **Shelf life:** 6 months

Curcumin suppositories 400 mg — €20.00*

Item number: 08165517 | **Contents:** 1 item | **Base price:** € 20.00 / 1 item | **Available only in pharmacies**
Dosage form: Suppositories for rectal or vaginal use
Ingredients: Curcumin 400, excipients q.s.
Note: Store away from light at 2–8°C | **Shelf life:** 6 months

Curcumin/DMSO suppositories 250 mg — €15,90*

Item number: 08165502 | **Contents:** 1 item | **Base price:** € 25.00 / 1 item | **Prescription-only**
Dosage form: Suppositories for rectal use
Ingredients: Curcumin 250 mg, DMSO 14%, excipients q.s.
Note: Store away from light at 2–8°C | **Shelf life:** 6 months

Curcumin powder — €42,90* / €109,90*

Item number: 08165538/39 | **Contents:** 30 g / 3x 30 g | **Base price:** €133.00 or 111.00 € / 100 g | **Available only in pharmacies**
Dosage form: Powder for oral use after diluting with water
Ingredients: Curcumin 30 g
Note: Store away from light at 15–25°C | **Shelf life:** 6 months

You do not need any special infusion equipment and do not need to administer cortisone beforehand. Container for low-germ removal as a single dose by a healthcare professional. Use after dilution in sterile isotonic saline solution. Intended for immediate consumption.

Sources

1. Aggarwal, B.B., et al., Curcumin: the Indian solid gold. Adv Exp Med Biol, 2007. 595: p. 1-75.
2. Kunnumakkara A.B. et al., Curcumin, the golden nutraceutical: multitargeting for multiple chronic diseases, Br J Pharmacol. 2017 Jun; 174 (11):1325-1348.
3. Liu X.F. et al, Curcumin, a potential therapeutic candidate for anterior segment eye diseases: A Review, Front Pharmacol. 2017 Feb 14;8:66
4. Anand P. et al, Curcumin and cancer: an "old-age" disease with an "age-old" solution, Cancer Lett. 2008 Aug 18;267(1):133-64
5. Cheng, Y.; Kozubek, A.; Ohlsson, L.; Sternby, B.; Duan, R.D. Curcumin decreases acid sphingomyelinase activity in colon cancer caco-2 cells. Planta Med. 2007, 73, 725–730.
6. Yu, T.; Li, J.; Qiu, Y.; Sun, H. 1-Phenyl-2-decanoylamino-3-morpholino-1-propanol (PDMP) facilitates curcumin-induced melanoma cell apoptosis by enhancing ceramide accumulation, JNK activation, and inhibiting PI3K/AKT activation. Mol. Cell. Biochem. 2012, 361, 47–54.
7. Jiang AJ, Jiang G, Li LT, Zheng JN. Curcumin induces apoptosis through mitochondrial pathway and caspases activation in human melanoma cells. Mol Biol Rep. 2015;42:267–75.
8. Thayyullathil, F.; Rahman, A.; Pallichankandy, S.; Patel, M.; Galadari, S. ROS-dependent prostate apoptosis response-4 (Par-4) up-regulation and ceramide generation are the prime signaling events associated with curcumin-induced autophagic cell death in human malignant glioma. FEBS Open Bio. 2014, 4, 763–776.
9. Hilchie, A.L.; Furlong, S.J.; Sutton, K.; Richardson, A.; Robichaud, M.R.J.; Giacomantonio, C.A.; Ridgway, N.D.; Hoskin, D.W. Curcumin-induced apoptosis in PC3 prostate carcinoma cells is caspase-independent and involves cellular ceramide accumulation and damage to mitochondria. Nutr. Cancer 2010, 62, 379–389.
10. Kizhakkayil, J.; Thayyullathil, F.; Chathoth, S.; Hago, A.; Patel, M.; Galadari, S. Glutathione regulates caspase-dependent ceramide production and curcumin-induced apoptosis in human leukemic cells. Free Radic. Biol. Med. 2012, 52, 1854–1864.
11. Scharstuhl, A.; Mutsaers, H.A.M.; Pennings, S.W.C.; Russel, F.G.M.; Wagener, F.A.D.T.G. Involvement of VDAC, Bax and ceramides in the efflux of AIF from mitochondria during curcumin-induced apoptosis. PLoS ONE 2009, 4, e6688.
12. Abdel Shakor, A.B.; Atia, M.; Ismail, I.A.; Alshehri, A.; El-Refaey, H.; Kwiatkowska, K.; Sobota, A. Curcumin induces apoptosis of multidrug-resistant human leukemia HL60 cells by complex pathways leading to ceramide accumulation. Biochim. Biophys. Acta Mol. Cell Biol. Lipids 2014, 1841, 1672–1682.
13. ang, Y.L.; Ji, C.; Cheng, L.; He, L.; Lu, C.C.;Wang, R.; Bi, Z.G. Sphingosine kinase-1 inhibition sensitizes curcumin-induced growth inhibition and apoptosis in ovarian cancer cells. Cancer Sci. 2012, 103, 1538–1545.
14. Wang, K.; Fan, H.; Chen, Q.; Ma, G.; Zhu, M.; Zhang, X.; Zhang, Y.; Yu, J. Curcumin inhibits aerobic glycolysis and induces mitochondrial-mediated apoptosis through hexokinase II in human colorectal cancer cells in vitro. Anticancer Drugs 2015, 26, 15–24.
15. Saha, A.; Kuzuhara, T.; Echigo, N.; Fujii, A.; Suganuma, M.; Fujiki, H. Apoptosis of human lung cancer cells by curcumin mediated through up-regulation of "Growth arrest and DNA damage inducible genes 45 and 153". Biol. Pharm. Bull. 2010, 33, 1291–1299.
16. Kao, H.; Wu, C.; Won, S.; Shin, J.-W.; Liu, H.-S.; Su, C.-L. Kinase gene expression and subcellular protein expression pattern of protein kinase c isoforms in curcumin-treated human hepatocellular carcinoma hep 3B cells. Plant Foods Hum. Nutr. 2011, 66, 136–142.
17. Limtrakul, P.; Lipigorngoson, S.; Namwong, O.; Apisariyakul, A.; Dunn, F.W. Inhibitory effect of dietary curcumin on skin carcinogenesis in mice. Cancer Lett. 1997, 116, 197–203.
18. Kawamori, T.; Lubet, R.; Steele, V.E.; Kelloff, G.J.; Kaskey, R.B.; Rao, C.V.; Reddy, B.S. Chemopreventive effect of curcumin, a naturally occurring anti-inflammatory agent, during the promotion/progression stages of colon cancer. Cancer Res. 1999, 59, 597–601.
19. Chuang, S.E.; Kuo, M.L.; Hsu, C.H.; Chen, C.R.; Lin, J.K.; Lai, G.M.; Hsieh, C.Y.; Cheng, A.L. Curcumin-containing diet inhibits diethylnitrosamine-induced murine hepatocarcinogenesis. Carcinogenesis 2000, 21, 331–335.
20. Huang, M.T.; Lou, Y.R.; Xie, J.G.; Ma, W.; Lu, Y.P.; Yen, P.; Zhu, B.T.; Newmark, H.; Ho, C.T. Effect of dietary curcumin and dibenzoylmethane on formation of 7,12-dimethylbenz[a]anthracene-induced mammary tumors and lymphomas/leukemias in Sencar mice.
21. Joe, B. and B.R. Lokesh, Role of capsaicin, curcumin and dietary n-3 fatty acids in lowering the generation of reactive oxygen species in rat peritoneal macrophages. Biochim Biophys Acta, 1994. 1224(2): p. 255-63.
22. Chan, M.M., et al., In vivo inhibition of nitric oxide synthase gene expression by curcumin, a cancer preventive natural product with anti-inflammatory properties. Biochem Pharmacol, 1998. 55(12): p. 1955-62
23. Li L, Aggarwal BB, Shishodia S, Abbruzzese J, Kurzrock R. Nuclear factor-kappaB and IkappaB kinase are constitutively active in human pancreatic cells, and their down-regulation by curcumin (diferuloylmethane) is associated with the suppression of proliferation and the induction of apoptosis. Cancer. 2004; 101:2351–62.
24. Jurenka, J.S., Anti-inflammatory properties of curcumin, a major constituent of Curcuma longa: a review of preclinical and clinical research. Altern Med Rev, 2009. 14(2): p. 141-53.
25. Garg, A. and B.B. Aggarwal, Nuclear transcription factor-kappaB as a target for cancer drug development. Leukemia, 2002. 16(6): p. 1053-68.
26. Aggarwal, B.B., et al., Curcumin suppresses the paclitaxel-induced nuclear factor-kappaB pathway in breast cancer cells and inhibits lung metastasis of human breast cancer in nude mice. Clin Cancer Res, 2005. 11(20): p. 7490-8.
27. Brennan, P. and L.A. O'Neill, Inhibition of nuclear factor kappaB by direct modification in whole cells--mechanism of action of nordihydroguaiaritic acid, curcumin and thiol modifiers. Biochem Pharmacol, 1998. 55(7): p. 965-73.
28. Wang, D., et al., Liposome-encapsulated curcumin suppresses growth of head and neck squamous cell carcinoma in vitro and in xenografts through the inhibition of nuclear factor kappaB by an AKT-independent pathway. Clin Cancer Res, 2008. 14(19): p. 6228-36.
29. Gilmore, T.D., Introduction to NF-kappaB: players, pathways, perspectives. Oncogene, 2006. 25(51): p. 6680-4.
30. Brasier, A.R., The NF-kappaB regulatory network. Cardiovasc Toxicol, 2006. 6(2): p. 111-30.
31. Plummer, S.M., et al., Inhibition of cyclo-oxygenase 2 expression in colon cells by the chemopreventive agent curcumin involves inhibition of NF-kappaB activation via the NIK/IKK signalling complex. Oncogene, 1999. 18(44): p. 6013-20.
32. Baharuddin, P.; Satar, N.; Fakiruddin, K.S.; Zakaria, N.; Lim, M.N.; Yusoff, N.M.; Zakaria, Z.; Yahaya, B.H. Curcumin improves the efficacy of cisplatin by targeting cancer stem-like cells through p21 and cyclin D1-mediated tumour cell inhibition in non-small cell lung cancer cell lines. Oncol. Rep. 2016, 35, 13–25.
33. Duarte, V.M.; Han, E.; Veena, M.S.; Salvado, A.; Jeffrey, D.; Liang, L.; Faull, K.F.; Srivatsan, E.S.;Wang, M.B. Curcumin enhances the effect of cisplatin in suppression of head and neck squamous cell carcinoma via inhibition of IKK protein of the nuclear factor kB pathway. Mol. Cancer Ther. 2010, 9, 2665–2675.
34. Chen, J.; Wang, G.; Wang, L.; Kang, J.; Wang, J. Curcumin p38-dependently enhances the anticancer activity of valproic acid in human leukemia cells. Eur. J. Pharm. Sci. 2010, 41, 210–218
35. Epelbaum, R.; Schaffer, M.; Vizel, B.; Badmaev, V.; Bar-Sela, G. Curcumin and gemcitabine in patients with advanced pancreatic cancer. Nutr. Cancer 2010, 62, 1137–1141.
36. Ferguson, J.E.; Orlando, R.A. Curcumin reduces cytotoxicity of 5-Fluorouracil treatment in human breast cancer cells. J. Med. Food 2015, 18, 497–502.
37. Pandey, A.; Vishnoi, K.; Mahata, S.; Tripathi, S.C.; Misra, S.P.; Misra, V.; Mehrotra, R.; Dwivedi, M.; Bharti, A.C. Berberine and curcumin target survivin and STAT-3 in gastric cancer cells and synergize actions of standard chemotherapeutic 5-fluorouracil. Nutr. Cancer 2015, 67, 1293–1304.
38. Yu, Y.; Kanwar, S.S.; Patel, B.B.; Nautiyal, J.; Sarkar, F.H.; Majumdar, A.P. Elimination of colon cancer stem-like cells by the combination of curcumin and FOLFOX. Transl. Oncol. 2009, 2, 321–328
39. Gao, J.-Z.; Du, J.-L.;Wang, Y.-L.; Li, J.;Wei, L.-X.; Guo, M.-Z. Synergistic effects of curcumin and bevacizumab on cell signaling pathways in hepatocellular carcinoma. Oncol. Lett. 2015, 9, 295–299.
40. Guo, Y.; Li, Y.; Shan, Q.; He, G.; Lin, J.; Gong, Y. Curcumin potentiates the anti-leukemia effects of imatinib by downregulation of the AKT/mTOR pathway and BCR/ABL gene expression in Ph+ acute lymphoblastic leukemia. Int. J. Biochem. Cell Biol. 2015, 65, 1–11.
41. Hossain, M.M.; Banik, N.L.; Ray, S.K. Synergistic anti-cancer mechanisms of curcumin and paclitaxel for growth inhibition of human brain tumor stem cells and LN18 and U138MG cells. Neurochem. Int. 2012, 61, 1102–1113.
42. De Ruiz Porras, V.; Bystrup, S.; Martínez-Cardús, A.; Pluvinet, R.; Sumoy, L.; Howells, L.; James, M.I.; Iwuji, C.; Manzano, J.L.; Layos, L.; et al. Curcumin mediates oxaliplatin-acquired resistance reversion in colorectal cancer cell lines through modulation of CXC-Chemokine/NF-B signalling pathway. Sci. Rep.2016, 6, 24675.
43. Zanotto-Filho, A.; Braganhol, E.; Klafke, K.; Figueiró, F.; Terra, S.R.; Paludo, F.J.; Morrone, M.; Bristot, I.J.; Battastini, A.M.; Forcelini, C.M.; et al. Autophagy inhibition improves the efficacy of curcumin/temozolomide combination therapy in glioblastomas. Cancer Lett. 2015, 358, 220–231.
44. Lee, J.Y.; Lee, Y.M.; Chang, G.C.; Yu, S.L.; Hsieh,W.Y.; Chen, J.J.W.; Chen, H.W.; Yang, P.C. Curcumin induces EGFR degradation in lung adenocarcinoma and modulates p38 activation in intestine: The versatile adjuvant for gefitinib therapy. PLoS ONE 2011, 6, e23756.
45. Bachmeier B.E., Killian P.H., Melchart D. The Role of Curcumin in Prevention and Management of Metastatic Disease. Int J Mol Sci. 2018 Jun 9;19(6). pii: E1716. doi: 10.3390/ijms19061716
46. Chendil D, Ranga RS, Meigooni D, Sathishkumar S, Ahmed MM. Curcumin confers radiosensitizing effect in prostate cancer cell line PC-3. Oncogene. 2004;23: 1599–607.

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CURCUMIN

BRIEF INFORMATION

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Curcumin

Curcumin is a lipophilic polyphenol found in turmeric (*Curcuma longa*), which gives it its characteristic deep yellow colour. Turmeric, or yellow root, belongs to the ginger family *(Zingiberaceae)* and is native to Southeast Asia. Turmeric is valued and used as a spice, as well as in Indian Ayurvedic medicine for its antioxidant,antiseptic, analgesic and anti-inflammatory properties [1].
We distinguish between three pharmacologically active ingredients, known as "curcuminoids", in turmeric root extract. The best study data shows the isolated active ingredient curcumin (diferuloylmethane [1,7-bis(4-hydroxy-3-methoxy-phenyl)-hepta-1,6-diene-3,5-dione]).
In addition to curcumin, the root extract also contains demethoxycurcumin (DMC) and bisdemethoxycurcumin (BDMC). The proportion of pure curcumin in the total root extract, however, amounts to only a few percent.

We only use the pure active ingredient curcumin from natural sources in our formulations.

Areas of application

In addition to its main area of application in complementary cancer therapy and inflammatory processes,curcumin is also a useful supplement to existing treatments for gastrointestinal, skin, neurodegenerative,cardiovascular and metabolic diseases. Even for anterior segment eye diseases and neurological depressive disorders, curcumin is now considered a promising therapeutic approach [2,3].

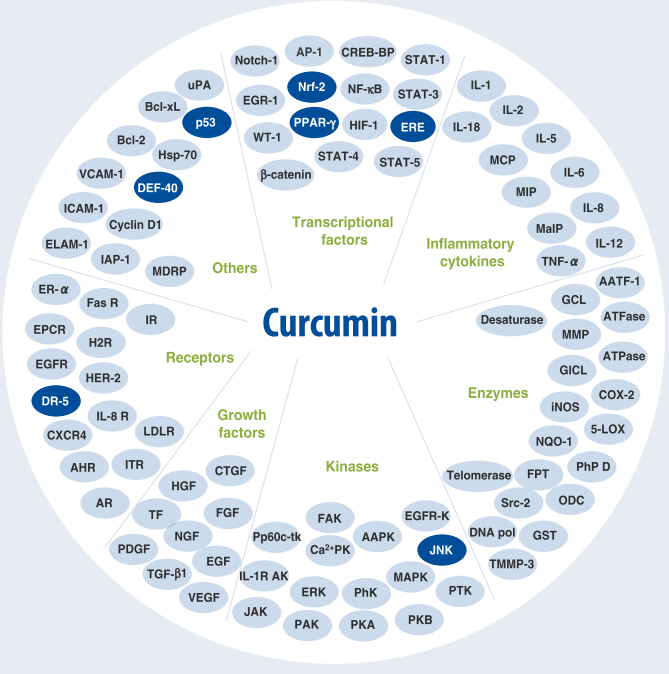
Curcumin has been part of clinical research for years. There is no polyphenol with a broader body of data than curcumin regarding its use in various diseases. Curcumin, artesunate and resveratrol are considered promising adjuvant therapies for the improved treatment of serious illnesses.

Mode of action

Curcumin acts as an epigenetic regulator targeting a wide range of molecular targets and signaling pathways. It has an influence on transcription factors, inflammatory mediators, protein kinases and enzymes.

Due to its numerous effects, curcumin has broad preventive and therapeutic significance. The following effects are described in a number of studies [4]:

- anti-parasitic, anti-bacterial
- immunostimulatory
- anti-arthritic
- anti-arteriosclerotic
- cholagogue
- anti-oxidative, anti-inflammatory
- neuroprotective, cardioprotective, hepatoprotective, nephroprotective, pulmoprotective
- radiation and chemosensitising
- radiation and chemoprotective
- anti-septic
- anti-diabetic
- anti-depressive
- pain-relieving



Molecular targets upregulated by curcumin

Molecular targets downregulated by curcumin

Fig.: Selective influence of curcumin on molecular targets, modified from [4]

Curcumin as a synergistic and sensitising component of therapy

A large number of studies confirm that curcumin, when used in combination therapy with chemotherapeutic agents, improves treatment effectiveness and side effect management both in vitro and in vivo:

POLYPHENOL	CHEMOTHERAPY	TYPE OF CANCER	SOURCE
Curcumin	Cisplatin	Lung	[32]
Curcumin	Cisplatin	Head and neck	[33]
Curcumin	Valproic acid	Leukaemia	[34]
Curcumin	Gemcitabine	Pancreas	[35]
Curcumin	5-Fluorouracil	Breast	[36]
Curcumin	5-Fluorouracil	Stomach	[37]
Curcumin	5-Fluorouracil + Oxaliplatin	Colon	[38]
Curcumin	Bevacizumab	Liver	[39]
Curcumin	Imatinib	Leukaemia	[40]
Curcumin	Paclitaxel	Brain	[41]
Curcumin	Oxaliplatin	Colon	[42]
Curcumin	Temozolomide	Glioblastoma	[43]
Curcumin	Gefitinib	Lung	[44]

(Fig. modified from [45])

A sensitising effect in combination with curcumin and radiotherapy was also demonstrated in prostate PC-3 cancer cells [46].

Curcumin in cancer therapy

Curcumin has been shown in a variety of clinical studies to induce anti-tumoural effects such as apoptosis and proliferation inhibition in melanoma, glioblastoma, prostate, colorectal, lung, liver, leukaemia and ovarian carcinoma cells [5-16].

Curcumin showed in vivo anti-tumoural effects in cancers of the breast, skin and liver as well as in colon cancer and its metastases [17-20]. In tumours, the activity of transcription factors such as NF-κB is often increased and associated with angiogenesis, tumour promotion and metastasis [21]. Curcumin was able to inhibit angiogenesis and metastasis by inhibiting proliferative stimuli via the NF-κB pathway [22, 23].

One of the most significant effects of curcumin is the selective induction of apoptosis in tumour cells. Curcumin achieves this by firstly upregulating p53 expression and secondly by initiating the mitochondrial intrinsic apoptosis pathway [24, 25].

However, curcumin also influences extrinsic apoptosis pathways, i.e. the binding of apoptotic ligands to their receptors [26]. Curcumin was also able to induce cell death through initiated autophagy [27, 28]. However, the broad spectrum of effects ofcurcumin goes far beyond these important influences.

The antioxidant and anti-inflammatory properties of curcumin also play an important role in cancer prevention [29]. The influence on phase I and II enzymes of the detoxification cycle contributes to protection against the development of cancer. Curcumin has been shown to inhibit Phase I enzymes such as cytochrome P450, which, while essential for detoxification, are also responsible for the activation of secondary carcinogens [30].

In contrast, curcumin induces phase II enzymes such as glutathione transferases, peroxidases and reductases, which enable the detoxification of metabolites through conjugation [31].

Advantages of our formulations using cyclodextrin

- Non-metabolisable, non-diabetogenic or glucose-releasing solubiliser
- Rapid renal clearance, remains extracellular after parenteral administration
- Minimal risk of anaphylactic shock
- Safety and tolerability confirmed by healthcare professionals
- No ethanol and therefore gentle on the liver, well tolerated
- No prior administration of cortisone or special infusion equipment required
- Use of pure, natural raw materials

Do not use these formulations in the following cases:

- Kidney damage
- in patients under 2 years of age
- If there are known intolerances to any of the ingredients
- CAVE: Curcumin has a cholagogue effect.

Dosage (based on previous therapeutic experience, indication assessment and further therapy):

1-2 times per week for 10 applications/treatment cycle, repeat as needed.