

# Ginger - Zingiber officinale

## **Common Indications**

- Nausea and vomiting from any source
- Gastric distress
- Antioxidant and anti-inflammatory
- Arthritis
- Infection
- Chemoprotection

#### **General Comments**

Ginger has a long history of use not only in cooking but as a medicinal herb. There is a large body of research and it continue to this day looking at ginger for a host of issues including use in cancer and as chemoprotective.

#### **Benefits & Mechanism of Action**

Nausea and vomiting associated with chemotherapy, surgery, motion sickness or pregnancy.

Ginger's antiemetic activity has been compared to both drug and placebo and shown effectiveness. <sup>1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17</sup> Ginger was compared to Dramamine (dimenhydrinate) in a double blind randomized controlled trial of 170 pregnant women and found to be just as effective.<sup>18</sup> It also presented fewer side effects and caused less drowsiness as it relieved nausea. A sperate meta-analysis also proved its merit in easing nausea and vomiting. <sup>19</sup>

Ginger has been studied in chemotherapy patients with good results. <sup>11,20,21,22</sup> Ginger was found to be more effective than Zofran (odansetron) in chemotherapy patients receiving cisplatin. Ginger decreased the delay in gastric emptying times. When given with a small meal, ginger was shown helpful in reducing nausea and the need for medication.<sup>23</sup>

Hyperemesis gravidarum occurrence in pregnancy has also been studied with good impact. When compared to Reglan (metoclopramide) for surgically induced

nausea, Ginger had good impact reducing nausea and vomiting.

### Antioxidant

Ginger has shown significant antioxidant effects both directly and indirectly. One study showed that ginger significanly lowered free radical levels and increased the activity of endogenous antioxidants superoxide dismutase and catalase.<sup>25</sup> Ginger also demonstrated a sparing effect on vitamins C and E.<sup>25</sup> It also protects against lipid peroxidation in the liver and kidney.<sup>26,27</sup>

Inflammation; may be used for inflammatory conditions such as arthritis.

Ginger's structural phenols are anti- inflammatory may have an effect on lipopolysaccharide induced COX-2 and PGE2 production.<sup>28</sup> In animal studies, aqueous extract of ginger significantly lowered thromboxane B2 levels and serum PGE<sub>2</sub>.<sup>29</sup> Ginger also inhibits 5-lipoxygenase and thromboxane synthase.<sup>31</sup> Genes that encode for cytokines, chemokines, and the inducible enxyme COX-2 have been inhibited with ginger supplementation.<sup>30,31</sup>

Multiple compounds in ginger contribute to the anti-inflammatory effect. Constituents include gingerols, shogaols, gingerenone A, 6-gingerdiol, hexahydrocurcumin, zingerone, diarylheptanoids, and gingerdione.<sup>32,33,34</sup> Gingerol and 8-gingerol showed capsaicin-like effects on intracellular Ca<sup>2+</sup> ion currents and are considered a valid alternative to topical capsaicin.<sup>35,36</sup>

## Gastroprotection

Ginger increases saliva, bile and gastric secretions.<sup>37,38,39</sup> In both animal and human studies, ginger increased gastrointestinal motility, accelerated gastric emptying, and stimulated antral contractions.<sup>10,40,41</sup> Ginger has cholinergic agonistic activity on  $M_3$  receptors in the gut, postsynaptically, and inhibititory effects presynaptically.<sup>42</sup> When used to treat occasional diarrhea, the mechanism is likely modification of bacterial cell walls and human epithelial cells, discouraging colonization.<sup>43</sup>

## Infection

In vivo and in vitro studies of ginger have show efficacy against bacteria and parasites. Ginger therapy was effective against *Staphylococcus aureus, Streptococcus pyogenes, Streptocuccus pneumoniae, Haemophilus, Penicillium spp., Escherichia coli, Bacillus subtilis, Helicobacter pylori,* and the larvae of mosquito associated with dengue fever, *Aedes aegypti.*<sup>44,45,46,47,48,49</sup> There are also studies showing antiviral and antifungal effects with additional activity of preventing plaque formation.<sup>48,50,51,52,53</sup>

## Chemoprotection

Ginger has shown chemoprotective effects in both human and animal models. There is demonstrated evidence of inhibition in breast cancer, ovarian, promyelocitic leukemia, prostate, colon, and pancreatic cancer cell lines.<sup>54,55,56,57,58,59,60,61,62</sup> Ginger has apoptotic activity and reduces proliferation and cell transformation.<sup>63</sup> 6-gingerol, 6-paradol, shogaols, zerumbone and zingerone have antitumor properties.<sup>64</sup> Mechanism activity includes modulation of proteins involved in apoptosis, arrested development in the sub-G1 phase, angiogenesis inhibition from reduced blood supply, intracellular oxidative stress mediated cascade, and down-regulation of transcription by NF-kappaB activation.<sup>54,61,65,66,67</sup>

#### Dose:

#### General

- Standardized extract 75 to 2000mg in divided doses with food
- Fresh root 1 to 4gm of the fresh root daily in divided doses
- Liquid extract (1:2) 0.7 to 4 ml/day
- Dried root 1 to 3 grams daily in divided doses
- Infusion 4 to 6 slices of fresh ginger steeped in boiling water for 30 minutes

## Pediatric (ages 6-12)

• Use 1/3 of adult dosage

Note: There are various products with different dosages and standardizations to choose from. When choosing a dietary supplement, select those from reputable manufacturers.

#### Standardization:

Ginger supplements should be standardized to contain 4% volatile oils or 5% total pungent compounds including 6-gingerol and/or 6-shogaol.

#### **Cautions & Side Effects:**

Ginger has been reported to be safe in recommended doses. Common minor adverse effects include heartburn, bloating, and dermatitis of fingertips with topical use.

Medications with increased effects while taking ginger include:

- Anticoagulant medications<sup>68</sup>
- Procardia case reported<sup>69</sup>
- Antibiotics<sup>70</sup>

Patients with the following disease states or conditions should use ginger:

Bleeding disorders

- Gastric ulcers
- GERD
- Gallstones

# References:

Nausea and Vomiting

- 1. Portnoi G, Chng LA, Karimi-Tabesh L, et al. Prospective comparative study of the safety and effectiveness of ginger for the treatment of nausea and vomiting in pregnancy. Am J Obstet Gynecol 2003;189(5):1374-1377.
- Sripramote M, Lekhyananda N. A randomized comparison of ginger and vitamin B6 in the treatment of nausea and vomiting of pregnancy. J Med Assoc Thai 2003;86(9):846-853.
- 3. Vutyavanich T, Kraisarin T, Ruangsri R. Ginger for nausea and vomiting in pregnancy: randomized, double-masked, placebo-controlled trial. Obstet Gynecol 2001;97(4):577-582.
- 4. Arfeen Z et al. A double-blind randomised controlled trial of ginger for the prevention of postoperative nausea and vomiting. Anaesth Intensive Care 23.4 (1995): 449–452.
- 5. Bone ME et al. Ginger root: a new antiemetic: the effect of ginger root on postoperative nausea and vomiting after major gynaecological surgery. Anaesthesia 45.8 (1990): 669–671.
- 6. Fischer-Rasmussen W et al. Ginger treatment of hyperemesis gravidarum. Eur J Obstet Gynecol Reprod Biol 38.1 (1990): 19–24.
- 7. Grontved A, Hentzer E. Vertigo-reducing effect of ginger root: a controlled clinical study. ORL J Otorhinolaryngol Relat Spec 48.5 (1986): 282–286.
- 8. Keating A, Chez RA. Ginger syrup as an antiemetic in early pregnancy. Altern Ther Health Med 8.5 (2002): 89–91.
- 9. Lien HC et al. Effects of ginger on motion sickness and gastric slow-wave dysrhythmias induced by circular vection. Am J Physiol Gastrointest Liver Physiol 284.3 (2003): G481–G489.
- 10. Phillips S et al. Zingiber officinale (ginger): an antiemetic for day case surgery. Anaesthesia 48.8 (1993): 715–7117.
- 11. Meyer K et al. Zingiber officinale (ginger) used to prevent 8-Mop associated nausea. Dermatol Nurs 7.4 (1995): 242–244.
- 12. Mowrey D, Clayson D. Motion sickness, ginger and psychosis. Lancet 319.8273 (1982): 655–657.
- 13. Schmid R et al. Comparison of seven commonly used agents for prophylaxis of seasickness. J Travel Med 1.4 (1994): 203–206.
- 14. Smith C et al. A randomized controlled trial of ginger to treat nausea and vomiting in pregnancy. Obstet Gynecol 103.4 (2004): 639–645.
- Willetts KE, Ekangaki A, Eden JA. Effect of a ginger extract on pregnancy-induced nausea: a randomised controlled trial. Aust NZ J Obstet Gynaecol 43.2 (2003): 139–144.

- Visalyaputra S et al. The efficacy of ginger root in the prevention of postoperative nausea and vomiting after outpatient gynaecological laparoscopy. Anaesthesia 53.5 (1998): 506–510.
- 17. Palatty PL, Haniadka R, Valder B, et al. Ginger in the prevention of nausea and vomiting: a review. Crit Rev Food Sci Nutr. 2013;53(7):659-69.
- Pongrojpaw D, Somprasit C, Chanthasenanont A. A randomized comparison of ginger and dimenhydrinate in the treatment of nausea and vomiting in pregnancy. J Med Assoc Thai. 2007 Sep;90(9):1703-9.
- 19. Ernst E, Pittler MH. Efficacy of ginger for nausea and vomiting: a systematic review of randomized clinical trials. Br J Anaesth 2000;84(3):367-371.
- 20. Manusirivithaya S et al. Antiemetic effect of ginger in gynecologic oncology patients receiving cisplatin. Int J Gynecol Cancer 14.6 (2004): 1063–1069.
- Ryan JL et al. Ginger (Zingiber officinale) reduces acute chemotherapy-induced nausea: a URCC CCOP study of 576 patients. Support Care Cancer 20.7 (2012): 1479–489.
- 22. Sontakke S et al. Ginger as an antiemetic in nausea and vomiting induced by chemotherapy: a randomized, cross-over, double blind study. Indian J Pharmacol 35.1 (2003): 32–36.
- 23. Levine ME, Gillis MG, Koch SY, et al. Protein and ginger for the treatment of chemotherapy-induced delayed nausea. J Altern Complement Med. 2008 Jun;14(5):545-51.
- 24. Zick SM, Ruffin MT, Lee J, et al. Phase II trial of encapsulated ginger as a treatment for chemotherapy- induced nausea and vomiting. Support Care Cancer. 2009 May;17(5):563-72. Epub 2008 Nov 13.

# Antioxidant

- 25. Jeyakumar SM et al. Antioxidant activity of ginger (Zingiber officinale Rosc.) in rats fed a high fat diet. Med Sci Res 27.5 (1999): 341–344.
- Asnani V, Verma RJ. Antioxidative effect of rhizome of Zinziber officinale on paraben induced lipid peroxidation: an in vitro study. Acta Pol Pharm 64.1 (2007): 35–37.
- 27. Ahmed RS et al. Protective effects of dietary ginger (Zingiber officinale Rosc.) on lindane-induced oxidative stress in rats. Phytother Res 22.7 (2008): 902–906.

# Inflammation

- 28. Kobayashi M, Shoji N, Ohizumi Y. Gingerol, a novel cardiotonic agent, activates the Ca2+-pumping ATPase in skeletal and cardiac sarcoplasmic reticulum. Biochim Biophys Acta 903.1 (1987): 96–102.
- 29. Thomson M, Al Qattan KK, Al Sawan SM, et al. The use of ginger (Zingiber officinale Rosc.) as a potential anti-inflammatory and antithrombotic agent. Prostaglandins Leukot Essent Fatty Acids 2002;67(6):475-478.
- 30. Langner E et al. Ginger: history and use. Adv Ther 15.1 (1998): 25-44.
- 31. Grzanna R et al. Ginger: an herbal medicinal product with broad anti-

inflammatory actions. J Med Food 8.2 (2005): 125–132.

- 32. Schuhbaum H, Franz G. Ginger: spice and versatile medicinal plant. Z Phytother 21.4 (2000): 203–209 [in German].
- 33. Flynn DL et al. Inhibition of human neutrophil 5-lipoxygenase activity by gingerdione, shogaol, capsaicin and related pungent compounds. Prostaglandins Leukot Med 24.2–3 (1986): 195–198.
- 34. Kiuchi F et al. Inhibition of prostaglandin and leukotriene biosynthesis by gingerols and diarylheptanoids.Chem Pharm Bull 40.2 (1992): 387–391.
- 35. Dedov VN et al. Gingerols: a novel class of vanilloid receptor (VR1) agonists. Br J Pharmacol 137.6 (2002): 793–798.
- 36. Onogi T et al. Capsaicin-like effect of (6)-shogaol on substance P-containing primary afferents of rats: a possible mechanism of its analgesic action. Neuropharmacology 31.11 (1992): 1165–1169.

# Gastroprotection

- 37. Platel, Kalpana, and K Srinivasan. "Influence of dietary spices or their active principles on digestive enzymes of small intestinal mucosa in rats." International journal of food sciences and nutrition 47.1 (1996): 55-59.
- 38. Platel K, Srinivasan K. Studies on the influence of dietary spices on food transit time in experimental rats. Nutr Res 21.9 (2001): 1309–1314.
- 39. Yamahara J et al. Cholagocic effect of ginger and its active constituents. J Ethnopharmacol 13.2 (1985): 217–225.
- 40. Micklefield GH et al. Effects of ginger on gastroduodenal motility. Int J Clin Pharmacol Ther 37.7 (1999): 341–346.
- 41. Gupta YK, Sharma M. Reversal of pyrogallol-induced delay in gastric emptying in rats by ginger (Zingiber officinale). Methods Find Exp Clin Pharmacol 23.9 (2001): 501–503.
- 42. Ghayur MN et al. Muscarinic, Ca(++) antagonist and specific butyrylcholinesterase inhibitory activity of dried ginger extract might explain its use in dementia. J Pharm Pharmacol 60.10 (2008): 1375–1383.
- 43. Daswani PG et al Antidiarrhoeal activity of Zingiber officinale (Rosc). Current Science 98.2 (2010): 222–229.

## Infection

- 44. Akoachere JF, Ndip RN, Chenwi EB, et al. Antibacterial effect of Zingiber officinale and Garcinia kola on respiratory tract pathogens. East Afr Med J 2002;79(11):588-592.
- 45. Mahady GB, Pendland SL, Yun GS, et al. Ginger (Zingiber officinale Roscoe) and the gingerols inhibit the growth of Cag A+ strains of Helicobacter pylori. Anticancer Res 2003;23(5A):3699-3702.
- 46. Bellik Y Total antioxidant activity and antimicrobial potency of the essential oil and oleoresin of Zingiber officinale Roscoe. Asian Pac J Trop Dis 4.1 (2014): 40–44.
- 47. Kalaivani K et al. Biological activity of selected Lamiaceae and Zingiberaceae

plant essential oils against the dengue vector Aedes aegypti L. (Diptera: Culicidae). Parasitol Res 110 (2012): 1261–1268.

- 48. Martins AP et al. Essential oil composition and antimicrobial activity of three Zingiberaceae from S.Tome e Principle. Planta Med 67.6 (2001): 580–584.
- 49. Kumar S et al. Evaluation of 15 local plant species as larvicidal agents against an Indian strain of dengue fever mosquito, Aedes aegypti L.(Diptera: Culicidae). Frontiers in Phys. 3 (2012) Art 104.
- 50. Henry CJ, Piggott SM. Effect of ginger on metabolic rate. Hum Nutr Clin Nutr 41.1 (1987): 89–92.
- 51. Denyer CV et al. Isolation of antirhinoviral sesquiterpenes from ginger (Zingiber officinale). J Nat Prod 57.5 (1994): 658–662.
- 52. Koch C et al. Inhibitory effect of essential oils against herpes simplex virus type 2. Phytomedicine 15.1–2 (2008): 71–78.
- 53. Schnitzler P et al. Susceptibility of drug-resistant clinical herpes simplex virus type 1 strains to essential oils of ginger, thyme, hyssop, and sandalwood. Antimicrob Agents Chemother 51.5 (2007): 1859–1862.

# Chemoprotection

- Brown AC et al. Ginger's (Zingiber officinale Roscoe) inhibition of rat colonic adenocarcinoma cells proliferation and angiogenesis in vitro. Phytother Res 23.5 (2008): 640–645.
- 55. Ishiguro K et al. Ginger ingredients reduce viability of gastric cancer cells via distinct mechanisms. Biochem Biophys Res Commun 362.1 (2007): 218–223.
- 56. Lee HS et al. [6]-Gingerol inhibits metastasis of MDA-MB-231 human breast cancer cells. J Nutr Biochem 19.5 (2008): 313–3119.
- 57. Park YJ et al. [6]-Gingerol induces cell cycle arrest and cell death of mutant p53expressing pancreatic cancer cells. Yonsei Med J 47.5 (2006): 688–697.
- 58. Rhode J et al. Ginger inhibits cell growth and modulates angiogenic factors in ovarian cancer cells. BMC Complement Altern Med 7 (2007): 44.
- 59. Sabli F et al Cytotoxic Properties of selected Etlingera spp. and Zingiber spp. (Zingiberaceae) endemic to Borneo. Pertanika J. Trop. Agric. Sci. 35.3 (2012): 663–671.
- 60. Shukla Y et al. In vitro and in vivo modulation of testosterone mediated alterations in apoptosis related proteins by [6]-gingerol. Mol Nutr Food Res 51.12 (2007): 1492–1502.
- 61. Yagihashi S et al. Inhibitory effect of gingerol on the proliferation and invasion of hepatoma cells in culture. Cytotechnology 57.2 (2008): 129–136.
- 62. Wei QY et al. Cytotoxic and apoptotic activities of diarylheptanoids and gingerolrelated compounds from the rhizome of Chinese ginger. J Ethnopharmacol 102.2 (2005): 177–184.
- 63. Bode AM et al. Inhibition of epidermal growth factor-induced cell transformation and activator protein 1 activation by [6]-gingerol. Cancer Res 61.3 (2001): 850– 853.
- 64. Kim SO et al. [6]-Gingerol inhibits COX-2 expression by blocking the activation of

p38 MAP kinase and NF-kappaB in phorbol ester-stimulated mouse skin. Oncogene 24.15 (2005): 2558–2567.

- 65. Chen CY et al. 6-shogaol (alkanone from ginger) induces apoptotic cell death of human hepatoma p53 mutant Mahlavu subline via an oxidative stress-mediated caspase-dependent mechanism. J Agric Food Chem 55.3 (2007): 948–954.
- 66. Ling H et al. 6-Shogaol, an active constituent of ginger, inhibits breast cancer cell invasion by reducing matrix metalloproteinase-9 expression via blockade of nuclear factor-kB activation. British J Pharma 161 (2010): 1763–1777.
- 67. Sabli F et al Cytotoxic Properties of selected Etlingera spp. and Zingiber spp. (Zingiberaceae) endemic to Borneo. Pertanika J. Trop. Agric. Sci. 35.3 (2012): 663–671.

Medications

- 68. Vaes LP, Chyka PA. Interactions of warfarin with garlic, ginger, ginkgo, or ginseng: nature of the evidence. Ann Pharmacother 2000;34(12):1478-1482.
- 69. Young HY, Liao JC, Chang YS, Luo YL, Lu MC, Peng WH. Synergistic effect of ginger and nifedipine on human platelet aggregation: a study in hypertensive patients and normal volunteers. Am J Chin Med. 2006;34(4):545-51.
- 70. Kesawarni K, Gupta R. Bioavailability enhancers of herbal origin. Asian Pac J Trop Biomed 3.4 (2013): 253–266.