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Anti-Oxidative and Anti-Inflammatory Effects of Ginger in Health and Physical Activity: Review of Current Evidence

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Abstract

Go to:

Background:

Ginger (Zingiber officinale Rosc.) belongs to the family Zingiberaceae. The health-promoting perspective of ginger is attributed to its rich phytochemistry. This study aimed to review the current evidence on ginger effects as an anti-inflammatory and anti-oxidative.

Methods:

We searched MEDLINE for related publications using “ginger” and “anti-oxidative” and “ginger” and “anti-inflammatory” as keywords. This search had considered Papers that had been published between 2000 and 2010 without any filter.

Conclusions:

The anticancer potential of ginger is well documented and its functional ingredients like gingerols, shogaol, and paradols are the valuable ingredients which can prevent various cancers. This review concludes to favor ginger but some ambiguities necessitate further research before claiming its efficacy.

Keywords: Anti-inflammatory, anti-oxidative, ginger, reactive oxygen species.

INTRODUCTION

Go to:

Ginger (Zingiber officinale Rosc.) belongs to the family Zingiberaceae. It originated in South-East

Asia and then used in many countries as a spice and condiment to add flavor to food.[1] Besides this, the rhizome of ginger has also been used in traditional herbal medicine. The health-promoting perspective of ginger is attributed to its rich phytochemistry.[2] Jolad *et al*. grouped fresh ginger into two wide range categories, i.e. volatiles and non-volatiles. Volatiles include sesquiterpene and monoterpenoid hydrocarbons providing the distinct aroma and taste of ginger. On the contrary, non-volatile pungent compounds include gingerols, shogaols, paradols, and zingerone.[3]

Ginger has staring potential for treating a number of ailments including degenerative disorders (arthritis and rheumatism), digestive health (indigestion, constipation and ulcer), cardiovascular disorders (atherosclerosis and hypertension), vomiting, diabetes mellitus, and cancer. It also has anti-inflammatory and anti-oxidative properties for controlling the process of aging. Furthermore, it has antimicrobial potential as well which can help in treating infectious diseases.[2,4–6] Generation of free radicals or reactive oxygen species (ROS) during metabolism beyond the antioxidant capacity of a biological system results in oxidative stress,[7] which plays an essential role in heart diseases, neurodegenerative diseases, cancer, and in the aging process.[7,8] The bioactive molecules of ginger like gingerols have shown antioxidant activity in various modules.[9]

Inflammatory disorders such as gastritis, esophagitis, and hepatitis, which are caused not only by infectious agents such as viruses, bacteria, and parasites but also by physical and chemical agents like heat, acid, cigarette smoke, and foreign bodies, are recognized as risk factors for human cancer. Ginger consumption before exercise might reduce naturally occurring quadriceps muscle pain during moderate-intensity cycling exercise. This effect may be due to anti-inflammatory effect of ginger and further investigation need to prove it in human.[10]

This study aimed to review the current evidence on ginger effects as an anti-inflammatory and anti-oxidative.

METHODS

Go to:

We conducted a comprehensive search in the following databases: MEDLINE, EMBASE, in order to identify relevant studies. The electronic search was conducted in July 2012, and developed in collaboration with an experienced librarian. Time restriction were applied to year of publication from 2000-2012 and we used literatures only from English language and studied both human and animal models. All titles and abstracts were examined that met our search terms and full publications were reviewed, when necessary. Medline search with the terms: [Ginger] AND [anti-oxidative] and [Ginger] AND [anti-inflammatory], then we had 211 articles. Review articles were only included in this review if they offered new insights or opinions. We could achieve only to 59 articles from these articles and summarized 12 full text studies in the table.

DISCUSSION

Go to:

Anti-oxidative stress effects

The rich phytochemistry of ginger includes components that scavenge free radicals produced in biological systems. For the purpose of energy production, some free radicals which generated during the process of oxidation are essential.[11] Increased production of free radicals results in oxidative stress that can lead to DNA damage.[12] In such circumstances of imbalance, extra antioxidant supplementation through dietary modules is essential for organism vitality.[13] The anti-oxidative properties of ginger and its components have been explored in various *in vitro* and *in vivo* tests.

Strengthening the body's defenses by improving the antioxidant status will undoubtedly protect human against many chronic diseases.[2] 6-Shogaol has exhibited the most potent antioxidant and anti-inflammatory properties in ginger, which can be attributed to the presence of alpha, beta-unsaturated ketone moiety.[9] Animal modeling showed that ginger significantly lowered induced lipid peroxidation and raised the levels of antioxidant enzymes, together with serum glutathione.[14] Furthermore, feeding ginger to rats at 1% w/w during administration of malathion (20 ppm) for 4 weeks significantly attenuated malathion-induced lipid peroxidation.[15] Concomitant dietary feeding of ginger (1%w/w) significantly attenuated lindane-induced lipid peroxidation, reduced glutathione (GSH), and the GSH-dependent enzymes glutathione peroxidase, glutathione reductase, and glutathione S-transferase.[16] *In vitro*, zingerone scavenged O^{2-} and OH and suppressed lipid peroxidation, so it can possibly value in treatment of Parkinson's disease.[17]

Ethanol significantly decreased the superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, and glutathione content in the hepatic tissue. This effect was improved by a treatment with 1% dietary ginger 1 month in rats which suggest that ginger may have protective role against the ethanol induced hepatotoxicity.[18] Ginger and Arabic Gum showed renoprotective effects in renal failure. These protective effects may be attributed to their anti-inflammatory properties by attenuating serum C-reactive protein levels and antioxidant effects by reducing lipid peroxidation marker, malondialdehyde levels, and increasing renal superoxide dismutase activity. They could be beneficial adjuvant therapy in patients with acute and chronic renal failure to prevent disease progression and delay the need for renal replacement therapy.[19]

In one study, ethanol extract of *Z. officinale* alone and in combination with vitamin E partially ameliorated cisplatin-induced nephrotoxicity. This protection is mediated by renal antioxidant defense system.[20]

In the other study, the protective effect of the ginger extract was examined on CCl (4) and acetaminophen-induced liver damage and indicated that *Z. officinale* could be useful in preventing acute liver injury.[21]

The overall evaluation of one study concludes that both spices ginger and cumin have good antioxidant potential, particularly fresh ginger. Methanol extracts of all the samples were found to have better antioxidant action than the *n*-hexane extracts. There was also a good correlation between the total phenolic content and antioxidant activities of the non-volatile extracts.[22]

Rat studies showed that ginger has an equal antioxidant effect to that of ascorbic acid.[15]

Ghasemzadeh *et al*. validated the medicinal potential of the leaves and young rhizome of *Z. officinale* (Halia Bara) and the positive relationship between total phenolics content and antioxidant activities in *Z. officinale*.[23]

Anti-inflammatory effects

In ancient cultures, medical practitioners focused on herbs for promoting the immune systems of body. In many countries ginger and its products raise the immune system.[13]

Gingerol, shogaol, and other structurally-related substances in ginger inhibit prostaglandin and leukotriene biosynthesis through suppression of 5-lipoxygenase or prostaglandin synthetase. Additionally, they can also inhibit synthesis of pro-inflammatory cytokines such as IL-1, TNF-α, and IL-8.[24,25] In another investigation, Pan *et al*. showed that in macrophages,[6] shogaol can down-

regulate inflammatory iNOS and COX-2 gene expression.[26] Jung *et al*. indicated that rhizome hexane fraction extract of *Z. officinale* inhibited the excessive production of NO, PGE (2), TNF-alpha, and IL-1beta.[27] Because of potent compounds in ginger rhizome for inhibiting allergic reactions, it may be useful for the treatment and prevention of allergic diseases.[28]

Habib *et al*. showed that ginger extract can reduce the elevated expression of NFκB and TNF-α in rats with liver cancer.[29] The activation of NF-κB is linked to a variety of inflammatory diseases, including cancer, atherosclerosis, myocardial infarction, diabetes, allergy, asthma, arthritis, Crohn's disease, multiple sclerosis, Alzheimer's disease, osteoporosis, psoriasis, septic shock, and AIDS.[30]

Lantz *et al*. showed that gingerols can inhibit LPS-induced COX-2 expression while shogaol containing extracts has no effect on COX-2 expression. These data demonstrate that important compounds in ginger are capable of inhibiting PGE (2) production.[31]

Studies evaluating the effectiveness of ginger in patients with osteoarthritis have controversial results. One study showed ginger extract to have a statistically significant effect on reducing symptoms of osteoarthritis of the knee.[32] In another study, the effect of ginger in osteoarthritis was significant only in the first period of treatment.[33] In gout as a rheumatic disease of joints, [6]-shogaol has strong anti-inflammatory and antioxidant effects and can be used as a curative agent.[34]

Black *et al*. showed that treatment of patients with has hypo-algesic effects. They used 2 g of ginger supplementation for 11 days of on 36 participants to cure muscle pain. They proved that daily consumption of raw and heat-treated ginger resulted in moderate-to-large reductions in muscle pain. [35]

However, cohort studies and controlled trails in sort of *in vivo* and *in vitro* need to be to warrant the pharmacological applications of ginger.

Anti-cancer effects

The mechanism of ginger for acting as chemopreventive spice remains a matter of conflict among researchers. Ingredients like [6]-gingerol,[6]-shogaol, [6]-paradol, and zerumbone in ginger exhibits anti-inflammatory and antitumorigenic activities.[36,37] Ginger and its bioactive molecules are effective in controlling the extent of colorectal, gastric, ovarian, liver, skin, breast, and prostate cancers. [36,38–43]

Colorectal cancer is more prevalent in vegetarians and ginger could be effective in reducing the extent of this disease. Manju and Nalini studied the efficacy of ginger against 1, 2 dimethylhydrazine (DMH)-induced colon cancer. They observed that ginger supplementation can activate various enzymes such as glutathione peroxidase, glutathione-S-transferase, and glutathione reductase and suppress colon carcinogenesis.[44] Kim *et al*. administered Zerumbone orally in mouse models and observed inhibition in multiplicity of colonic adenocarcinomas through suppression of colonic inflammation in a dose-dependent manner. The mechanism of that includes inhibition of proliferation, induction of apoptosis, and suppression of NF-κB and heme oxygenase (HO)-1 expression.[41]

In gastric cancer, the tumor necrosis factor-related inducing apoptosis ligand (TRIALS) plays a major role by promoting apoptosis. Cascades of caspase proteins activate by ginger and its functional components.[45] Ishiguro *et al*. explained a model for [6]-gingerol and[6]-shogaol action against gastric cancer cells. They observed that [6]-gingerol inhibits TRAIL-induced NF-κB activation by impairing the nuclear translocation of NF-κB, suppresses cIAP1 expression, and increases TRAIL-

induced caspase-3/7 activation.[38]

Yagihashi *et al*. reported that [6]-gingerol can inhibit both proliferation and invasion of hepatoma cells. Cell cycle arrest and apoptosis induction are the main causes of [6]-gingerol in these cancerous cells. [46] Habib *et al*. suggested that ginger extract can reduce the elevated expression of NF-κB and TNF-alpha in rats with liver cancer.[29]

Inhibition of angiogenesis in the mouse skin is the mechanism of ginger for treating of skin cancer.[47 [6]-Gingerol exhibited considerable cytotoxicity by growth inhibition of human epidermoid carcinoma cells mediated via reactive oxygen species (ROS) induced apoptosis.[48]

The effectiveness of ginger and its biomolecules has been demonstrated for controlling of ovarian cancer. Ginger inhibited NF-κB activation and diminished the secretion of VEGF and IL-8 helping to treat ovarian cancer.[49]

Zhang *et al*. showed that zerumbone induced apoptosis in pancreatic carcinoma cells through p53 signal pathway, formation of apoptotic bodies, condensed nuclei, and the increased activity of caspase-3. So, zerumbone is a new therapeutic candidate for controlling of pancreatic cancer.[50] Lee *et al*. indicated that ginger can cure breast cancer via inhibiting cell adhesion invasion motility.[42 [6]-gingerol can affect prostate cancer models by modulation of proteins involved in apoptosis pathway. [51]

Anti-diabetic effects

Some research studies have proved the effectiveness of ginger against diabetes and its complications. Weidner and Sigwart conducted an experimental study and indicated that ginger extract with a high content of gingerols and shogaols did not induce significant changes in blood glucose, blood coagulation, blood pressure, and heart rate in rat models.[52] However, ginger significantly lowered blood glucose, serum total cholesterol, LDL, VLDL, and triglycerides, and raised HDL in hyperglycemic rats, in models that are diabetic, deficient in the apolipoprotein E gene or those that have been fed a high lipid diet.[53] Bhandari *et al*. showed that ethanolic extract of *Zingiber officinale* fed orally for 20 days produced a significant antihyperglycaemic effect ($P < 0.01$) in diabetic rats.[54] Additionally, Nammi *et al*. indicated that the ethanolic extract of ginger reduced body weights and levels of glucose, insulin, total cholesterol, LDL cholesterol, triglycerides, free fatty acids, and phospholipids in high-fat diets.[55] Heimes *et al*. supported from this hypoglycemic potential, too.[56] Insulinoptropic properties of ginger and glucose-lowering potential were explained by Islam and Choi. [56–61]

We summarized 12 studies from these articles in Table 1.

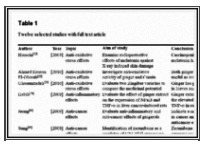

Table 1

Twelve selected studies with full text article

CONCLUSIONS

Go to:

The health-promoting perspectives of ginger are well known. It can treat a wide range of diseases via immunonutrition and anti-inflammatory responses. As a result of anti-inflammatory effect of ginger, it can reduce muscle pain after intense physical activity. Likewise, the anticancer potential of ginger is

well documented and its functional ingredients like gingerols, shogaol, and paradols are the valuable ingredients which can prevent various cancers, angiogenesis and metastasis, induction of apoptosis, and inhibition of cell-cycle progression. Besides these, it improves cardiovascular disorders, diabetes mellitus, and gastrointestinal health.

This review concludes to favor ginger but some ambiguities necessitate further research before claiming its efficacy.

Footnotes

Go to:

Source of Support: Nil

Conflict of Interest: None declared

REFERENCES

Go to:

1. Park EJ, Pizzuto JM. Botanicals in cancer chemoprevention. Cancer Metast Rev. 2002;21:231–55. [PubMed]

2. Shukla Y, Singh M. Cancer preventive properties of ginger: A brief review. Food Chem Toxicol. 2007;45:683–90. [PubMed]

3. Jolad SD, Lantz RC, Solyom AM, Chen GJ, Bates RB, Timmermann BN. Fresh organically grown ginger (*Zingiber officinale*): Composition and effects on LPS-induced PGE2 production. Phytochemistry. 2004;65:1937–54. [PubMed]

4. Jiang H, Xie Z, Koo HJ, McLaughlin SP, Timmermann BN, Gang DR. Metabolic profiling and phylogenetic analysis of medicinal Zingiber species: Tools for authentication of ginger (Zingiber officinale Rosc.) Phytochemistry. 2006;67:232–44. [PubMed]

5. Ali BH, Blunden G, Tanira MO, Nemmar A. Some phytochemical, pharmacological and toxicological properties of ginger (Zingiber officinale Roscoe): A review of recent research. Food Chem Toxicol. 2008;46:409–20. [PubMed]

6. Nicoll R, Henein MY. Ginger (Zingiber officinale Roscoe): A hot remedy for cardiovascular disease? Int J Cardiol. 2009;131:408–9. [PubMed]

7. Zheng W, Wang SY. Antioxidant activity and phenolic compounds in selected herbs. J Agric Food Chem. 2001;49:5165–70. [PubMed]

8. Astley SB. Dietary antioxidants past, present and future. Trends Food Sci Technol. 2003;14:93–8.

9. Dugasani S, Pichika MR, Nadarajah VD, Balijepalli MK, Tandra S, Korlakunta JN. Comparative antioxidant and anti-inflammatory effects of [6]-gingerol, [8]-gingerol, [10]-gingerol and [6]-shogaol. J Ethnopharmacol. 2010;127:515–20. [PubMed]

10. Ohshima H, Tatemicho M, Sawa T. Chemical basis of inflammation-induced carcinogenesis. Arch Biochem Biophys. 2003;417:3–11. [PubMed]

11. Ramaa CS, Shirode AR, Mundada AS, Kadam VJ. Nutraceuticals an emerging era in the treatment and prevention of cardiovascular diseases. Curr Pharm Biotechnol. 2006;7:15–23. [PubMed]

12. Hussein MR, Abu-Dief EE, Abd El-Reheem MH, Abd-Elrahman A. Ultrastructural evaluation of the radioprotective effects of melatonin against X-ray-induced skin damage in Albino rats. Int J Exp

Pathol. 2005;86:45–55. [PMC free article] [PubMed]

13. Barta I, Smerak P, Polıvkova Z, Sestakova H, Langova M, Turek B, et al. Current trends and perspectives in nutrition and cancer prevention. Neoplasma. 2006;53:19–25. [PubMed]

14. El-Sharaky AS, Newairy AA, Kamel MA, Eweda SM. Protective effect of ginger extract against bromobenzene-induced hepatotoxicity in male rats. Food Chem Toxicol. 2009;47:1584–90. [PubMed]

15. Ahmed RS, Seth V, Banerjee BD. Influence of dietary ginger (Zingiber officinales Rosc) on antioxidant defense system in rat: Comparison with ascorbic acid. Indian J Exp Biol. 2000;38:604–6. [PubMed]

16. Ahmed RS, Suke SG, Seth V, Chakraborti A, Tripathi AK, Banerjee BD. Protective effects of dietary ginger (Zingiber officinales Rosc.) on lindane-induced oxidative stress in rats. Phytother Res. 2008;22:902–6. [PubMed]

17. Kabuto H, Nishizawa M, Tada M, Higashio C, Shishibori T, Kohno M. Zingerone [4-(4-hydroxy-3-methoxyphenyl)-2-butanone] sprevents 6-hydroxydopamine-induced dopamine depression in mouse striatum and increases superoxide scavenging activity in serum. Neurochem Res. 2005;30:325–32. [PubMed]

18. Mallikarjuna K, Sahitya Chetan P, Sathyavelu Reddy K, Rajendra W. Ethanol toxicity: Rehabilitation of hepatic antioxidant defense system with dietary ginger. Fitoterapia. 2008;79:174–8. [PubMed]

19. Mahmoud MF, Diaai AA, Ahmed F. Evaluation of the efficacy of ginger, Arabic gum, and Boswellia in acute and chronic renal failure. Ren Fail. 2012;34:73–82. [PubMed]

20. Ajith TA, Nivitha V, Usha S. Zingiber officinale Roscoe alone and in combination with alpha-tocopherol protect the kidney against cisplatin-induced acute renal failure. Food Chem Toxicol. 2007;45:921–7. [PubMed]

21. Yemitan OK, Izegbu MC. Protective effects of Zingiber officinale (Zingiberaceae) against carbon tetrachloride and acetaminophen-induced hepatotoxicity in rats. Phytother Res. 2006;20:997-–1002. [PubMed]

22. El-Ghorab AH, Nauman M, Anjum FM, Hussain S, Nadeem M. A comparative study on chemical composition and antioxidant activity of Ginger (Zingiber officinale) and Cumin (Cuminum cyminum) J Agric Food Chem. 2010;58:8231–7. [PubMed]

23. Ghasemzadeh A, Jaafar HZ, Rahmat A. Antioxidant activities, total phenolics and flavonoids content in two varieties of Malaysia young Ginger (*Zingiber officinale* Roscoe) Molecules. 2010;15:6231–43. [PubMed]

24. Tjendraputra E, Tran VH, Liu-Brennan D, Roufogalis BD, Duke CC. Effect of ginger constituents and synthetic analogues on cyclooxygenase-2 enzyme in intact cells. Bioorganic Chem. 2001;29:156–63. [PubMed]

25. Verma SK, Singh M, Jain P, Bordia A. Protective effect of ginger, Zingiber officinale Rosc on experimental atherosclerosis in rabbits. Indian J Exp Biol. 2004;42:736–8. [PubMed]

26. Pan MH, Hsieh MC, Kuo JM, Lai CS, Wu H, Sang S, et al. [6]-Shogaol induces apoptosis in human colorectal carcinoma cells via ROS production, caspase activation, and GADD 153 expression.

Mol Nutr Food Res. 2008;52:527–37. [PubMed]

27. Jung HW, Yoon CH, Park KM, Han HS, Park YK. Hexane fraction of Zingiberis Rhizoma Crudus extract inhibits the production of nitric oxide and proinflammatory cytokines in LPS-stimulated BV2 microglial cells via the NF kappaB pathway. Food Chem Toxicol. 2009;47:1190–7. [PubMed]

28. Chen BH, Wu PY, Chen KM, Fu TF, Wang HM, Chen CY. Antiallergic potential on RBL-2H3 cells of some phenolic constituents of Zingiber officinale (Ginger) J Nat Prod. 2009;72:950–3. [PubMed]

29. Habib SH, Makpol S, Abdul Hamid NA, Das S, Ngah WZ, Yusof YA. Ginger extract (*Zingiber officinale*) has anti-cancer and anti-inflammatory effects on ethionine-induced hepatoma rats. Clinics (Sao Paulo) 2008;63:807–13. [PMC free article] [PubMed]

30. Aggarwal BB, Shishodia S. Molecular targets of dietary agents for prevention and therapy of cancer. Biochem Pharmacol. 2006;71:1397–421. [PubMed]

31. Lantz RC, Chen GJ, Sarihan M, Sólyom AM, Jolad SD, Timmermann BN. The effect of extracts from ginger rhizome on inflammatory mediator production. Phytomedicine. 2007;14:123–8. [PubMed]

32. Altman RD, Marcussen KC. Effects of a ginger extract on knee pain in patients with osteoarthritis. Arthritis Rheum. 2001;44:2531–8. [PubMed]

33. Bliddal H, Rosetzsky A, Schlichting P, Weidner MS, Andersen LA, Ibfelt HH, et al. A randomised, placebo controlled, cross-over study of ginger extracts and Ibuprofen in osteoarthritis. J Pain. 2000;8:9–12. [PubMed]

34. Grzanna R, Lindmark L, Frondoza CG. Ginger: An herbal medicinal product with broad anti-inflammatory actions. J Med Food. 2005;8:125–32. [PubMed]

35. Black CD, Herring MP, Hurley DJ, O'Connor PJ. Ginger (Zingiber officinale) reduces muscle pain caused by eccentric exercise. J Pain. 2010;11:894–903. [PubMed]

36. Jeong CH, Bode AM, Pugliese A, Cho YY, Kim HG, Shim JH. [6]gingerol suppresses colon cancer growth by targeting leukotriene a4 hydrolase. Cancer Res. 2009;69:5584–91. [PubMed]

37. Hung JY, Hsu YL, Li CT, Ko YC, Ni WC, Huang MS, et al. [6]-Shogaol, an active constituent of dietary ginger, induces autophagy by inhibiting the AKT/mTOR pathway in human non-small cell lung cancer A549 cells. J Agric Food Chem. 2009;57:9809–16. [PubMed]

38. Ishiguro K, Ando T, Maeda O, Ohmiya N, Niwa Y, Kadomatsu K, et al. Ginger ingredients reduce viability of gastric cancer cells via distinct mechanisms. Biochem Biophys Res Commun. 2007;362:218–23. [PubMed]

39. Sung B, Jhurani S, Ahn KS, Mastuo Y, Yi T, Guha S, et al. Zerumbone down-regulates chemokine receptor CXCR4 expression leading to inhibition of CXCL12-induced invasion of breast and pancreatic tumor cells. Cancer Res. 2008;68:8938–44. [PubMed]

40. Brown AC, Shah C, Liu J, Pham JT, Zhang JG, Jadus MR. Ginger's (*Zingiber officinale Roscoe*) inhibition of rat colonic adenocarcinoma cells proliferation and angiogenesis *in vitro*. Phytother Res. 2009;23:640–5. [PubMed]

41. Kim M, Miyamoto S, Yasui Y, Oyama T, Murakami A, Tanaka T. Zerumbone, a tropical ginger sesquiterpene, inhibits colon and lung carcinogenesis in mice. Int J Cancer. 2009;124:264–71.

[PubMed]

42. Lee HS, Seo EY, Kang NE, Kim WK. [6]-Gingerol inhibits metastasis of MDA-MB-231 human breast cancer cells. J Nutr Biochem. 2008;19:313–9. [PubMed]

43. Sung B, Murakami A, Oyajobi BO, Aggarwal BB. Zerumbone abolishes RANKL-induced NF-kappaB activation, inhibits osteoclastogenesis, and suppresses human breast cancer-induced bone loss in athymic nude mice. Cancer Res. 2009;69:1477–84. [PubMed]

44. Manju V, Nalini N. Chemopreventive efficacy of ginger, a naturally occurring anticarcinogen during the initiation, post-initiation stages of 1,2 dimethylhydrazine-induced colon cancer. Clin Chim Acta. 2005;358:60–7. [PubMed]

45. Yodkeeree S, Sung B, Limtrakul P, Aggarwal BB. Zerumbone enhances TRAIL-induced apoptosis through the induction of death receptors in human colon cancer cells: Evidence for an essential role of reactive oxygen species. Cancer Res. 2009;69:6581–9. [PMC free article] [PubMed]

46. Yagihashi S, Miura Y, Yagasaki K. Inhibitory effect of gingerol on the proliferation and invasion of hepatoma cells in culture. Cytotechnology. 2008;57:129–36. [PMC free article] [PubMed]

47. Kim EC, Min JK, Kim TY, Lee SJ, Yang HO, Han S, et al. [6]-Gingerol, a pungent ingredient of ginger, inhibits angiogenesis *in vitro* and *in vivo*. Biochem Biophys Res Commun. 2005;335:300–8. [PubMed]

48. Nigam N, Bhui K, Prasad S, George J, Shukla Y. [6]-Gingerol induces reactive oxygen species regulated mitochondrial cell death pathway in human epidermoid carcinoma A431 cells. Chem Biol Interact. 2009;181:77–84. [PubMed]

49. Rhode J, Fogoros S, Zick S, Wahl H, Griffith KA, Huang J, et al. Ginger inhibits cell growth and modulates angiogenic factors in ovarian cancer cells. BMC Complement Altern Med. 2007;7:44. [PMC free article] [PubMed]

50. Zhang S, Liu Q, Liu Y, Qiao H, Liu Y. Zerumbone, a Southeast Asian Ginger Sesquiterpene, induced apoptosis of pancreatic carcinoma cells through p53 signaling pathway. Evid Based Complement Alternat Med. 2012;2012:936030. [PMC free article] [PubMed]

51. Shukla Y, Prasad S, Tripathi C, Singh M, George J, Kalra N. *In vitro* and *in vivo* modulation of testosterone mediated alterations in apoptosis related proteins by [6]-gingerol. Mol Nutr Food Res. 2007;51:1492–502. [PubMed]

52. Weidner MS, Sigwart K. The safety of a ginger extract in the rat. J Ethnopharmacol. 2000;73:513–20. [PubMed]

53. Fuhrman B, Rosenblat M, Hayek T, Coleman R, Aviram M. Ginger extract consumption reduces plasma cholesterol, inhibits LDL oxidation and attenuates development of atherosclerosis in atherosclerotic, apolipoprotein E-deficient mice. J Nutr. 2000;130:1124–231. [PubMed]

54. Bhandari U, Kanojia R, Pillai KK. Effect of ethanolic extract of Zingiber officinale on dyslipidaemia in diabetic rats. J Ethnopharmacol. 2005;97:227–30. [PubMed]

55. Nammi S, Sreemantula S, Roufogalis BD. Protective effects of ethanolic extract of Zingiber officinale rhizome on the development of metabolic syndrome in high-fat diet-fed rats. Basic Clin Pharmacol Toxicol. 2009;104:366–73. [PubMed]

56. Heimes K, Feistel B, Verspohl EJ. Impact of the 5-HT receptor channel system for insulin secretion and interaction of ginger extracts. Eur J Pharmacol. 2009;624:58–65. [PubMed]

57. Islam MS, Choi H. Comparative effects of dietary ginger (Zingiber officinale) and garlic (Allium sativum) investigated in a type 2 diabetes model of rats. J Med Food. 2008;11:152–9. [PubMed]

58. Sekiya K, Ohtani A, Kusano S. Enhancement of insulin sensitivity in adipocytes by ginger. Biofactors. 2004;22:153–6. [PubMed]

59. Goyal RK, Kadnur SV. Beneficial effects of Zingiber officinale on goldthioglucose induced obesity. Fitoterapia. 2006;77:160–3. [PubMed]

60. Moin P, Khalighinejad N, Yusefi A, Farajzadegan Z, Barekatain M. Converting three general-cognitive function scales into persian and assessment of their validity and reliability. Int J Prev Med. 2011;2:82–7. [PMC free article] [PubMed]

61. Amiri M. Early life Conditions and trends in mortality at later life: Is there any relationship? Int J Prev Med. 2011;2:53–5. [PMC free article] [PubMed]
