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Ginger (*Zingiber officinale*) and its Bioactive Components with Protective and Therawpeutic Potential against Cancer

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ABSTRACT

Ginger can be an important complementary medicine for prevention and treatment of different types of cancers, owing to its natural origin, safety, and low cost relative to synthetic cancer drugs. Ginger contains volatile oils, anthocyanins, tannins, phenolic compounds and sesquiterpenes anticancer effects of ginger may arise from the ability to induce changes in a number of cellular processes, including cell division, apoptosis and differentiation. In this study, anticancer activity of ginger extract against various cancer cells both *in vitro* and *in vivo* were investigated. The evidence in this review suggests that ginger and its compounds in diet may lower cancer risk and affect tumor behavior.

INTRODUCTION

There has been a resurgence of whole food-based therapeutics categorized as natural medicines in prevention and treatment of chronic diseases like cancer. Although surgery and chemotherapy have been the most common treatment for cancer, cancer chemoprevention with dietary factors has received attention as the most effective approach. Ginger (*Zingiber officinale*) a key component in traditional herbal medicine, where its potential has been intensely exploited in health benefits. The bioactive components of ginger include volatile oils, anthocyanins, tannins, and pungent phenolic compounds known as gingerols, shogaols, and sesquiterpenes [1-3]. Ginger contains fragrant oil and the main constituents are sesquiterpenoids with (−)-zingiberene. Ginger and its pungent bioactive components, which include gingerols and shogaols, can be used in the prevention and treatment of cancer [4-7].

The health attributes associated with ginger may arise from its pharmacological properties, its anticancer effects may arise from the ability to induce changes in a number of cellular processes, including cell division, apoptosis and differentiation. The main pharmacological actions of active compounds extracted from ginger root reported by *in vitro* and *in vivo* test attributed to its active phytocompounds were: anti-inflammatory, antioxidant, antiemetic, anticancer, anticoagulant, immunomodulatory, antihyperglycemic, hypolipidemic, analgesic, and cardioprotective properties [5]. Evidence that ginger and ginger-derived compounds have inhibitory effects on various cancers is increasingly being reported in the

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scientific literature. The potential mechanisms of action involve the inhibition of proliferation and the induction of apoptosis in cancer [8,9]. 6-gingerol [5-hydroxy-1-(40-hydroxy-30-methoxyphenyl)-3-decanone] is the most abundant compound in fresh ginger and is widely investigated anticancer potential [10,11]. This review reports the anticancer activity of ginger and its compounds which may be associated with the reduction of cell viability and induction of apoptosis in various cancer cells.

Sources and methodology

The search was done in electronic databases of PubMed, Scopus, ScienceDirect, Web of Science and Google Scholar for studies using the key terms: anticancer potential, ginger, gingerol, zingerone, paradols and shogaols. The inclusion was based reported articles on anticancer activity of ginger and its compounds whose mechanism of action are discussed in detail. All the data were extracted and explained in respective subheadings.

Breast cancer

Breast cancer is the most common type of cancer and the leading cause of cancer-related death in women [12]. Although early detection methods and multimodal approaches for breast cancer treatment have been made, there has been only modest progress in improving clinical outcomes for women with metastases.

Lee, et al. [13] studied the effect of 6-gingerol on adhesion, invasion, and motility activity was assessed by measuring the levels of MMP-2 and -9 in cultured human breast cancer cells. Anticancer effect of 6-gingerol may contribute to the inhibition of metastasis by decreasing the activities and expressions of MMP-2 and MMP-9. Ling, et al. [14] evaluated the effect of shogaols on the viability of MDA-MB-231 breast cancer cells using the CCK-8 assay. The results demonstrated that sublethal doses of 6-, 8- and 10-shogaol, by reducing MMP-9 expression and secretion, have an inhibitory effect on PMA-induced breast cancer cell invasion. Further, 6-shogaol impairs breast cancer cell invasion, at least in part, through targeting the NF-κB activation cascade.

Human breast cancer cell lines MCF-7 and MDA–MB–231 are considerably more sensitive to growth suppression than the normal mammary line MCF–10A when treated with ginger extracts [15]. Ginger treatment downregulated expression of prosurvival genes, such as NF-κB, Bcl-X, Mcl-1, and Survivin, and cell cycle-regulating proteins, including cyclin D1 and Cyclin-Dependent Kinase-4 (CDK-4). On the other hand, it increased expression of CDK inhibitor, p21. It also inhibited the expression of the two prominent molecular targets of cancer, c-Myc and the human Telomerase Reverse Transcriptase (hTERT).

Joo, et al. [16] investigated the regulatory effects and signaling pathways of 10-gingerol on cell proliferation and invasion in MDA-MB-231 breast cancer cells. 10-gingerol treatment inhibited cell proliferation through downregulation of cell cycle regulatory proteins such as cyclin-dependent kinases and cyclins, and subsequent induction of G1 phase arrest. In addition, 10-gingerol treatment blocked cell invasion in response to mitogenic stimulation. These antitumor activities of 10-gingerol were mediated through inactivation of Akt and p38MAPK activity, and suppression of epidermal growth factor receptor expression.

Bernard, et al. [17] compared 10-gingerol with 8-gingerol and 6-gingerol in terms of their ability to inhibit the growth of human and mouse mammary carcinoma cells. The inhibitory effect of 10-gingerol on the growth of MDA-MB-231 cells was associated with a reduction in the number of rounds of cell division and evidence of S phase-cell cycle arrest, as well as induction of apoptosis due to mitochondrial outer membrane permeabilization and the release of apoptogenic molecules.

Liver cancer

Kaewtunjai, et al. [18] found that *Zingiber officinale* extract induced telomere shortening and cellular senescence in A549 cells. The results suggest that these paradols and shogaols are likely the active compounds in zinger extract that suppress hTERT expression and telomerase activity in these cells. Likewise, Yusof, et al. [19] investigated the effect of ginger in ethionine induced rat hepatocarcinogenesis. It was found that ginger supplementation suppressed liver carcinogenesis by scavenging the free radical formation, and by reducing lipid peroxidation. Ginger polysaccharide could promote apoptosis and arrest cells in G0-G1 phase of hepatocellular carcinoma HepG2 cells. Real-time fluorescence quantification and Western blot revealed that GP could up-regulate the expression of Bax, Fas, FasL, caspase-3, p21 and p53, and down-regulate the expression of Bcl-2 [20].

Habib, et al. [21] tested the potential anti-inflammatory and anti-cancer effects of ginger extract by using an immunohistochemistry technique to detect the presence of the inflammatory marker TNF-α and the transcription factor NFκB. Ginger extract significantly reduced the elevated expression of NFκB and TNF-α in rats with liver cancer. Ginger may act as an anti-cancer and anti-inflammatory agent by inactivating NFκB through the suppression of the pro-inflammatory TNF-α. Weng, et al. [22] evaluated the anti-invasion activity of 6-shogaol and 6-gingerol, two compounds found in ginger, on hepatoma cells. The migratory and invasive abilities of Phorbol 12-Myristate 13-Acetate (PMA)-treated HepG2 and PMA-untreated Hep3B cells were both reduced in a dose-dependent manner by treatment with 6-shogaol and 6-gingerol. Upon incubation of PMA-treated HepG2 cells and PMA-untreated Hep3B cells with 6-shogaol and 6-gingerol, Matrix

Metalloproteinase (MMP)-9 activity decreased, whereas the expression of Tissue Inhibitor Metalloproteinase Protein (TIMP)-1 increased in both cell types. Further, 6-Shogaol and 6-gingerol effectively inhibit invasion and metastasis of hepatocellular carcinoma through diverse molecular mechanisms, including inhibition of the MAPK and PI3k/Akt pathways and NF-κB and STAT3 activities to suppress expression of MMP-2/-9 and uPA and block angiogenesis [23].

Cervical cancer

6-gingerol was found to reduce the viability of HeLa (human cervical carcinoma) cells as shown by morphological changes in cells. HeLa cells treated with 6-gingerol showed altered nuclear and cellular morphology, cell shrinkage, and membrane blebbing, which are characteristics of apoptotic cell death. Additionally, an increase in chromatin condensation and fragmentation of HeLa cells was observed with increased dose of 6-gingerol during treatment [24]. A study involving 6-gingerol extracted from Tongling White Ginger led to several morphological changes with increased dose and longer treatment and resulted in cell cycle arrest in G0/G1-phase [25]. The mRNA and protein expression significantly decreased in cyclin A, cyclin D1 and cyclin E, while, there was slight decrease in CDK-1, p21 and p27 and cyclin B1 and E1 protein remain unchanged. Likewise, 10-gingerol inhibited the proliferation of HeLa cells at IC_{50} (29.19 μM) and IC_{80} (50.87 μM) with altered cell morphology, increased cytotoxicity, and arrested cell cycle in the G0/G1 phase. Most cell cycle related genes and protein expression significantly decreased, followed by a slight decrease in a few without affecting cyclin B1 and cyclin E1 (protein). Both death receptors significantly up-regulated and activated apoptosis indicators (caspase family). Furthermore, significant changes in mitochondria-dependent pathway markers were observed and led to cell death. 10-gingerol led to PI3K/AKT inhibition and AMPK activation to induce mTOR-mediated cell apoptosis in HeLa cells [26].

Rastogi, et al. [27] explored the molecular mechanism of action of 6-gingerol in human cervical cancer cells *in vitro* and *in vivo*. 6-gingerol potently inhibited proliferation of the HPV positive cervical cancer cells. 6-gingerol was found to inhibit the chymotrypsin activity of proteasomes; induce reactivation of p53; increase levels of p21; induce DNA damage and G2/M cell cycle arrest and alter expression levels of p53-associated apoptotic markers like, cleaved caspase-3 and PARP. Ansari, et al. [28] demonstrated that ZOME inhibited the proliferation and colony formation in HeLa cells in a dose- and time-dependent manner and induced typical changes in nuclear morphology, chromatin condensation and fragmentation, membrane shrinkage and blebbing in both cells indicated apoptotic property of *Z. officinale*.

Colon cancer

The anticancer effects of 6-gingerol on human colon cancer cell (LoVo) was studied by Lin, et al. [29]. Results showed that 6-gingerol significantly induces cell cycle arrest at the G2/M phase; has little influence on the sub–G1 phase; and decreases the levels of cyclin A, cyclin B1, and CDK1. However, treatment with 6-gingerol increased levels of negative cell cycle regulators p27Kip1 and p21Cip1 and enhanced ROS levels and phosphorylation of p53. These results highlight the importance of 6-gingerol in the treatment of colon cancer.

The effects of zingerone on suppressing cell proliferation and enhancing apoptosis in colon cancer cells (HCT116) was explored by Su, et al. [30]. The results indicated that zingerone significantly enhances the production of reactive oxygen species, lipid peroxidation (Thiobarbituric Acid Reactive Substance [TBARS]), and loss of cell viability; and reduces mitochondrial membrane potential and antioxidant levels (SOD, CAT, and GSH) in ZO-treated HCT116 cells in a dose-dependent (2.5, 5, and 10 μM) manner. Abdullah, et al. [31] reported G0/G1 arrest and apoptosis induced by ginger extract in case of HCT 116 and HT 29 colon cancer cell lines. Chemopreventive efficacy of ginger extract was also described against hepatoma HepG2 and HLE cell lines [32].

Qi, et al. [33] observed that 6-shogaol (15 mg/kg) significantly inhibited colorectal tumor growth in a xenograft mouse model. 6-shogaol inhibited HCT-116 and SW-480 cell proliferation with IC50 of 7.5 and 10 μM, respectively. Growth of HCT-116 cells was arrested at the G2/M phase of the cell cycle, primarily mediated by the up-regulation of p53, the CDK inhibitor p21(waf1/cip1) and GADD45α, and by the down-regulation of cdc2 and cdc25A.

Colorectal cancer

Treatment of human HCT116 (colorectal) cancer cells with EG caused morphological and biochemical characteristics of apoptotic cell death. Induction of apoptosis was associated with mitochondrial cytochrome c release, increased Bax:Bcl2 ratio, activation of caspase–3 and –9, and PARP cleavage. Furthermore, EG (a) decreased the expression levels of antiapoptotic proteins including Bcl2, BclX, Mcl–1, survivin, and XIAP; (b) elevated expression levels of the onco-suppressive proteins, p53, p21, and p27; (c) reduced the expression of cyclin D1 and cyclin/Cdk–4; and (d) decreased expression of c–Myc [34].

Exposure of ginger leaf extract to human colorectal cancer cells (HCT116, SW480 and LoVo cells) reduced the cell viability and induced apoptosis in a dose-dependent manner. In addition, ginger leaf reduced cell viability in MCF-7, MDA-MB-231 and HepG-2 cells. Ginger leaf increased Activating Transcription Factor 3 (ATF3) expressions in both protein and mRNA level and activated ATF3 promoter activity, indicating transcriptional activation of ATF3 gene [35].

Endometrial cancer

Treatment of the endometrial cancer cells with the steam distilled extract of ginger results in significant increase in intracellular calcium, decrease in the mitochondrial membrane potential, increase in the expression of caspase 3, phosphorylation of P53, and a significant decrease in the expression of Bcl-2 [32]. The data demonstrated that ginger extract treatment results in a rapid increase in the levels of intracellular calcium and in the activation of p53. Furthermore, inhibition of p53 attenuates the ability of ginger extract to induce apoptosis in the endometrial cancer cells.

Melanoma skin cancer

Antiproliferative and proapoptotic activity of ginger extracts in murine melanoma B164A5 cell line was reported by earlier [36]. A possible signaling pathway involved in 6-gingerol mediated depigmentation was investigated by means of specific inhibitors [37]. The results indicated that 6-gingerol has a more potent inhibitory effect on melanin formation in B16F10 melanoma cells than kojic acid does which might lead to the activation of the Akt/protein kinase B pathway. In another study, treatment of B16F10 mouse melanoma cells with 6-shogaol reduced the melanin content in a concentration-dependent manner. It significantly decreased the intracellular tyrosinase activity, and markedly suppressed the expression levels of tyrosinase and MITF proteins in the cells. Huang, et al. [38] investigated the effects of 8-gingerol on mushroom tyrosinase activity, the expression of melanogenesis-related proteins, and melanin content in B16F10 and B16F1 melanoma cells. It was determined that 8-gingerol significantly inhibits tyrosinase activity and decreases melanin synthesis. Moreover, 8-gingerol also expresses intracellular free radical scavenging activity. The results suggest that 8-gingerol decreases melanin production, which may be attributed to its inhibitory action upon the signalling pathway that regulates tyrosinase activity or by the depletion of cellular RS and ROS. Further, the results demonstrated that 8-gingerol decreases melanogenesis in melanoma cells by inactivating PKA and MAPK signalling pathways, reducing MITF expression and inhibiting tyrosinase activity.

Cojocaru, et al. [39] investigated the cytotoxicity of a fresh ginger extract on skin tumor cells and the amelanotic melanoma cells displayed profound changes in cell morphology such as cell shrinkage, rounding-up and membrane blebbing and a decrease in cell viability in a dose-dependent manner. Furthermore, 6-shogaol (10 μmol/L) activated ERK, which was known to negatively regulate melanin synthesis in mouse melanoma cells [40].

Pancreatic cancer

Park, et al. [41] investigated the action of 6-gingerol on two human pancreatic cancer cell lines. The experiments described that 6-gingerol induces apoptotic cell death in p53-mutant cancer cells. The death mechanism was characterized, revealing that 6-gingerol not only initiated cell cycle arrest but ultimately caused cell death through apoptosis. Thus, 6-gingerol, is capable of killing cancer cells expressing mutant p53, overcoming the phenotypic resistance to chemotherapy- and irradiation-induced cell death. Further, 6-gingerol regulates TJ-related proteins and suppresses invasion and metastasis through NF-κ B/Snail inhibition via inhibition of the ERK pathway thus suppress the invasive activity of PANC-1 cells [42].

Zerumbone, a component of subtropical ginger against angiogenesis in pancreatic cancer [43]. Zerumbone blocked the pancreatic cancer associated angiogenesis through the inhibition of NF-κB and NF-κB-dependent proangiogenic gene products. Further, zerumbone induced apoptosis in pancreatic carcinoma cells through p53 signal pathway [44].

Akimoto, et al. [45] examined the anticancer activity of ginger extract against pancreatic cancer cells both *in vitro* and *in vivo* and investigated its potential mechanism. They reported that ginger extract leads to the reduction of cell viability and tumor growth of Panc-1 cells mainly through ROS-mediated autosis. Zhou, et al. [46] investigated whether 6-shogaol could suppress pancreatic cancer progress. 6-shogaol inhibited TLR4 signalling resulting in a reduced activation of NF-κB, which led to a delayed growth of pancreatic cancer. Moreover, pre-treatment with 6-shogaol resulted in an inhibition of constitutive and gemcitabine-induced NF-κB activity.

Prostate cancer

Karna, et al. [47] showed that ginger extracts exhibits substantial growth-inhibitory effect and induced death in a panel of prostate cancer cells. Additionally, the extract reduced cell cycle progression, decreased the capacity to reproduce, and initiated a caspase-driven, mitochondrially mediated apoptosis. IN another study, treatment of androgen-dependent and -independent human prostate cancer cells in culture with 6-Shogaol inhibits survival and induces apoptosis [48]. These effects of 6-Shogaol were associated with inhibition of both STAT3 and NF-κB signalling and possibly other signalling pathways.

CONCLUSION

Cancers are not an inevitable consequence of aging and changing lifestyle but are preventable diseases. Ginger can be an important complementary medicine for prevention and treatment of different types of cancers, owing to its natural origin, safety, and low cost relative to synthetic cancer drugs. The evidence in this review suggests that ginger and its compounds in diet may lower cancer risk and affect tumor behavior. Thus, ginger alone or in combination with other chemotherapeutic drugs could be an alternative drug in treating different cancers.

References

1. Semwal RB, Semwal DK, Combrinck S, Viljoen AM. Gingerols and shogaols: Important nutraceutical principles from ginger. Phytochemistry. 2015 Sep;117:554-568. doi: 10.1016/j.phytochem.2015.07.012. Epub 2015 Jul 27. PMID: 26228533.

2. Langner E, Greifenberg S, Gruenwald J. Ginger: history and use. Adv Ther. 1998 Jan-Feb;15(1):25-44. PMID: 10178636.

3. Ault A. On food and cooking. The science and lore of the kitchen by Harold McGee. Scribner, New York. 2003; pp. 425-426

4. Wilson R, Haniadka R, Sandhya P, Palatty PL, Baliga MS. Ginger (*Zingiber officinale* Roscoe) the dietary agent in skin care: A Review. In bioactive dietary factors and plant extracts in dermatology. Edited by: Watson RR, Zibadi S. Karnataska: Humana Press. 2013: 103-111.

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 Feb;46(2):409-20. doi: 10.1016/j.fct.2007.09.085. Epub 2007 Sep 18. PMID: 17950516.

6. Wang B, Sun J, Ma Y, Wu G, Tian Y, Shi Y, Le G. Resveratrol preserves mitochondrial function, stimulates mitochondrial biogenesis, and attenuates oxidative stress in regulatory T cells of mice fed a high-fat diet. J Food Sci. 2014 Sep;79(9):H1823-31. doi: 10.1111/1750-3841.12555. Epub 2014 Aug 23. PMID: 25156660.

7. Wang S, Sun X, Jiang L, Liu X, Chen M, Yao X, Sun Q, Yang G. 6-Gingerol induces autophagy to protect HUVECs survival from apoptosis. Chem Biol Interact. 2016 Aug 25;256:249-56. doi: 10.1016/j.cbi.2016.07.020. Epub 2016 Jul 20. PMID: 27451028.

8. Liu CM, Kao CL, Tseng YT, Lo YC, Chen CY. Ginger Phytochemicals Inhibit Cell Growth and Modulate Drug Resistance Factors in Docetaxel Resistant Prostate Cancer Cell. Molecules. 2017 Sep 5;22(9):1477. doi: 10.3390/molecules22091477. PMID: 28872603; PMCID: PMC6151784.

9. Tahir AA, Sani NF, Murad NA, Makpol S, Ngah WZ, Yusof YA. Combined ginger extract & Gelam honey modulate Ras/ERK and PI3K/AKT pathway genes in colon cancer HT29 cells. Nutr J. 2015 Apr 1;14:31. doi: 10.1186/s12937-015-0015-2. PMID: 25889965; PMCID: PMC4390091.

10. Lee SH, Cekanova M, Baek SJ. Multiple mechanisms are involved in 6-gingerol-induced cell growth arrest and apoptosis in human colorectal cancer cells. Mol Carcinog. 2008 Mar;47(3):197-208. doi: 10.1002/mc.20374. PMID: 18058799; PMCID: PMC2430145.

11. Poltronieri J, Becceneri AB, Fuzer AM, Filho JC, Martin AC, Vieira PC, Pouliot N, Cominetti MR. [6]-gingerol as a cancer chemopreventive agent: a review of its activity on different steps of the metastatic process. Mini Rev Med Chem. 2014 Apr;14(4):313-21. doi: 10.2174/1389557514666140219095510. PMID: 24552266.

12. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin. 2015 Mar;65(2):87-108. doi: 10.3322/caac.21262. Epub 2015 Feb 4. PMID: 25651787.

13. Lee HS, Seo EY, Kang NE, Kim WK. [6]-Gingerol inhibits metastasis of MDA-MB-231 human breast cancer cells. J Nutr Biochem. 2008 May;19(5):313-9. doi: 10.1016/j.jnutbio.2007.05.008. Epub 2007 Aug 1. PMID: 17683926.

14. Ling H, Yang H, Tan SH, Chui WK, Chew EH. 6-Shogaol, an active constituent of ginger, inhibits breast cancer cell invasion by reducing matrix metalloproteinase-9 expression via blockade of nuclear factor-κB activation. Br J Pharmacol. 2010 Dec;161(8):1763-77. doi: 10.1111/j.1476-5381.2010.00991.x. PMID: 20718733; PMCID: PMC3010581.

15. Elkady AI, Abuzinadah OA, Baeshen NA, Rahmy TR. Differential control of growth, apoptotic activity, and gene expression in human breast cancer cells by extracts derived from medicinal herbs Zingiber officinale. J Biomed Biotechnol. 2012;2012:614356. doi: 10.1155/2012/614356. Epub 2012 Aug 26. PMID: 22969274; PMCID: PMC3433172.

16. Joo JH, Hong SS, Cho YR, Seo DW. 10-Gingerol inhibits proliferation and invasion of MDA-MB-231 breast cancer cells through suppression of Akt and p38MAPK activity. Oncol Rep. 2016 Feb;35(2):779-84. doi: 10.3892/or.2015.4405. Epub 2015 Nov 9. PMID: 26554741.

17. Bernard MM, McConnery JR, Hoskin DW. [10]-Gingerol, a major phenolic constituent of ginger root, induces cell cycle arrest and apoptosis in triple-negative breast cancer cells. Exp Mol Pathol. 2017 Apr;102(2):370-376. doi: 10.1016/j.yexmp.2017.03.006. Epub 2017 Mar 16. PMID: 28315687.

18. Kaewtunjai N, Wongpoomchai R, Imsumran A, Pompimon W, Athipornchai A, Suksamrarn A, Lee TR, Tuntiwechapikul W. Ginger Extract Promotes Telomere Shortening and Cellular Senescence in A549 Lung Cancer Cells. ACS Omega. 2018 Dec 27;3(12):18572-18581. doi: 10.1021/acsomega.8b02853. PMID: 32010796; PMCID: PMC6988994.

19. Yusof YA, Ahmad N, Das S, Sulaiman S, Murad NA. Chemopreventive efficacy of ginger (*Zingiber officinale*) in ethionine induced rat hepatocarcinogenesis. Afr J Tradit Complement Altern Med. 2008 Oct 25;6(1):87-93. doi: 10.4314/ajtcam.v6i1.57078. PMID: 20162046; PMCID: PMC2816532.

20. Wang Y, Wang S, Song R, Cai J, Xu J, Tang X, Li N. Ginger polysaccharides induced cell cycle arrest and apoptosis in human hepatocellular carcinoma HepG2 cells. Int J Biol Macromol. 2019 Feb 15;123:81-90. doi: 10.1016/j.ijbiomac.2018.10.169. Epub 2018 Nov 8. PMID: 30414900.

21. 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 Dec;63(6):807-13. doi: 10.1590/s1807-59322008000600017. PMID: 19061005; PMCID: PMC2664283.

22. Weng CJ, Wu CF, Huang HW, Ho CT, Yen GC. Anti-invasion effects of 6-shogaol and 6-gingerol, two active components in ginger, on human hepatocarcinoma cells. Mol Nutr Food Res. 2010 Nov;54(11):1618-27. doi: 10.1002/mnfr.201000108. PMID: 20521273.

23. Weng CJ, Chou CP, Ho CT, Yen GC. Molecular mechanism inhibiting human hepatocarcinoma cell invasion by 6-shogaol and 6-gingerol. Mol Nutr Food Res. 2012 Aug;56(8):1304-14. doi: 10.1002/mnfr.201200173. Epub 2012 Jun 20. PMID: 22714996.

24. Chakraborty D, Bishayee K, Ghosh S, Biswas R, Mandal SK, Khuda-Bukhsh AR. [6]-Gingerol induces caspase 3 dependent apoptosis and autophagy in cancer cells: drug-DNA interaction and expression of certain signal genes in HeLa cells. Eur J Pharmacol. 2012 Nov 5;694(1-3):20-9. doi: 10.1016/j.ejphar.2012.08.001. Epub 2012 Aug 24. PMID: 22939973.

25. Zhang F, Zhang JG, Qu J, Zhang Q, Prasad C, Wei ZJ. Assessment of anti-cancerous potential of 6-gingerol (Tongling White Ginger) and its synergy with drugs on human cervical adenocarcinoma cells. Food Chem Toxicol. 2017 Nov;109(Pt 2):910-922. doi: 10.1016/j.fct.2017.02.038. Epub 2017 Feb 27. PMID: 28249781.

26. Zhang F, Thakur K, Hu F, Zhang JG, Wei ZJ. 10-Gingerol, a Phytochemical Derivative from "Tongling White Ginger", Inhibits Cervical Cancer: Insights into the Molecular Mechanism and Inhibitory Targets. J Agric Food Chem. 2017 Mar 15;65(10):2089-2099. doi: 10.1021/acs.jafc.7b00095. Epub 2017 Mar 1. PMID: 28230361.

27. Rastogi N, Duggal S, Singh SK, Porwal K, Srivastava VK, Maurya R, Bhatt ML, Mishra DP. Proteasome inhibition mediates p53 reactivation and anti-cancer activity of 6-gingerol in cervical cancer cells. Oncotarget. 2015 Dec 22;6(41):43310-25. doi: 10.18632/oncotarget.6383. PMID: 26621832; PMCID: PMC4791234.

28. Ansari JA, Ahmad MK, Khan AR, Fatima N, Khan HJ, Rastogi N, Mishra DP, Mahdi AA. Anticancer and Antioxidant activity of *Zingiber officinale* Roscoe rhizome. Indian J Exp Biol. 2016 Nov;54(11):767-773. PMID: 30179422.

29. Lin CB, Lin CC, Tsay GJ. 6-Gingerol Inhibits Growth of Colon Cancer Cell LoVo via Induction of G2/M Arrest. Evid Based Complement Alternat Med. 2012;2012:326096. doi: 10.1155/2012/326096. Epub 2012 Jun 7. PMID: 22719783; PMCID: PMC3375166.

30. Su P, Veeraraghavan VP, Krishna Mohan S, Lu W. A ginger derivative, zingerone-a phenolic compound-induces ROS-mediated apoptosis in colon cancer cells (HCT-116). J Biochem Mol Toxicol. 2019 Dec;33(12):e22403. doi: 10.1002/jbt.22403. Epub 2019 Nov 12. PMID: 31714660.

31. Abdullah S, Abidin SAZ, Murad NA, Makpol S, Ngah WZW, Yusof YAM. Ginger extract (*Zingiber offi cinale*) triggers apoptosis and G0/G1 cells arrest in HCT 116 and HT 29 colon cancer cell lines. Afr J Biochem Res. 2010; 4: 134-142. https://rb.gy/3ipnnc

32. Liu Y, Whelan RJ, Pattnaik BR, Ludwig K, Subudhi E, Rowland H, Claussen N, Zucker N, Uppal S, Kushner DM, Felder M, Patankar MS, Kapur A. Terpenoids from Zingiber officinale (Ginger) induce apoptosis in endometrial cancer cells through the activation of p53. PLoS One. 2012;7(12):e53178. doi: 10.1371/journal.pone.0053178. Epub 2012 Dec 31. PMID: 23300887; PMCID: PMC3534047.

33. Qi LW, Zhang Z, Zhang CF, Anderson S, Liu Q, Yuan CS, Wang CZ. Anti-Colon Cancer Effects of 6-Shogaol Through G2/M Cell Cycle Arrest by p53/p21-cdc2/cdc25A Crosstalk. Am J Chin Med. 2015;43(4):743-56. doi: 10.1142/S0192415X15500469. Epub 2015 Jun 28. PMID: 26119958.

34. Elkady AI, Hussein RA, Abu-Zinadah OA. Effects of crude extracts from medicinal herbs Rhazya stricta and Zingiber officinale on growth and proliferation of human brain cancer cell line in vitro. Biomed Res Int. 2014;2014:260210. doi: 10.1155/2014/260210. Epub 2014 Jul 22. PMID: 25136570; PMCID: PMC4130191.

35. Park GH, Park JH, Song HM, Eo HJ, Kim MK, Lee JW, Lee MH, Cho KH, Lee JR, Cho HJ, Jeong JB. Anti-cancer activity of Ginger (Zingiber officinale) leaf through the expression of activating transcription factor 3 in human colorectal cancer cells. BMC Complement Altern Med. 2014 Oct 23;14:408. doi: 10.1186/1472-6882-14-408. PMID: 25338635; PMCID: PMC4210498.

36. Danciu C, Vlaia L, Fetea F, Hancianu M, Coricovac DE, Ciurlea SA, Şoica CM, Marincu I, Vlaia V, Dehelean CA, Trandafirescu C. Evaluation of phenolic profile, antioxidant and anticancer potential of two main representants of Zingiberaceae family against B164A5 murine melanoma cells. Biol Res. 2015 Jan 12;48(1):1. doi: 10.1186/0717-6287-48-1. PMID: 25654588; PMCID: PMC4417255.

37. Huang HC, Chiu SH, Chang TM. Inhibitory effect of [6]-gingerol on melanogenesis in B16F10 melanoma cells and a possible mechanism of action. Biosci Biotechnol Biochem. 2011;75(6):1067-72. doi: 10.1271/bbb.100851. Epub 2011 Jun 13. PMID: 21670536.

38. Huang HC, Chou YC, Wu CY, Chang TM. [8]-Gingerol inhibits melanogenesis in murine melanoma cells through down-regulation of the MAPK and PKA signal pathways. Biochem Biophys Res Commun. 2013 Aug 23;438(2):375-81. doi: 10.1016/j.bbrc.2013.07.079. Epub 2013 Jul 25. PMID: 23892040.

39. Cojocaru SI, Stan M, Stoian G, Dinischiotu A. EFFECTS OF ZINGIBER OFFICINALE ROSCOE FRESH EXTRACT ON AMELANOTIC MELANOMA AND NORMAL SKIN FIBROBLASTS. Rev Med Chir Soc Med Nat Iasi. 2015 Apr-Jun;119(2):592-6. PMID: 26204672.

40. Yao C, Oh JH, Oh IG, Park CH, Chung JH. [6]-Shogaol inhibits melanogenesis in B16 mouse melanoma cells through activation of the ERK pathway. Acta Pharmacol Sin. 2013 Feb;34(2):289-94. doi: 10.1038/aps.2012.134. Epub 2012 Nov 5. PMID: 23123645; PMCID: PMC4011614.

41. Park YJ, Wen J, Bang S, Park SW, Song SY. [6]-Gingerol induces cell cycle arrest and cell death of mutant p53-expressing pancreatic cancer cells. Yonsei Med J. 2006 Oct 31;47(5):688-97. doi: 10.3349/ymj.2006.47.5.688. PMID: 17066513; PMCID: PMC2687755.

42. Kim SO, Kim MR. [6]-Gingerol Prevents Disassembly of Cell Junctions and Activities of MMPs in Invasive Human Pancreas Cancer Cells through ERK/NF- κ B/Snail Signal Transduction Pathway. Evid Based Complement Alternat Med. 2013;2013:761852. doi: 10.1155/2013/761852. Epub 2013 Sep 24. PMID: 24204396; PMCID: PMC3800596.

43. Shamoto T, Matsuo Y, Shibata T, Tsuboi K, Nagasaki T, Takahashi H, Funahashi H, Okada Y, Takeyama H. Zerumbone inhibits angiogenesis by blocking NF-κB activity in pancreatic cancer. Pancreas. 2014 Apr;43(3):396-404. doi: 10.1097/MPA.0000000000000039. PMID: 24622069.

44. 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. doi: 10.1155/2012/936030. Epub 2012 Jan 29. PMID: 22454691; PMCID: PMC3290912.

45. Akimoto M, Iizuka M, Kanematsu R, Yoshida M, Takenaga K. Anticancer Effect of Ginger Extract against Pancreatic Cancer Cells Mainly through Reactive Oxygen Species-Mediated Autotic Cell Death. PLoS One. 2015 May 11;10(5):e0126605. doi: 10.1371/journal.pone.0126605. PMID: 25961833; PMCID: PMC4427290.

46. Zhou L, Qi L, Jiang L, Zhou P, Ma J, Xu X, Li P. Antitumor activity of gemcitabine can be potentiated in pancreatic cancer through modulation of TLR4/NF-κB signaling by 6-shogaol. AAPS J. 2014 Mar;16(2):246-57. doi: 10.1208/s12248-013-9558-3. Epub 2014 Jan 15. PMID: 24424498; PMCID: PMC3933586.

47. Karna P, Chagani S, Gundala SR, Rida PC, Asif G, Sharma V, Gupta MV, Aneja R. Benefits of whole ginger extract in prostate cancer. Br J Nutr. 2012 Feb;107(4):473-84. doi: 10.1017/S0007114511003308. Epub 2011 Aug 18. PMID: 21849094; PMCID: PMC3426621.

48. Saha A, Blando J, Silver E, Beltran L, Sessler J, DiGiovanni J. 6-Shogaol from dried ginger inhibits growth of prostate cancer cells both in vitro and in vivo through inhibition of STAT3 and NF-κB signaling. Cancer Prev Res (Phila). 2014 Jun;7(6):627-38. doi: 10.1158/1940-6207.CAPR-13-0420. Epub 2014 Apr 1. PMID: 24691500.

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