



[rexresearch.com](http://rexresearch.com)

---

## Ginger vs Cancer

---

<http://www.healthnutnews.com/new-study-shows-ginger-is-10000x-stronger-than-chemo-and-only-kills-cancer-cells>

2 November 2015

[ Excerpts ]

**NEW STUDY SHOWS GINGER IS 10,000X STRONGER THAN CHEMO (AND ONLY KILLS CANCER CELLS)**

by

**Erin Elizabeth**

[ A study conducted by Georgia State University found that 6-Shogaol ( extract of ginger ) reduced mouse prostate tumor size by 56%... Another study showed it to be superior to chemotherapy against breast cancer stem cells, at concentrations that are non-toxic to normal cells. 6-shogaol increases apoptosis -- cancer cell death -- by inducing of autophagy, and it inhibits the formaton of breast cancer lumps... The cancer drug taxol is not nearly as effective as 6-shogaol, which is 10,000 times more effective at killing cancer stem cells, inhibits tumor formation, and prevents the formation of tumors. ]

---

<http://www.Wikipedia.org/>

### Shogaol

Names

IUPAC name : (E)-1-(4-Hydroxy-3- methoxyphenyl)dec-4-en-3-one

Other names :

(6)-Shogaol

Identifiers

CAS Registry Number : 555-66-8 Yes

ChEMBL ChEMBL25948

ChemSpider : 4445106

PubChem : 5281794

UNII : 83DNB5FIRF

Chemical formula : C<sub>17</sub>H<sub>24</sub>O<sub>3</sub>

Molar mass : 276.38 g·mol<sup>-1</sup>

Except where otherwise noted, data are given for materials in their standard state (at 25 °C

[77 °F], 100 kPa).  
Hottest-chili-rating  
Heat (SR: 160,000)

Shogaol, also known as (6)-shogaol, is a pungent constituent of ginger similar in chemical structure to gingerol. Like zingerone, it is produced when ginger is dried or cooked.[1]

Shogaols are artifacts formed during storage or through excess heat, probably created by a dehydration reaction of the gingerols. The ratio of shogaols to gingerols sometimes is taken as an indication of product quality.[2]

The name 'shogaol' is derived from the Japanese name for ginger (生姜、shōga).

Shogaol is rated 160,000 SHU on Scoville scale. When compared to other pungent compounds, shogaol is moderately more pungent than piperine, but less than capsaicin.

Compound	Scoville Heat Units (SHU)
Capsaicin	15,000,000[3]
(6)-Shogaol	160,000
Piperine	100,000
(6)-Gingerol	60,000

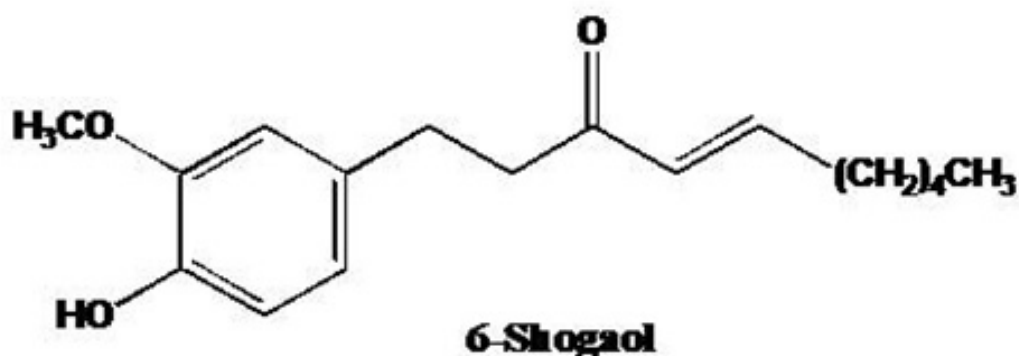
## Pharmacology

Among ginger constituents, it has a very strong antitussive (anti-cough) effect.[medical citation needed] Both shogaol and gingerols reduced blood pressure and gastric contraction.[4] Shogaol has been shown to induce apoptosis (kill) in human colorectal carcinoma cells via reactive oxygen species.[5] It is broken down into 16 metabolites via the mercapturic acid pathway.[4] Acetylcysteine was found to reduce effectiveness of shogaol's apoptotic properties.[5]

## References

- Harold McGee (2004). *On Food and Cooking: The Science and Lore of the Kitchen* (2nd ed.). New York: Scribner. pp. 425–426.
- NSF International Determination of Gingerols and Shogaols in *Zingiber officinale* rhizome and powdered extract by High-Performance Liquid Chromatography[full citation needed]
- Ula (1996). "The HPLC measures the capsaicinoid(s) in ppm, which can then be converted to Scoville units using a conversion factor of 15, 20 or 30 depending on the capsaicinoid." Missing or empty |title= (help)[full citation needed] This would make capsaicin 15,000,000 SHU.
- Suekawa, M; Ishige, A; Yuasa, K; Sudo, K; Aburada, M; Hosoya, E (1984). "Pharmacological studies on ginger. I. Pharmacological actions of pungent constituents, (6)-gingerol and (6)-shogaol". *Journal of pharmacobio-dynamics* 7 (11): 836–48. PMID 6335723.
- Pan, Min-Hsiung; Hsieh, Min-Chi; Kuo, Jen-Min; Lai, Ching-Shu; Wu, Hou; Sang, Shengmin; Ho, Chi-Tang (2008). "6-Shogaol induces apoptosis in human colorectal carcinoma cells via ROS production, caspase activation, and GADD 153 expression". *Molecular Nutrition & Food Research* 52 (5): 527. doi:10.1002/mnfr.200700157.
-

## 6-Shogaol



A bioactive ingredient of ginger root (*Zingiber officinale*), a medicinal plant having anti-nausea, anti-inflammatory, and anti-carcinogenic properties and a carminative effect

Catalog No: APH-02034

CAS Number: 555-66-8

Chemical Formula: C<sub>17</sub>H<sub>24</sub>O<sub>3</sub>

Molecular Weight: 276.37

Purity: > 95% determined by HPLC

Appearance: Viscous yellow liquid

Solubility: Soluble in methanol and ethanol

Stability: Unstable at room temperature in the presence of oxygen and light. Stable over extended period at -20°C.

Storage: -20°C

Shipping: On ice (5°C)

Handling: Avoid exposure to oxygen and direct sunlight.

---

**Br J Pharmacol. 2010 Dec; 161(8): 1763–1777.**

**doi: 10.1111/j.1476-5381.2010.00991.x**

**PMCID: PMC3010581**

### **6-Shogaol, an active constituent of ginger, inhibits breast cancer cell invasion... KEY RESULTS**

Shogaols (6-, 8- and 10-shogaol) inhibited PMA-stimulated MDA-MB-231 cell invasion with an accompanying decrease in MMP-9 secretion. 6-Shogaol was identified to display the greatest anti-invasive effect in association with a dose-dependent reduction in MMP-9 gene activation, protein expression and secretion. The NF-κB transcriptional activity was decreased by 6-shogaol; an effect mediated by inhibition of IκB phosphorylation and degradation that subsequently led to suppression of NF-κB p65 phosphorylation and nuclear translocation. In addition, 6-shogaol was found to inhibit JNK activation with no resulting reduction in activator protein-1 transcriptional activity. By using specific inhibitors, it was demonstrated that ERK and NF-κB signalling, but not JNK and p38 signalling, were involved

in PMA-stimulated MMP-9 activation.

## **CONCLUSIONS AND IMPLICATIONS**

6-Shogaol is a potent inhibitor of MDA-MB-231 cell invasion, and the molecular mechanism involves at least in part the down-regulation of MMP-9 transcription by targeting the NF- $\kappa$ B activation cascade. This class of naturally occurring small molecules thus have potential for clinical use as antimetastatic treatments.

---

<http://www.ncbi.nlm.nih.gov/pubmed/17950516>

**Food Chem Toxicol.** 2008 Feb;46(2):409-20. Epub 2007 Sep 18.

**Some phytochemical, pharmacological and toxicological properties of ginger (*Zingiber officinale* Roscoe): a review of recent research.**

**Ali BH, Blunden G, Tanira MO, Nemmar A.**

### **Abstract**

Ginger (*Zingiber officinale* Roscoe, Zingiberaceae) is a medicinal plant that has been widely used in Chinese, Ayurvedic and Tibb-Unani herbal medicines all over the world, since antiquity, for a wide array of unrelated ailments that include arthritis, rheumatism, sprains, muscular aches, pains, sore throats, cramps, constipation, indigestion, vomiting, hypertension, dementia, fever, infectious diseases and helminthiasis. Currently, there is a renewed interest in ginger, and several scientific investigations aimed at isolation and identification of active constituents of ginger, scientific verification of its pharmacological actions and of its constituents, and verification of the basis of the use of ginger in some of several diseases and conditions. This article aims at reviewing the most salient recent reports on these investigations. The main pharmacological actions of ginger and compounds isolated therefrom include immuno-modulatory, anti-tumorigenic, anti-inflammatory, anti-apoptotic, anti-hyperglycemic, anti-lipidemic and anti-emetic actions. Ginger is a strong anti-oxidant substance and may either mitigate or prevent generation of free radicals. It is considered a safe herbal medicine with only few and insignificant adverse/side effects. More studies are required in animals and humans on the kinetics of ginger and its constituents and on the effects of their consumption over a long period of time.

---

<http://www.ncbi.nlm.nih.gov/pubmed/17706603>

**Biochem Biophys Res Commun.** 2007 Oct 12;362(1):218-23. Epub 2007 Aug 10.

**Ginger ingredients reduce viability of gastric cancer cells via distinct mechanisms.**

**Ishiguro K, Ando T, Maeda O, Ohmiya N, Niwa Y, Kadomatsu K, Goto H.**

### **Abstract**

Ginger has been used throughout the world as spice, food and traditional herb. We found that 6-gingerol, a phenolic alkanone isolated from ginger, enhanced the TRAIL-induced viability

reduction of gastric cancer cells while 6-gingerol alone affected viability only slightly. 6-Gingerol facilitated TRAIL-induced apoptosis by increasing TRAIL-induced caspase-3/7 activation. 6-Gingerol was shown to down-regulate the expression of cIAP1, which suppresses caspase-3/7 activity, by inhibiting TRAIL-induced NF-kappaB activation. As 6-shogaol has a chemical structure similar to 6-gingerol, we also assessed the effect of 6-shogaol on the viability of gastric cancer cells. Unlike 6-gingerol, 6-shogaol alone reduced the viability of gastric cancer cells. 6-Shogaol was shown to damage microtubules and induce mitotic arrest. These findings indicate for the first time that in gastric cancer cells, 6-gingerol enhances TRAIL-induced viability reduction by inhibiting TRAIL-induced NF-kappaB activation while 6-shogaol alone reduces viability by damaging microtubules.

---

<http://pubs.acs.org/doi/abs/10.1021/jf504934m>

J. Agric. Food Chem., 2015, 63 (6), pp 1730–1738

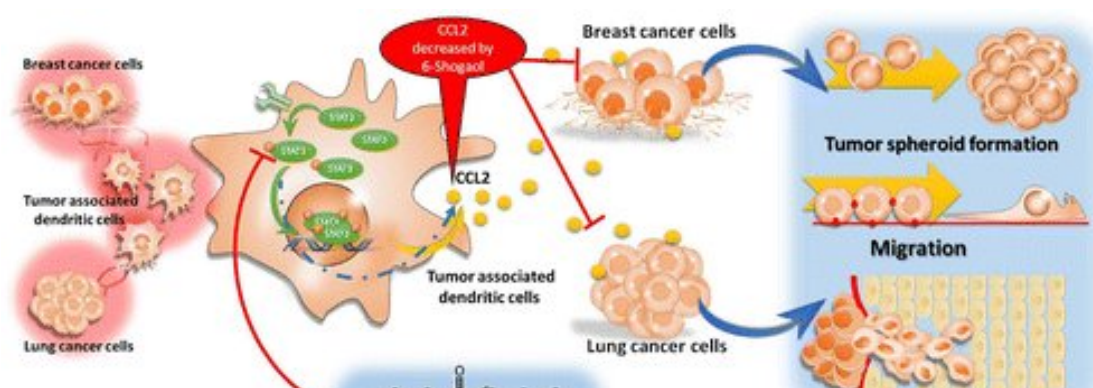
DOI: 10.1021/jf504934m

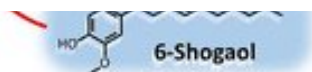
February 9, 2015

### 6-Shogaol, an Active Constituent of Dietary Ginger, Impairs Cancer Development and Lung Metastasis...

Ya-Ling Hsu, Jen-Yu Hung, Ying-Ming Tsai, Eing-Mei Tsai, Ming-Shyan Huang, Ming-Feng Hou, and Po-Lin Kuo

This study has two novel findings: it is not only the first to demonstrate that tumor-associated dendritic cells (TADCs) facilitate lung and breast cancer metastasis in vitro and in vivo by secreting inflammatory mediator CC-chemokine ligand 2 (CCL2), but it is also the first to reveal that 6-shogaol can decrease cancer development and progression by inhibiting the production of TADC-derived CCL2. Human lung cancer A549 and breast cancer MDA-MB-231 cells increase TADCs to express high levels of CCL2, which increase cancer stem cell features, migration, and invasion, as well as immunosuppressive tumor-associated macrophage infiltration. 6-Shogaol decreases cancer-induced up-regulation of CCL2 in TADCs, preventing the enhancing effects of TADCs on tumorigenesis and metastatic properties in A549 and MDA-MB-231 cells. A549 and MDA-MB-231 cells enhance CCL2 expression by increasing the phosphorylation of signal transducer and activator of transcription 3 (STAT3), and the activation of STAT3 induced by A549 and MDA-MB-231 is completely inhibited by 6-shogaol. 6-Shogaol also decreases the metastasis of lung and breast cancers in mice. 6-Shogaol exerts significant anticancer effects on lung and breast cells in vitro and in vivo by targeting the CCL2 secreted by TADCs. Thus, 6-shogaol may have the potential of being an efficacious immunotherapeutic agent for cancers.





Invasion

<http://dmd.aspetjournals.org/content/40/4/742.full>

## Metabolism of [6]-Shogaol in Mice and in Cancer Cells

Huadong Chen, Lishuang Lv, Dominique Soroka, Renaud F. Warin, Tiffany A. Parks, Yuhui Hu, Yingdong Zhu, Xiaoxin Chen and Shengmin Sang

### Abstract

Ginger has received extensive attention because of its antioxidant, anti-inflammatory, and antitumor activities. However, the metabolic fate of its major components is still unclear. In the present study, the metabolism of [6]-shogaol, one of the major active components in ginger, was examined for the first time in mice and in cancer cells. Thirteen metabolites were detected and identified, seven of which were purified from fecal samples collected from [6]-shogaol-treated mice. Their structures were elucidated as 1-(4'-hydroxy-3'-methoxyphenyl)-4-decen-3-ol (M6), 5-methoxy-1-(4'-hydroxy-3'-methoxyphenyl)-decan-3-one (M7), 3',4'-dihydroxyphenyl-decan-3-one (M8), 1-(4'-hydroxy-3'-methoxyphenyl)-decan-3-ol (M9), 5-methylthio-1-(4'-hydroxy-3'-methoxyphenyl)-decan-3-one (M10), 1-(4'-hydroxy-3'-methoxyphenyl)-decan-3-one (M11), and 5-methylthio-1-(4'-hydroxy-3'-methoxyphenyl)-decan-3-ol (M12) on the basis of detailed analysis of their <sup>1</sup>H, <sup>13</sup>C, and two-dimensional NMR data. The rest of the metabolites were identified as 5-cysteinyl-M6 (M1), 5-cysteinyl-[6]-shogaol (M2), 5-cysteinylglycyl-M6 (M3), 5-N-acetylcysteinyl-M6 (M4), 5-N-acetylcysteinyl-[6]-shogaol (M5), and 5-glutathiol-[6]-shogaol (M13) by analysis of the MS<sub>n</sub> (n = 1–3) spectra and comparison to authentic standards. Among the metabolites, M1 through M5, M10, M12, and M13 were identified as the thiol conjugates of [6]-shogaol and its metabolite M6. M9 and M11 were identified as the major metabolites in four different cancer cell lines (HCT-116, HT-29, H-1299, and CL-13), and M13 was detected as a major metabolite in HCT-116 human colon cancer cells. We further showed that M9 and M11 are bioactive compounds that can inhibit cancer cell growth and induce apoptosis in human cancer cells. Our results suggest that 1) [6]-shogaol is extensively metabolized in these two models, 2) its metabolites are bioactive compounds, and 3) the mercapturic acid pathway is one of the major biotransformation pathways of [6]-shogaol.

...Shogaols have gained interest because of recent discoveries revealing their higher anticancer potencies over gingerols. It is reported that [6]-, [8]-, and [10]-gingerols had little to no effect but [6]-shogaol significantly inhibited the growth of A-2780 ovarian cancer cells (Rhode et al., 2007). Kim et al. (2008) reported that [6]-shogaol exhibited much stronger growth-inhibitory effects on A-549 human lung cancer cells, SK-OV-3 human ovarian cancer cells, SKMEL-2 human skin cancer cells, and HCT-15 human colon cancer cells than [4]-, [6]-, [8]-, and [10]-gingerols. A study from our group has also demonstrated that [6]-, [8]-, and [10]-shogaols exhibited much higher antiproliferative potency than [6]-, [8]-, and [10]-gingerols against H-1299 human lung cancer cells with IC<sub>50</sub> values of 8 μM for [6]-shogaol and 150 μM for [6]-gingerol (Sang et al., 2009). Along with our collaborators, we have reported that [6]-shogaol was more effective than [6]-gingerol in inhibiting 12-O-tetradecanoylphorbol-13-acetate-induced tumor promotion in mice (Wu et al., 2010).



Furthermore, Dugasani et al. (2010) found that [6]-shogaol showed the most potent antioxidative activity with an IC<sub>50</sub> value of approximately 8 µM, whereas [6]-, [8]-, and [10]-gingerols had IC<sub>50</sub> values of 28, 20, and 12 µM, respectively.

---

<http://www.ncbi.nlm.nih.gov/pubmed/19367122>

Forum Nutr. 2009;61:182-92. doi: 10.1159/000212750. Epub 2009 Apr 7.

## **Ginger-derived phenolic substances with cancer preventive and therapeutic potential.**

**Kundu JK, Na HK, Surh YJ.**

### **Abstract**

Ginger, the rhizomes of *Zingiber officinale* Roscoe (Zingiberaceae), has widely been used as a spice and condiment in different societies. Besides its food-additive functions, ginger has a long history of medicinal use for the treatment of a variety of human ailments including common colds, fever, rheumatic disorders, gastrointestinal complications, motion sickness, diabetes, cancer, etc. Ginger contains several nonvolatile pungent principles viz. gingerols, shogaols, paradols and zingerone, which account for many of its health beneficial effects. Studies conducted in cultured cells as well as in experimental animals revealed that these pungent phenolics possess anticarcinogenic properties. This chapter summarizes updated information on chemopreventive and chemotherapeutic effects of ginger-derived phenolic substances and their underlying mechanisms.

---

<http://molecular-cancer.biomedcentral.com/articles/10.1186/1476-4598-12-135>

Molecular Cancer 2013 12:135

DOI: 10.1186/1476-4598-12-135

## **6-Shogaol induces apoptosis in human leukemia cells through a process involving caspase-mediated cleavage of eIF2 $\alpha$**

**Qun Liu, Yong-Bo Peng, Ping Zhou, Lian-Wen Qi, Mu Zhang, Ning Gao, E-Hu Liu and Ping Li**

### **Abstract**

#### **Background**

6-Shogaol is a promising antitumor agent isolated from dietary ginger (*Zingiber officinale*). However, little is known about the efficacy of 6-shogaol on leukemia cells. Here we investigated the underlying mechanism of 6-shogaol induced apoptosis in human leukemia cells in vitro and in vivo.

#### **Methods**

Three leukemia cell lines and primary leukemia cells were used to investigate the apoptosis effect of 6-shogaol. A shotgun approach based on label-free proteome with LC-CHIP Q-TOF

MS/MS was employed to identify the cellular targets of 6-shogaol and the differentially expressed proteins were analyzed by bioinformatics protocols.

## Results

The present study indicated that 6-shogaol selectively induced apoptosis in transformed and primary leukemia cells but not in normal cells. Eukaryotic translation initiation factor 2 alpha (eIF2 $\alpha$ ), a key regulator in apoptosis signaling pathway, was significantly affected in both Jurkat and U937 proteome profiles. The docking results suggested that 6-shogaol might bind well to eIF2 $\alpha$  at Ser51 of the N-terminal domain. Immunoblotting data indicated that 6-shogaol induced apoptosis through a process involving dephosphorylation of eIF2 $\alpha$  and caspase activation-dependent cleavage of eIF2 $\alpha$ . Furthermore, 6-shogaol markedly inhibited tumor growth and induced apoptosis in U937 xenograft mouse model.

## Conclusion

The potent anti-leukemia activity of 6-shogaol found both in vitro and in vivo in our study make this compound a potential anti-tumor agent for hematologic malignancies.

---

<https://rucore.libraries.rutgers.edu/rutgers-lib/21328/>

## Isolation of gingerols and shogaols from ginger and evaluation of their chemopreventive activity on prostate cancer cells...

**Ramji, Divya; ho, chi ; Huang, Qingron Rafi, Mohamed; Huang, Mou**  
**Rutgers University; Graduate School-New Brunswick**

## Description

Ginger, obtained from the rhizome of *Zingiber officinale* (Family Zingiberaceae), has been used extensively as a spice and in traditional medicine. The compounds in ginger primarily responsible for its medicinal properties are the gingerols. Gingerols can undergo dehydration, during storage and processing, to form the corresponding shogaols. Studies conducted so far have primarily focused on the biological activities of ginger and 6-gingerol. The main objectives of this research were to evaluate the anti-inflammatory and chemopreventive activities of gingerols and shogaols.

The crude ginger extract was subjected to column chromatography to obtain a mixture of gingerols, a mixture of shogaols, 6- gingerol, 8-gingerol and 6-shogaol which were characterized using high pressure liquid chromatography and nuclear magnetic resonance spectroscopy.

The anti-inflammatory activity of 6-gingerol and 6-shogaol was evaluated using the 12-O-tetradecanoylphorbol-13-acetate-induced mouse ear inflammatory model. Both 6-gingerol and 6-shogaol inhibited ear edema as well as the levels of proinflammatory cytokines.

The primary focus of this study was to evaluate the chemopreventive potential of these compounds on prostate cancer cells (LNCaP and PC-3). We hypothesized that gingerols and shogaols exhibit their chemopreventive potential through the modulation of the intrinsic



pathway of apoptosis. Cell viability studies indicated that, among the compounds tested, 6-shogaol, 8-gingerol and shogaol mixture were the most effective in inhibiting cell growth in both cell lines. Morphological assessment, cell cycle, Annexin V staining and western blot analysis showed that 8-gingerol and 6-shogaol induced apoptosis in both the cell lines. Western blot analysis further confirmed our hypothesis that 8-gingerol and 6-shogaol induced apoptosis through activation of the intrinsic pathway of apoptosis as seen by caspase-9 cleavage. In addition, 8-gingerol and 6-shogaol induced the production of reactive oxygen species (ROS) which correlated well with the induction of apoptosis. This suggests that production of ROS could be one of the mechanisms of apoptosis induction by these compounds.

In conclusion, our study shows for the first time that gingerols and shogaols isolated from ginger were able to inhibit the growth of prostate cancer cells. 6-shogaol and 8-gingerol were able to induce apoptosis in both cell lines by activation of the intrinsic pathway of apoptosis.

---

<http://www.sciencedirect.com/science/article/pii/S0378874109006448>

doi:10.1016/j.jep.2009.10.004

Journal of Ethnopharmacology

Volume 127, Issue 2, 3 February 2010, Pages 515–520

**Comparative antioxidant and anti-inflammatory effects of [6]-gingerol, [8]-gingerol, [10]-gingerol and [6]-shogaol**

**Swarnalatha Dugasania, Mallikarjuna Rao Pichikac, Vishna Devi Nadarajahc, Madhu Katyayani Balijepallic, Satyanarayana Tandraa, Jayaveera Narsimha Korlakuntab**

## **Abstract**

### **Ethnopharmacological relevance**

*Zingiber officinale* Rosc. (Zingiberaceae) has been traditionally used in Ayurvedic, Chinese and Tibb-Unani herbal medicines for the treatment of various illnesses that involve inflammation and which are caused by oxidative stress. Although gingerols and shogaols are the major bioactive compounds present in *Zingiber officinale*, their molecular mechanisms of actions and the relationship between their structural features and the activity have not been well studied...

### **Conclusions**

6-Shogaol has exhibited the most potent antioxidant and anti-inflammatory properties which can be attributed to the presence of  $\alpha,\beta$ -unsaturated ketone moiety. The carbon chain length has also played a significant role in making 10-gingerol as the most potent among all the gingerols. This study justifies the use of dry ginger in traditional systems of medicine.

---

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2553670/>

# **Inhibitory effect of gingerol on the proliferation and invasion of hepatoma cells in culture**

**Satoru Yagihashi, Yutaka Miura, and Kazumi Yagasaki**

## **Abstract**

Effect of [6]-gingerol, a major pungent component in ginger, on the proliferation of a rat ascites hepatoma AH109A cells was investigated by measuring [3H]thymidine incorporation into acid-insoluble fraction of the cultured cells and that on the invasion by co-culturing the hepatoma cells with rat mesentery-derived mesothelial cells. [6]-Gingerol inhibited both the proliferation and invasion of hepatoma cells in a dose-dependent manner at concentrations of 6.25–200  $\mu$ M (proliferation) and 50–200  $\mu$ M (invasion). [6]-Gingerol accumulated cells in S phase and elongated doubling time of hepatoma cells, and increased the rate of apoptosis. Hepatoma cells previously cultured with hypoxanthine (HX) and xanthine oxidase (XO) or with hydrogen peroxide showed increased invasive activities. [6]-Gingerol suppressed the reactive oxygen species-potentiated invasive capacity by simultaneously treating AH109A cells with [6]-gingerol, HX and XO or with [6]-gingerol and hydrogen peroxide. Furthermore, [6]-gingerol reduced the intracellular peroxide levels in AH109A cells. These results suggest that the suppression of hepatoma cell proliferation by [6]-gingerol may be due to cell cycle arrest and apoptosis induction. They also suggest that the anti-oxidative property of [6]-gingerol may be involved in its anti-invasive activity of hepatoma cells.

---

## **6-Shogaol Patents**

**KR20150068008**

### **PREPARATION METHOD OF GINGER WITH INCREASED SHOGAOL CONTENT**

The present invention relates to a method for increasing shogaol in ginger by processing gingers under high pressure and a ginger with improved shogaol content manufactured by the method wherein the manufacturing method is allowed to economically turn ginger roll into shogaol in an efficient manner, and the increased shogaol is used in various uses like improving recognition function or for turning into paradol as a substrate.

**JP2015044767**

### **METHOD OF PRODUCING GINGER EXTRACT PROCESSED PRODUCT**

**PROBLEM TO BE SOLVED:** To provide a method which makes it possible to efficiently produce a ginger extract processed product with increased content of shogaol in ginger extract.**SOLUTION:** A method of producing a ginger extract processed product comprises a step in which ginger extract is heated at 90-150 DEG C in the presence of acid selected from hydrochloric acid, sulfuric acid, phosphoric acid and inositol hexaphosphate in the state of moisture content in the system being 10-50%.

**JP2015044766**

### **METHOD OF PRODUCING GINGER EXTRACT PROCESSED PRODUCT**

**PROBLEM TO BE SOLVED:** To provide a method which makes it possible to efficiently produce a ginger extract processed product with increased content of shogaol in ginger extract.**SOLUTION:** A method of producing a ginger extract processed product comprises a

step in which ginger extract is heated at 110-150 DEG C in the presence of organic acid selected from citric acid, succinic acid and malic acid in the state of moisture content in the system being 5-10%.

#### **JP2015023878**

##### **GINGER EXTRACT**

**PROBLEM TO BE SOLVED:** To provide a ginger extract in which 6-shogaol is largely included than 6-gingerol, and excellent in stability in such a manner that the ratio between the 6-gingerol and the 6-shogaol is not changed even in preservation over a long period, and a method for producing the ginger extract. **SOLUTION:** Provided is a ginger extract characterized in that the weight ratio of 6-shogaol to 6-gingerol is 1.6 or higher.

#### **KR20150000354**

##### **ZINGIBER EXTRACT HAVING INCREASED SHOGAOL CONTENT, METHOD OF PRODUCING THE SAME, AND A COMPOSITION COMPRISING THE SAME**

In the present invention, provided are a ginger extract with increased shogaol content obtained by microwave emission, a manufacturing method thereof and a composition including the same. In the present invention, a method for manufacturing the ginger extract comprises the steps of emitting microwave to gingers and using a solvent wherein the microwave emission is made between 120 and 200 degrees Celsius for 30 to 60 minutes under 2 to 100 bars. The shogaol is included in the ginger extract and is well known for having memory improving effects, anti-inflammatory effects and anti-oxidant effects.

#### **JP2015010083**

##### **METHOD OF PRODUCING GINGER EXTRACT PROCESSED PRODUCT**

**PROBLEM TO BE SOLVED:** To provide a method which makes it possible to efficiently produce a ginger extract processed product with improved content of shogaol in ginger extract. **SOLUTION:** A method of producing ginger extract processed product comprises the step of heating ginger extract in the presence of lactic acid at 110-150 DEG C.

#### **CN104147557**

##### **Shogaol extract soft capsule and preparation method thereof**

The invention relates to a shogaol extract preparation and in particular relates to a shogaol extract soft capsule and a preparation method thereof. The shogaol extract soft capsule is prepared from the components in parts by weight: 3-10 parts of shogaol extract and 40-60 parts of oiliness matrix; preferentially, the shogaol extract soft capsule is prepared from the following components in parts by weight: 6 parts of shogaol extract and 54 parts of corn oil. As a supercritical CO<sub>2</sub> extraction method is adopted, the extraction method of a shogaol extract has the advantages of high extraction ratio and high content of 6-shogaol.

#### **JP2014152130**

##### **METHOD FOR PRODUCTION OF GINGER EXTRACT WITH HIGH CONTENT OF SHOGAOL**

**PROBLEM TO BE SOLVED:** To provide a method for producing the shogaol-containing extract which contains shogaol with high purity by changing gingerol in ginger extract into shogaol. **SOLUTION:** Shogaol, particularly shogaol-containing extract which contains [6]-shogaol with high purity is efficiently produced by heating dehydration under reduced pressure after adding organic acids, such as a malic acid, to ginger extract.

#### **CN103263433**

## **Medical application of natural product 6-shogaol in enhancing chemosensitivity of pancreatic cancer on gemcitabine and compound drug composite of natural product 6-shogaol**

The invention relates to the field of natural drugs, and discloses medical application of natural product 6-shogaol in enhancing the chemosensitivity of pancreatic cancer on gemcitabine and a compound drug composite of the natural product 6-shogaol. According to the invention, low-dose gemcitabine can generate biological effect under high dose through the combined administration of the 6-shogaol and the gemcitabine, so that the clinical usage amount of the gemcitabine can be greatly reduced, the toxic side effect can be reduced, the clinical treatment safety index can be enhanced, and good clinical application development prospect is achieved.

### **JP2013100253**

#### **ANTICANDIDAL ACTIVITY COMPOSITION INCLUDING GINGER COMPONENT**

**PROBLEM TO BE SOLVED:** To solve the problem that the candidiasis of a skin and a mucous membrane, particularly, any of the oral candidiasis of old persons and the vaginal candidiasis of women is infectious disease having a lot of numbers of patients and also easy to be relapsed, but, concerning to treatment with an antifungal agent, there is the risk of side effects or the appearance of resistant bacteria and its use over a long period is limited, and the suppression of relapse is difficult, and to provide a new anticandidal activity composition which has no need of considering the risk of side effects and the appearance of resistant bacteria to the candidiasis of a skin and a mucous membrane, and can be obtained and easily used by a patient. ;**SOLUTION:** Shogaol being a plant constituent exhibits strong anticandidal activity. Further, the plant constituent such as shogaol can easily obtain a product with high purity, and also, its utilization to foods has been approved. Thus, it can be applied to wide products from pharmaceutical agents to foods, and, when it is put to practical use, a patient can easily obtain any product and conveniently use the same. Though oral candidiasis and vaginal candidiasis are easy to be relapsed, the composition including the plant constituent can be utilized by a patient at ease without worrying about risk caused by the application of an antifungal agent.

### **CN103159599**

#### **Synthesis process of gingerol derivative**

The invention relates to a synthesis process of a gingerol derivative. A shogaol derivative is obtained by condensation of vanillin, aliphatic aldehyde and ketone in acid and base solvents in an appropriate ratio. The novel gingerol derivative is obtained by catalytic hydrogenation reduction of shogaol. The synthesis process disclosed by the invention is simple, and the gingerol derivative can be obtained through the reaction with one step-two steps and through a simple and convenient purification method.

### **JP2012249553**

#### **METHOD FOR PRODUCING GINGER PROCESSED PRODUCT**

**PROBLEM TO BE SOLVED:** To provide a method for rapidly and efficiently producing, for efficient and sufficient intake of shogaol known as a functional component of ginger, a ginger processed product which contains shogaol more than gingerol and is reduced in stimulative pungency or smell peculiar to ginger. ;**SOLUTION:** The method for producing a ginger processed product which contains shogaol more than gingerol includes performing heat treatment on dried ginger as raw material under a specific condition. According to the method, shogaol can be efficiently increased.

**WO2012075754****PHARMACEUTICAL COMPOSITION FOR TREATING ACUTE LYMPHOCYTIC LEUKEMIA**

The present invention discloses a pharmaceutical composition for treating acute lymphocytic leukemia which comprises 6-shogaol and Salubrinol. The combination of 6-shogaol and Salubrinol in low dose can obtain the biological effect of 6-shogaol in high dose, and can significantly reduce the clinical dose of 6-shogaol, and decrease the occurrence of the potential toxicity and side effect, and can increase the safety index of clinic therapeutics.

**KR20120020708****A METHOD FOR PRODUCING PROCESSED GINGER CONTAINING HIGHLY-CONCENTRATED [6]-SHOGAOL USING BY NOVEL TREATMENT METHOD**

**PURPOSE:** A method for preparing processed ginger or extract thereof containing a large amount of [6]-shogaol is provided to ensure anticancer, anti-inflammatory, and antioxidative activities. **CONSTITUTION:** A method for preparing processed ginger containing [6]-shogaol comprises: a step of steaming washed gingers at 70[deg.]C-150[deg.]C for 30 minutes to 24 hours to prepare primarily processed ginger; a step of drying in the dark or by hot wind; and a step of repeating the first and second steps 3-20 times more.

**JP2012051811****IMMUNOENHANCING AGENT**

**PROBLEM TO BE SOLVED:** To provide an immunoenhancing agent containing a ginger extract component as an active ingredient. ;**SOLUTION:** The immunoenhancing agent contains 6-shogaol as an active ingredient. The 6-shogaol is preferably contained in form of a ginger extract containing 6-shogaol and 6-gingerol, wherein 6-shogaol is 1.6 times or more 6-gingerol.

**TW201041639****Method of preparing 6-shogaol from Zingiber Officinal by using supercritical fluid**

A method of preparing 6-shogaol from ginger (Zingiber Officinal) by using supercritical fluid is disclosed. Dried ginger root powder is subjected to a critical reaction step and an extraction step in a supercritical fluid under specific process conditions, so as to obtain 6-shogaol with high yield. Since the aforementioned process use the supercritical fluid instead of organic solvents, the prior problems of the resulted extract with low yield and remained organic solvent therein can be effectively overcome, thereby achieving the application of the shogaol in food and medicine industries.

**TW200918085****Use of a potent product extracted from rhizomes of zingiber officinale in treating a disease associated with helicobacter pylori**

The present invention discloses a new use of a potent product extracted from rhizomes of Zingiber officinale in treating a disease associated with Helicobacter pylori such as gastritis, gastric ulcer or duodenal ulcer in a patient. The potent product is prepared by a process including the steps of (a) preparing a crude extract from rhizomes of Zingiber officinale, said crude extract comprising 6-gingerol and 6-shogaol; (b) introducing the crude extract to a reverse phase chromatography column, and eluting the column with a first eluent having a polarity lower than water to obtain a first potent fraction and a second eluent having a polarity lower than that of the first eluent to obtain a second potent fraction. Preferably, the second potent fraction is substantially free of both 6-gingerol and 6-shogaol.

**CN102091058**

**Medical application of 6-shogaol for treating cervical cancer**

The invention relates to the field of natural drugs, in particular to a medical application of 6-shogaol for treating cervical cancer. The research on the pharmacological activity of the 6-shogaol shows that: although the 6-shogaol has a curative activity on various kinds of tumors, the activity on different tumors has great difference. In multiple tumor-inhibiting tests, the 6-shogaol has a best effect on treating cervical cancer, breast cancer and leukemia, i.e. the effect on treating cervical cancer, breast cancer and leukemia by using the 6-shogaol is obviously better than the effect on treating other kinds of cancers by using the 6-shogaol.

**US2011136916**

**6-SHOGAOL FOR USING IN A METHOD FOR THE TREATMENT OF LEUKEMIA**

The present invention relates to the field of natural drugs, particularly to 6-shogaol for using in a method for the treatment of leukemia. The present invention provides a method for treating leukemia by applying a therapeutically effective dose of 6-shogaol and this therapeutic method can be used for treating leukemia in mammals including human being.

**US2010286283**

**MICROTUBULE-DISRUPTING AGENT AND CANCER CELL PROLIFERATION INHIBITOR CONTAINING THE SAME**

The present invention provides a novel microtubule-disrupting agent, and also provides a use of the microtubule-disrupting agent. A microtubule-disrupting agent containing an [alpha], [beta]-unsaturated carbonyl compound as an active ingredient is provided. Further, a cancer cell proliferation inhibitor containing the microtubule-disrupting agent is also provided. As the [alpha],[beta]-unsaturated carbonyl compound, 6-shogaol is preferably used.

**CN101912378**

**Medical application of 6-shogaol for preventing and curing radiation injury**

The invention relates to the field of natural medicines, particularly to application of 6-shogaol for preventing and curing radiation injury. Pharmacological test proves that the 6-shogaol can effectively cure and prevent the radiation injury.

**CN101735030**

**Method for preparing 6-shogaol**

The invention relates to the field of natural medicines, in particular to a method for preparing 6-shogaol, which is a method for preparing the efficient component 6-shogaol from the extract of ginger supercritical fluid. The method comprises the following steps of: mixing the extract of ginger supercritical fluid with an ethanol-containing acid water liquid before conversion, heating and refluxing, then separating and refining. The content of the 6-shogaol in the original extract of ginger supercritical fluid is about 2.5%, and the content of the 6-shogaol in the extract after the acid water reaction can reach 20%.

**KR20100060123**

**PHARMACEUTICAL COMPOSITION FOR PREVENTING OR TREATING PARKINSON'S DISEASES COMPRISING A GINGER EXTRACT OR SHOGAOL**

**PURPOSE:** A composition containing ginger extract or shogaol is provided to prevent or treat Parkinson's disease. **CONSTITUTION:** A pharmaceutical composition for preventing or treating Parkinson's disease contains ginger extract or shogaol and a pharmaceutically acceptable carrier. The composition is used in the form of a powder, granule, tablet, capsule, suspension, emulsion, or syrup. A method for extracting ginger extract comprises: a step of



extracting ginger with C1-C4 alcohol; a step of adding water and n-hexane to the extract; and a step of adding ethyl acetate to an aqueous layer to extract and to separate ethyl acetate layer.

#### **US2005238737**

##### **Use of one or more shogaol(s) as an aphrodisiac**

The present invention relates to the use of one or more shogaol(s) as aphrodisiacs.

Advantageously, the shogaol(s) correspond(s) to the general formula I: in which n is equal to 1, 2, 4, 6 or 8 and advantageously 1. The present invention also relates to a process for stimulating or arousing the libido in human beings, comprising the administration to a human being of an effective amount of one or more shogaol(s).

#### **JP2008189571**

##### **NEW THERAPEUTIC OR PROPHYLACTIC AGENT FOR DIABETES AND/OR OBESITY**

**PROBLEM TO BE SOLVED:** To provide a new therapeutic or prophylactic agent for diabetes and/or obesity. ;**SOLUTION:** The therapeutic or the prophylactic agent for diabetes and/or obesity comprises shogaol as an active ingredient. The shogaol is preferably 6-shogaol. The therapeutic or the prophylactic agent for diabetes and/or obesity can be used as a pharmaceutical, a food and drink and an external preparation for skin

#### **JP2008079562**

##### **METHOD FOR PRODUCING GINGER PROCESSED PRODUCT HIGHLY CONTAINING SHOGAOL**

**PROBLEM TO BE SOLVED:** To provide a method for producing a ginger processed product highly containing shogaol, enabling to obtain the ginger processed product highly containing shogaol without causing problems such as quality deterioration and property change, and to provide the ginger processed product highly containing shogaol obtained by the method.

**SOLUTION:** This method for producing the ginger processed product highly containing shogaol comprises heating ginger in a hermetically sealed container. As the ginger, *Zingiberis Rhizoma* is preferably used. The ginger processed product highly containing shogaol produced by the method is also provided.

#### **WO2005046630**

##### **HAIR RESTORER COMPOSITIONS AND ANTIPRURITIC AGENT**

Hair restorer compositions and an antipruritic agent which each contains shogaol, which has not been used as a hair-restoring ingredient. The hair restorer compositions contain shogaol. One of the hair restorer compositions further contains a specific ingredient and thereby has improved shogaol stability.

#### **JPH0196121**

##### **REMEDY FOR HYPERKERATOSIS**

**PURPOSE:** To obtain a remedy for hyperkeratosis, having remedying effect against hyperkeratosis, low toxicity and high safety, by using (6)-shogaol as an active component.

**CONSTITUTION:** The objective remedy contains, as an active component, (6)- shogaol of formula [1-(4-hydroxy-3-methoxyphenyl)-(E)-4-decen-3-one] having central nervous suppressing action and analgesic action, etc., and existing in KANKYO (dried rhizome of *Zingiber officinale*) or SHOKYO (raw rhizome of *Zingiber officinale*) which are Chinese herb drugs compounded in Chinese drug formulations SAIKO-KEIHI-KANKYO-TO, KOSEIRYU-TO, etc. The compound of formula is administered to animal or human as it is or together with conventional drug-preparation carrier. To attain the expected effect as a peroral

drug, it is preferable to administer 20-80mg of the compound of formula for adult daily in several divided doses. several times a day.

### **JPS6372625**

#### **BLOOD PLATELET AGGLUTINATION INHIBITOR**

**PURPOSE:**To obtain a blood platelet agglutination inhibitor, containing (6)- shogaol obtained from a dried rhizome of ginger as an active ingredient and useful for treating cerebral infarction, cerebral thrombosis, arteriosclerosis, angina pectoris, etc. **CONSTITUTION:**A blood platelet agglutination inhibitor obtained by extracting a dried rhizome of ginger with ether, etc., to give an extract essence, subjecting the resultant extract essence to column chromatography using silica gel as a solid support, carrying out development with a solvent, e.g. n-hexane, etc., to give (6)-shogaol [1-(4-hydroxy-3-methoxyphenyl)-4-decen-3-one] expressed by the formula and formulating the resultant shogaol as an active ingredient into an oral agent, e.g. tablet, capsule, granule, etc., or parenteral agent, e.g. injection suppository, etc. The dose thereof for adults is up to 3 times a day based on 20-80mg at a time as an oral agent and 0.25-10mg a month as a parenteral agent.

### **JPH0840970**

#### **PRODUCTION OF GINGEROL AND SHOGAOL**

**PURPOSE:**To industrially and simply obtain gingerol useful as a synthetic intermediate for shogaol, a perfume composition, etc., by reacting a specific gingerone with an aldehyde. **CONSTITUTION:**This gingerol of formula III is obtained by reacting a gingerone of formula I with a compound of formula II [(n) is 0-10] in the presence of an inert solvent such as a base such as sodium t-butoxide and an inert solvent such as THF. This shogaol of formula IV is obtained by heating the gingerol of formula III in the presence of an acid catalyst such as p-toluenesulfonic acid and an inert solvent such as toluene.

### **JPH024711**

#### **ANTIPARASITIC AGENT**

**PURPOSE:**To obtain an antiparasitic agent, containing [6]-shogaol and/or [6]- gingerol as an active ingredient and capable of exhibiting excellent anthelmintic effects on parasites, such as oxyurids or roundworms of *Anisaxis* spp., parasitic on human digestive tracts. **CONSTITUTION:**An antiparasitic agent, containing [6]-shogaol expressed by formula I and/or gingerol expressed by formula II as an active ingredient and having the above-mentioned effects.; The afore-mentioned compound is directly used or, together with a normally used pharmaceutical carrier, formed into an oral agent, e.g., tablet, capsule, granule, fine granule or powder, or a parenteral agent, such as injection, and can be administered to animals and humans and the following daily dose is considered as normally suitable for an adult. 100-500mg in the case of oral administration and 0.5-100mg in the case of parenteral administration.

### **JPS6032705**

#### **ANTIMICROBIAL AGENT**

**PURPOSE:**To provide an antimicrobial agent containing extract of ginger rhizome as an active component, exhibiting excellent bacteriostatic and bactericidal activity at a low dose, and useful especially as a preservative additive for foods. **CONSTITUTION:**The peices or powder of ginger obtained by cutting or grinding the rhizome of ginger, is extracted with a proper solvent such as alcohol, ketone, ester, etc. in hot state, and the extract is used as the active component usually in the form of liquid, and optionally after dispersing in a proper powdery carrier. An antimicrobial activity is attained by the synergistic effect of the pungent

taste components of the extract such as zingerone, ginerol, shogaol, zingiberene, etc., the essential oil of ginger, and other minor components. The desirable effect can be achieved without lowering the taste, color, and flavor of the food, by adding about 0.02-0.5% extract to the food

#### **WO03095424**

#### **PROCESS FOR PRODUCING SHOGAOL AND INTERMEDIATES FOR THE SYNTHESIS THEREOF**

It is intended to provide a process for industrially producing shogaols which are useful in the fields of foods, perfumes, drugs, quasi drugs, cosmetics and so on. Namely, a novel intermediates represented by the following general formula and a process for producing shogaols via these intermediates. According to this process, shogaols, which can be hardly produced on a mass scale by the existing method of extracting from natural ginger, can be easily produced. Intermediate: In the above chemical formula (1), R<1> represents hydrogen or methyl; R<2> represents optionally branched C1-18 alkyl; R<3> and R<4> independently represent each hydrogen, lower alkyl or a protective group of phenolic hydroxy; A represents C1-4 alkylene; and X represents benzenesulfonyl or toluenesulfonyl.

#### **CN1683316**

#### **Separating and purifying method for shogaol**

The shogaol separating and purifying process includes the following steps: 1. separating water, Kaempferia galanga oil and shogaol in the distilled mixture, and filtering to obtain coarse shogaol crystal; 2. adding alcohol or acetone in 1-3 times the weight of coarse shogaol crystal into the coarse shogaol crystal and adding distilled water in 15-35 times the weight; 3. regulating pH value of the solution to 4-8, setting for 20-40 hr to separate crystal; and 4. filtering and vacuum drying to obtain high purity shogaol crystal. The product is used in medicine.

---