Journal of Pharmacognosy and Phytochemistry

Available online at www.phytojournal.com

E-ISSN: 2278-4136
P-ISSN: 2349-8234
https://www.phytojournal.com
JPP 2023; 12(6): 267-271
Received: 13-09-2023
Accepted: 16-10-2023

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Review on ginger: Chemical constituents & biological effects

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DOI: https://doi.org/10.22271/phyto.2023.v12.i6c.14792

Abstract
Zingiber officinale Roscoeor ginger, is a common and extensively utilized spice. It is abundant in phenolic compounds, terpenes, polysaccharides, lipids, organic acids, and unprocessed fibers, among other chemical constituents. The phenolic compounds found in ginger, such as shogaols and gingerols, are primarily responsible for its health benefits. Research over time has shown that ginger has a wide range of biological properties, such as anti-inflammatory, antimicrobial, anticancer, neuroprotective, cardiovascular, respiratory, anti-obesity, antidiabetic, anti-nausea, and antiemetic effects. We provide an overview of the current understanding of ginger's bioactive substances and bioactivities in this review, and we also go over the mechanisms of action with this revised review paper, we hope to raise awareness of ginger and its potential uses going forward, such as in the creation of functional foods or nutraceuticals for the management and prevention of chronic illnesses. Considerable attention is being paid to the clinical uses of ginger with the hope of achieving therapeutic benefits. The goal of this systematic review is to present a thorough analysis of the clinical effects of ginger in all fields that have been studied.

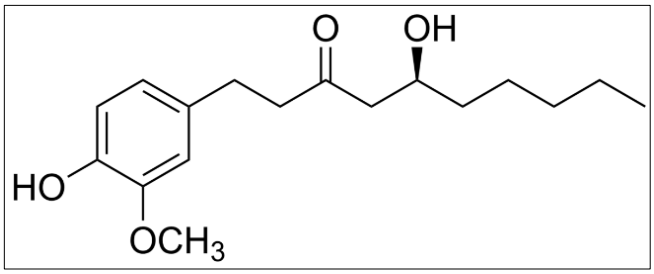
Keywords: Ginger, chemical constituents, health effects, biological activity, phytoconstituents

Introduction
Ginger, or Zingiber officinale Roscoe, is a member of the Zingiberaceae family and genus and has long been used as a spice and herbal medicine [1]. Common ailments like headaches, colds, nausea, and emesis can be mitigated and treated with ginger root. Terpene and phenolic compounds are just two of the numerous bioactive substances found in ginger that have been identified. All of ginger's different bioactivities are attributed to its phenolic compounds, primarily gingerols, shogaols, and paradols [2]. The biological properties of ginger, including anti-inflammatory [4], antimicrobial [5], antioxidant [3] and anti-cancer [6], have been discovered in recent years. Furthermore, a growing body of research has shown that ginger may help prevent and treat a number of illnesses, including neurological conditions [7], cardiovascular conditions [8], obesity [9], diabetes mellitus [10], nausea and vomiting brought on by chemotherapy [11], and respiratory issues [12]. We concentrate on the bioactive substances and bioactivities of ginger in this review, with particular attention to its mechanisms of action. The number of studies on the health benefits of ginger has significantly increased as a result of its possible pharmacological and physiological actions. In terms of clinical applications, there has been a growing body of research demonstrating the health benefits of ginger. In fact, an astounding number of randomized clinical trials (RCTs) have been carried out with the goal of determining the advantages of ginger by lowering symptoms. For instance, several randomized controlled trials assessed the efficacy of supplementing with ginger in lowering chemotherapy-induced nausea, vomiting, and dysmenorrhea in cancer patients. In addition, a number of systematic reviews and meta-analyses (SR-MA) that sought to evaluate the clinical efficacy of ginger have been finished.

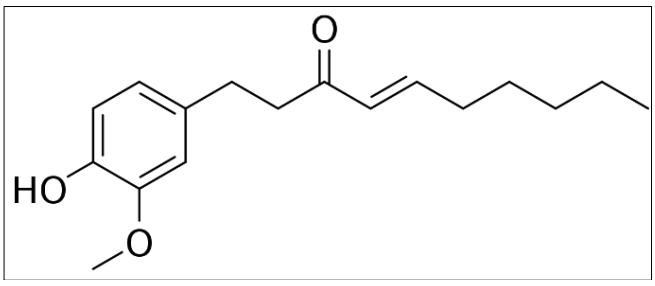
Ginger and Its Constituents
Members of the Zingiberaceae family, including ginger (Zingiber officinale), are widely used as spices throughout the world, particularly in most Asian nations [13]. Active ingredients like phenolic and terpene compounds are abundant in ginger. Gingerols, shogaols, and paradols make up the majority of the phenolic compounds found in ginger. The main polyphenols in fresh ginger are called gingerols, and they include 6-gingerol, 8-gingerol, and 10-gingerol. Gingerols can be converted into matching shogaols by applying heat treatment or storing them for a long period. Shohaols can change into paradols after hydrogenation.

Ginger contains a wide variety of additional phenolic compounds, including 6-dehydrogingerdione, zingerone, quercetin, and gingerenone-A. Additionally, ginger contains a number of terpene components, including β-bisabolene, α-curcumene, zingiberene, α-farnesene, and β-sesquiphellandrene, which are thought to be the primary ingredients of ginger essential oils. In addition to these, ginger also contains lipids, organic acids, polysaccharides, and raw fibers. Ginger has been found to contain over 400 different compounds, according to chemical analysis. Carbohydrates (50-70%), lipids (3-8%), terpenes, and phenolic compounds are the main components of ginger rhizomes [14]. Zingiberene, β-bisabolene, α-farnesene, β-sesquiphellandrene, and α-curcumene are among the terpene components of ginger, and gingerol, paradols, and shogaol are among the phenolic compounds. Compared to other varieties, these gingerols (23-25%) and shogaols (18-25%) are more prevalent. In addition to these, there are also amino acids, minerals, ash, protein, phytosterols, and vitamins (like A and Nicotinic Acid) [15, 16]. Zingiberene and bisabolene are examples of aromatic constituents, whereas gingerols and shogaols are examples of pungent constituents [17]. Additional compounds (1-10%) related to gingerol or shogaol have been found in the rhizome of ginger, such as diarylheptanoids [18, 19], 6-paradol, 1-dehydrogingerdione, 6-gingerdiol and 10-gingerdione, 4-gingerdiol, 6-gingerdiol, 8-gingerdiol, and 10-gingerdiol. A combination of volatile oils, including shogaols and gingerols, is responsible for the distinctive flavor and odor of ginger [20].

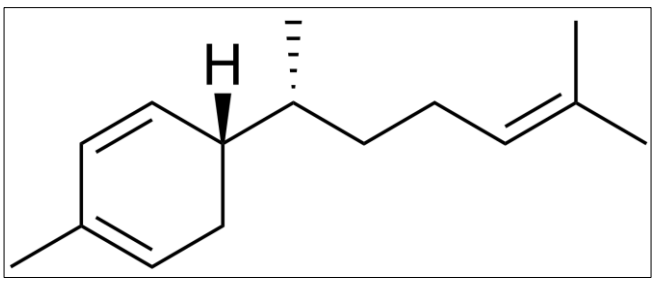
Gingrol



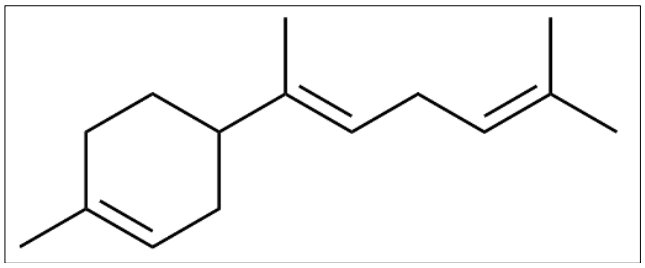
[6]-Shogaol



Zingeberene



Bisabolene



Traditional use

In ancient China and India, ginger was used both as a spice and a medicine. For its therapeutic qualities, it was also well-known in Europe by the ninth century and in England by the tenth. The rhizome of wild ginger has also been used by Native Americans to control heart rate and menstruation. It is believed that ginger reduces nausea by acting directly on the gastrointestinal tract. Consequently, it is used to stop nausea brought on by radiation therapy, car sickness, and surgery. One well-known treatment for nausea during pregnancy is ginger. Other GI issues like morning sickness, colic, upset stomach, gas, bloating, heartburn, flatulence, diarrhea, loss of appetite, and dyspepsia (discomfort after eating) are also treated with ginger. According to Indian Ayurvedic medicinal system, ginger is recommended to enhance the digestion of food.

Biological Activity

Antioxidant Activity

Overproduction of one type of free radical, reactive oxygen species (ROS), has been associated with the onset of many chronic illnesses. Numerous natural products have been demonstrated to possess antioxidant potential, such as fruits, vegetables, cereal grains, edible flowers, medicinal plants, and herbal infusions. Many studies have found that ginger has a high level of antioxidant activity [21]. The antioxidant activity of different types of ginger tended to be as follows: Different types of ginger: Fresh, carbonized, dried, and stir-fried. This was mainly associated with their polyphenolic contents. Heating fresh ginger resulted in dried ginger with higher antioxidant activity because fresh ginger has a higher moisture content than dried ginger.

However, when dried ginger was heated further to make stir-fried and carbonized ginger, the antioxidant activity decreased because the processing could turn gingerols into shogaols.

Neuroprotection

Alzheimer's disease (AD) and Parkinson's disease (PD) are two neurodegenerative diseases that some people, particularly the elderly, are more susceptible to. Ginger has been shown in numerous studies to have anti-inflammatory properties and to improve memory function. These properties may help prevent and treat neurodegenerative diseases [22]. Based on the activation of BV2 microglia culture model with lipopolysaccharide (LPS), 10-gingerol was found to be the primary compound responsible for the potent anti-neuroinflammatory properties of fresh ginger. By preventing NF-κB activation, it suppressed the expression of proinflammatory genes, resulting in a decrease in NO, IL-1β, IL-6, and TNF-α levels. Ginger and its bioactive constituents, including 6-shogaol, 6-dehydrogingerdione, and 10-gingerol, have been shown to have anti-AD and anti-PD properties. Ginger's anti-inflammatory and antioxidant properties supported neuroprotection.

Antiobesity Activity

Numerous chronic illnesses, including diabetes, hypertension, and cardiovascular disorders are made more likely by obesity. Ginger is useful in managing and preventing obesity, according to several studies [23]. Compared to gingerols and 6-shogaol, gingerenone A demonstrated a stronger inhibitory effect on adipogenesis and lipid accumulation in 3T3-L1 preadipocyte cells. Additionally, gingerenone A may lessen diet-induced obesity by modulating fatty acid metabolism through the *in vivo* activation of AMPK. The Antiobesity properties of ginger and its bioactive constituents, such as 6-shogaol, 6-gingerol, and gingerenone A, are primarily associated with the stimulation of fatty acid catabolism and the inhibition of adipogenesis.

Protective Effects against Respiratory Disorders

Ginger is one of the natural herbal medicines that have been used for a long time to treat respiratory conditions like asthma. Numerous studies have demonstrated the Broncho dilating and antihypertensive properties of ginger and its bioactive compounds. In the isolated human airway smooth muscle, ginger significantly and quickly relaxed the muscle. According to findings from trachea models in guinea pigs and humans, 6-gingerol, 8-gingerol, and 6-shogaol may cause precontracted airway smooth muscle to relax quickly. In mice, the nebulization of 8-gingerol decreased Ca2+ influx, thereby attenuating airway resistance. Additionally, an enteral diet rich in ginger facilitated gas exchange and shortened the need for mechanical ventilation in patients suffering from acute respiratory distress syndrome (ARDS) [24]. The aforementioned findings suggest that the bioactive components of ginger, such as 6-gingerol, 8-gingerol, 6-shogaol, citral, and eucalyptol, attenuate airway resistance and inflammation and induce relaxation in airway smooth muscle, which in turn has protective effects against respiratory disorders.

Prevention and Treatment of Gastrointestinal Cancer

Ginger and its active ingredients may inhibit the growth and trigger apoptosis of several cancer types, such as skin, ovarian, colon, breast, cervical, oral, renal, prostate, gastric, pancreatic, liver, and brain cancer, according to data from *in vitro*, animal, and epidemiological studies. These characteristics of ginger and its ingredients may be connected to various biological activities as well as anti-inflammatory, anti-mutagenic, and antioxidant qualities. In order to determine whether ginger and its active ingredients have chemo preventive and chemotherapeutic potential, this review has only focused on GI cancers.

According to preclinical research, ginger extract and its components have antitumor and chemo preventive effects on stomach cancer. An *in vitro* study revealed that 6-gingerol causes stomach cancer cells to undergo apoptosis. By enhancing caspase-3/7 activation, it promotes apoptosis induced by TNF-related apoptosis-inducing ligand (TRAIL). 6-gingerol induced apoptosis via cytosolic inhibitor of apoptosis (cIAP)-1 down regulation and blocking trail-induced nuclear factor-kappaB (NF-κB) activation. In addition to 6-gingerol, 6-shogaol also harmed microtubules, which decreased the viability of stomach cancer cells [25]. Ginger extract dramatically decreased the area of the gastric ulcer in Sprague-Dawley rats with ulcers caused by acetic acid. Moreover, the elevated levels of malondialdehyde (MDA) and xanthine oxidase and myeloperoxidase in the ulcerated mucosa were reduced by ginger extract. Therefore, ginger extract acts as an antioxidant to promote ulcer healing and shields the stomach mucosa from harm.

Studies conducted *in vitro* show that components of ginger are effective in preventing liver cancer. According to a study, 6-shogaol causes Mahlavu hepatoma cells to undergo apoptotic cell death through a caspase-dependent, oxidative stress-mediated mechanism. It has been demonstrated that a significant factor in mediating 6-shogaol-induced apoptosis of Mahlavu cells is glutathione (GSH) depletion. According to a recent study by Jeena *et al*. [26], giving mice ginger oil orally for a month increases the antioxidant enzymes SOD, GSH, and glutathione reductase in their blood as well as glutathione-S-transferase, glutathione peroxidase, and SOD in their liver. Additionally, ginger oil significantly reduced the acute inflammation caused by carrageenan and dextran as well as the chronic inflammation induced by formalin [26], suggesting that it may have a preventive effect on the development of liver cancer.

In addition to glutathione, ROS have been implicated in the apoptosis of HepG2 hepatoma cells induced by ginger extract. When HepG2 cells are exposed to 250 μg/mL of ginger extract, their morphology is significantly altered, including cell shrinkage and chromosome condensation. According to a different study, 6-gingerol caused human HepG2 cells to undergo apoptosis via the lysosomal-mitochondrial axis, and cathepsin D was essential to this process. 6-Cathepsin D was released from the mitochondria by gingerol before ROS were produced and cytochrome c was released. Additionally, it is said to shield liver tissue homogenate/mitochondria from lipid peroxidation. The ability of ginger extract to scavenge radicals can be linked to the protective mechanism. In an animal model, ginger prevents the production of free radicals and lowers lipid peroxidation to prevent ethionine-induced liver carcinogenesis. Thus, ginger prevents rat hepatocarcinogenesis.

Additionally effective against pancreatic cancer are ginger and its constituents. 6-gingerol, independent of p53 status, inhibits the growth of BxPC-3 and HPAC pancreatic cancer cells by cell cycle arrest at the G1 phase, as demonstrated by Park *et al*. [27]. Additionally, they discovered that 6-gingerol inhibited the expression of cyclin A and cyclin-dependent kinase (Cdk), which was followed by a decrease in the phosphorylation of retinoblastoma (Rb) and a blocking of the S phase entry. According to a different study, 6-gingerol inhibits the invasion and metastasis of pancreatic cancer cells and controls proteins linked to tight junctions. 6-gingerol's actions were facilitated by blocking the extracellular signal-regulated kinases (ERK) pathway, which in turn inhibited NF-κB/Snail. As a result, 6-gingerol inhibits PANC-1 cells' ability to invade.6-Shogaol, another ingredient in ginger, opens the TRPV1 channels in the pancreatic β-cells, causing Ca2+ signals to be triggered. 6-Shogaol increased intracellular Ca2+ in fura-2 loaded single rat insulinoma (INS-1E) cells in a concentration-dependent manner. The increase in intracellular Ca2+ resulting from 1 μM 6-shogaol was observed to be higher than that obtained from 10 mM glucose.

In addition to research conducted *in vitro*, investigations conducted on animals revealed that 6-shogaol inhibited the growth of pancreatic cancer and enhanced the effects of gemcitabine in preventing tumor growth. The inhibition of NF-κB, cyclooxygenase- (COX-) 2, cyclin D1, survivin, cIAP-1, X-linked inhibitor of apoptosis protein (XIAP), Bcl-2, and matrix metallopeptidase- (MMP-) 9 was the mechanism by which 6-shogaol caused antiproliferation and

sensitization to gemcitabine. Additionally, in a pancreatic cancer xenograft model, it suppressed tumour growth. 6-shogaol's suppression of the tumour's growth was linked to a rise in apoptosis and a drop in the proliferation index (Ki-67). Thus, 6-shogaol, a component of ginger, has antitumor activity in both vitro and *in vivo* models [27].

Conclusion

A natural spice called ginger is used all over the world to give food a strong taste. Moreover, ginger has been utilized as a herbal remedy for common medical issues. For the first time, randomized clinical trials (RCTs) pertaining to the effectiveness of ginger in a variety of human health conditions have been gathered exclusively for this systematic review. Six subsections have been established to address the clinical effects of ginger: Gastrointestinal function, pain, inflammation, metabolic syndromes, nausea and vomiting, and other symptoms. Most studies that have looked at the reduction of nausea and vomiting during pregnancy (NVP), improvement of the expression level of markers for colorectal cancer risk, and anti-inflammatory properties have reportedly found ginger to be beneficial. Trials have also shown that a number of other functions are helpful, with some surprising outcomes. Nonetheless, it is important to acknowledge a few shortcomings pertaining to the caliber of the trials, irregular assessment frameworks or parameters, and the generally modest sample sizes. Therefore, for future clinical trials to address the functional characteristics of ginger, well-designed research with thorough methodological descriptions and a large enough participant pool is required. Studies have shown that ginger can effectively combat a number of gastrointestinal cancers, including cholangiocarcinoma, gastric cancer, pancreatic cancer, liver cancer, and colorectal cancer. Its anticancer effects on pancreatic islet cell cancer and other GI cancers such as duodenal, esophageal, anal, and GI carcinoid Tumors are still unknown.

References

1. Han YA, Song CW, Koh WS, Yon GH, Kim YS, Ryu SY, *et al*. Anti-inflammatory effects of the *Zingiber officinale* Roscoe constituent 12-dehydrogingerdione in lipopolysaccharide-stimulated RAW 264.7 cells. Phytother Res. 2013;27:1200-1205.
2. Stoner GD. Ginger: Is it ready for prime time? Cancer Prev Res. 2013;6:257-262.
3. Nile SH, Park SW. Chromatographic analysis, antioxidant, anti-inflammatory, and xanthine oxidase inhibitory activities of ginger extracts and its reference compounds. Ind Crop Prod. 2015;70:238-244.
4. Zhang M, Viennois E, Prasad M, Zhang Y, Wang L, Zhang Z, *et al*. Edible ginger-derived nanoparticles: A novel therapeutic approach for the prevention and treatment of inflammatory bowel disease and colitis-associated cancer. Biomaterials. 2016;101:321-340.
5. Kumar NV, Murthy PS, Manjunatha JR, Bettadaiah BK. Synthesis and quorum sensing inhibitory activity of key phenolic compounds of ginger and their derivatives. Food Chem. 2014;159:451-457.
6. Citronberg J, Bostick R, Ahearn T, Turgeon DK, Ruffin MT, Djuric Z, *et al*. Effects of ginger supplementation on cell-cycle biomarkers in the normal-appearing colonic mucosa of patients at increased risk for colorectal cancer: Results from a pilot, randomized, and controlled trial. Cancer Prev Res. 2013;6:271-281.
7. Ho S, Chang K, Lin C. Anti-neuroinflammatory capacity of fresh ginger is attributed mainly to 10-gingerol. Food Chem. 2013;141:3183-3191.
8. Akinyemi AJ, Thome GR, Morsch VM, Stefanello N, Goularte JF, Bello-Klein A, *et al*. Effect of dietary supplementation of ginger and turmeric rhizomes on angiotensin-1 converting enzyme (ACE) and arginase activities in L-NAME induced hypertensive rats. J Funct Foods. 2015;17:792-801.
9. Suk S, Kwon GT, Lee E, Jang WJ, Yang H, Kim JH, *et al*. Gingerenone A, a polyphenol present in ginger, suppresses obesity and adipose tissue inflammation in high-fat diet-fed mice. Mol Nutr Food Res, 2017, 61(1700139).
10. Wei C, Tsai Y, Korinek M, Hung P, El-Shazly M, Cheng Y, *et al*. 6-Paradol and 6-shogaol, the pungent compounds of ginger, promote glucose utilization in adipocytes and myotubes, and 6-paradol reduces blood glucose in high-fat diet-fed mice. Int J Mol Sci, 2017, 18(168).
11. Walstab J, Krueger D, Stark T, Hofmann T, Demir IE, Ceyhan GO, *et al*. Ginger and its pungent constituents non-competitively inhibit activation of human recombinant and native 5-HT3 receptors of enteric neurons. Neurogastroent Motil. 2013;25:439-447.
12. Townsend EA, Siviski ME, Zhang Y, Xu C, Hoonjan B, Emala CW, *et al*. Effects of ginger and its constituents on airway smooth muscle relaxation and calcium regulation. Am J Resp Cell Mol. 2013;48:157-163.
13. Demin G, Yingying Z. Comparative antibacterial activities of crude polysaccharides and flavonoids from *Zingiber officinale* and their extraction. Am J Trop Med. 2010;5:235-238.
14. Grzanna R, Lindmark L, Frondoza CG. Ginger-an herbal medicinal product with broad anti-inflammatory actions. J Med Food. 2005;8(2):125-132.
15. Langner E, Greifenberg S, Gruenwald J. Ginger: History and use. Adv Ther. 1998;15(1):25-44.
16. Shukla Y, Singh M. Cancer preventive properties of ginger: A brief review. Food Chem Toxicol. 2007;45(5):683-690.
17. Tyler VE. The Therapeutic Use of Phytomedicinals. New York, NY: Pharmaceutical Products Press; c1994.
18. 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(2):409-420.
19. Govindarajan VS. Ginger-chemistry, technology, and quality evaluation. Part 1. Crit Rev Food Sci Nutr. 1982;17(1):1-96.
20. Harold M. On Food and Cooking: The Science and Lore of the Kitchen. 2nd Ed. New York, NY: Scribner; c2004.
21. Ji K, Fang L, Zhao H, Li Q, Shi Y, Xu C, *et al*. Ginger oleoresin alleviated gamma-ray irradiation-induced reactive oxygen species via the Nrf2 protective response in human mesenchymal stem cells. Oxid Med Cell Longev. 2017;2017:1480294. DOI: 10.1155/2017/1480294.
22. Huh E, Lim S, Kim HG, Ha SK, Park H, Huh Y, *et al*. Ginger fermented with *Schizosaccharomyces pombe* alleviates memory impairment via protecting hippocampal neuronal cells in amyloid beta (1-42) plaque injected mice. Food Funct. 2018;9:171-178. DOI: 10.1039/C7FO01149K.

23. Mahmoud RH, Elnour WA. Comparative evaluation of the efficacy of ginger and orlistat on obesity management, pancreatic lipase and liver peroxisomal catalase enzyme in male albino rats. Eur Rev Med Pharmaco. 2013;17:75-83.
24. Shariatpanahi ZV, Mokhtari M, Taleban FA, Alavi F, Surmaghi MHS, Mehrabi Y, *et al*. Effect of enteral feeding with ginger extract in acute respiratory distress syndrome. J Crit Care. 2013;28:217. e6.
25. Ishiguro K, Ando T, Maeda O. Ginger ingredients reduce viability of gastric cancer cells via distinct mechanisms. Biochem Biophys Res Commun. 2007;362(1):218-223.
26. Jeena K, Liju VB, Kuttan R. Antioxidant, anti-inflammatory and antinociceptive activities of essential oil from ginger. Indian J Physiol Pharmacol. 2013;57(1):51-62.
27. 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;47(5):688-697.