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

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Abstract

Background:

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

Methods:

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

Conclusions:

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

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

INTRODUCTION

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

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

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

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

METHODS

We conducted a comprehensive search in the following databases: MEDLINE, EMBASE, in order to identify relevant studies. The electronic search was conducted in July 2012, and developed in collaboration with an experienced librarian. Time restriction were applied to year of

publication from 2000-2012 and we used literatures only from English language and studied both human and animal models. All titles and abstracts were examined that met our search terms and full publications were reviewed, when necessary. Medline search with the terms: [Ginger] AND [anti-oxidative] and [Ginger] AND [anti-inflammatory], then we had 211 articles. Review articles were only included in this review if they offered new insights or opinions. We could achieve only to 59 articles from these articles and summarized 12 full text studies in the table.

DISCUSSION

Anti-oxidative stress effects

The rich phytochemistry of ginger includes components that scavenge free radicals produced in biological systems. For the purpose of energy production, some free radicals which generated during the process of oxidation are essential.[11] Increased production of free radicals results in oxidative stress that can lead to DNA damage.[12] In such circumstances of imbalance, extra antioxidant supplementation through dietary modules is essential for organism vitality.[13] The anti-oxidative properties of ginger and its components have been explored in various *in vitro* and *in vivo* tests. Strengthening the body's defenses by improving the antioxidant status will undoubtedly protect human against many chronic diseases.[2] 6-Shogaol has exhibited the most potent antioxidant and anti-inflammatory properties in ginger, which can be attributed to the presence of alpha, beta-unsaturated ketone moiety.[9] Animal modeling showed that ginger significantly lowered induced lipid peroxidation and raised the levels of antioxidant enzymes, together with serum glutathione.[14] Furthermore, feeding ginger to rats at 1% w/w during administration of malathion (20 ppm) for 4 weeks significantly attenuated malathion-induced lipid peroxidation.[15] Concomitant dietary feeding of ginger (1%w/w) significantly attenuated lindane-induced lipid peroxidation, reduced glutathione (GSH), and the GSH-dependent enzymes glutathione peroxidase, glutathione reductase, and glutathione S-transferase.[16] *In vitro*, zingerone scavenged O^{2-} and OH and suppressed lipid peroxidation, so it can possibly value in treatment of Parkinson's disease.[17]

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

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

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

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

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

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

Anti-inflammatory effects

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

Gingerol, shogaol, and other structurally-related substances in ginger inhibit prostaglandin and leukotriene biosynthesis through suppression of 5-lipoxygenase or prostaglandin synthetase. Additionally, they can also inhibit synthesis of pro-inflammatory cytokines such as IL-1, TNF-α, and IL-8.[24,25] In another investigation, Pan *et al*. showed that in macrophages,[6] shogaol can down-regulate inflammatory iNOS and COX-2 gene expression.[26] Jung *et al*. indicated that rhizome hexane fraction extract of *Z. officinale* inhibited the excessive production of NO, PGE (2), TNF-alpha, and IL-1beta.[27] Because of potent compounds in ginger rhizome for inhibiting allergic reactions, it may be useful for the treatment and prevention of allergic diseases.[28]

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

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

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

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

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

Anti-cancer effects

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

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

In gastric cancer, the tumor necrosis factor-related inducing apoptosis ligand (TRIALS) plays a major role by promoting apoptosis. Cascades of caspase proteins activate by ginger and its functional components.[45] Ishiguro *et al*. explained a model for [6]-gingerol and[6]-shogaol action against gastric cancer cells. They observed that [6]-gingerol inhibits TRAIL-induced NF-κB activation by impairing the nuclear translocation of NF-κB, suppresses cIAP1 expression, and increases TRAIL-induced caspase-3/7 activation.[38]

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

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

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

Zhang *et al*. showed that zerumbone induced apoptosis in pancreatic carcinoma cells through p53 signal pathway, formation of apoptotic

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

Anti-diabetic effects

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

We summarized 12 studies from these articles in Table 1.

CONCLUSIONS

The health-promoting perspectives of ginger are well known. It can treat a wide range of diseases via immunonutrition and anti-inflammatory responses. As a result of anti-inflammatory effect of ginger, it can reduce muscle pain after intense physical activity. Likewise, the anticancer potential of ginger is well documented and its functional ingredients like gingerols, shogaol, and paradols are the valuable ingredients which can prevent various cancers, angiogenesis and metastasis, induction of apoptosis, and inhibition of cell-cycle progression. Besides these, it improves cardiovascular disorders, diabetes mellitus, and gastrointestinal health.

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

Footnotes

Source of Support: Nil

Conflict of Interest: None declared

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Figures and Tables

Table 1

Author	Year	Topic	Aim of study	Conclusion
Hussein[12]	[2005]	Anti-oxidative stress effects	Examine radioprotective effects of melatonin against X-ray induced skin damage	Carcinogenic effects of X-ray and melatonin has radioprotective role
Ahmed Hassan El-Ghorab[22]	[2010]	Anti-oxidative stress effects	Investigate anti-oxidative activity of ginger and Cumin	Both ginger and Cumin can be useful as anti-oxidant in foods
Ghasemzadeh[23]	[2010]	Anti-oxidative stress effects	Evaluate two Zingiber varieties to compare the medicinal potential	Ginger has potential medicinal properties in leaves and young rhizomes
Habib[29]	[2008]	Anti-inflammatory effects	Evaluate the effect of ginger extract on the expression of NFκB and TNF-α in liver cancer-induced rats	Ginger extract significantly reduced the elevated expression of NFκB and TNF-α in rats with liver cancer
Jeong[36]	[2009]	Anti-cancer effects	Evaluate anti-inflammatory and anti-cancer effects of gingerols	Indicate a crucial role of LTA[4] H in cancer and also support the anticancer efficacy of [6]-gingerols
Sung[39]	[2008]	Anti-cancer effects	Identification of zerumbone as a regulator of CXCR[4] expression	Zerumbone has a potential in the suppression of cancer metastasis
Sung[43]	[2009]	Anti-cancer effects	Examined whether zerumbone could prevent human breast cancer-induced bone loss in animals	Zerumbone decreased osteolysis in a dose-dependent manner
Yodkeeree[45]	[2009]	Anti-cancer effects	Investigate zerumbone, can enhance the anticancer effects of TRAIL	Zerumbone can potentiate TRAIL-induced apoptosis and resulting in enhancement of the anticancer effects of TRAIL
Yagihashi[46]	[2008]	Anti-cancer effects	Investigate the effect of [6]-gingerol on the proliferation and invasion of AH[109]A cells in culture	Antioxidative property of [6]-gingerol may be involved in its anti-invasive activity of hepatoma cells
Rhode[49]	[2007]	Anti-cancer effects	Investigated the effect of ginger on tumor cell growth in ovarian cancer cells	Ginger inhibits growth and modulates secretion of angiogenic factors in ovarian cancer cells
Zhang[50]	[2012]	Anti-cancer effects	Investigate if zerumbone will produce the anticancer effects on pancreatic carcinoma cell lines	Zerumbone was able to induce apoptosis of pancreatic carcinoma cell lines

Twelve selected studies with full text article