ANTICANCER PROPERTIES OF ZINGIBER OFFICINALE – GINGER: A REVIEW

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ABSTRACT

Carcinogenesis and transformation of a normal cell to tumor is caused by many environmental, lifestyle and biological factors. Cancer incidence and death cases also increased gradually. Developing new, early detection methods, risk assessment, creating awareness on healthy food habits, preventive measures may help in prevention of many diseases including cancer. Providing effective anticancer drugs to treat cancer is one of the major requirements in cancer therapy.

Many plants and their products have active anticancer agents. Ginger is considered as an important spice with many clinical potential activities. Ginger and its compounds display anti-inflammatory, antioxidant, antimetastatic and anticancer agent. The anticancer activity of ginger components is reviewed in this article due to its versatile therapeutic nature.

KEYWORDS: Cytotoxic, Carcinoma, Zinger, Natural Products and Anticancer Drugs, Cancer, Signaling, Medicinal Plants, Inhibitors

INTRODUCTION

Zingiber officinale (ginger) belongs to Zingiberaceae is an essential spice, condiment and traditional medicine for many human ailments and is used worldwide since ancient period. Indian and Jamaican ginger are considered superior followed by the West African variety. Jamaican ginger possesses delicate and flavor and is sometimes as first grade. Nigerian dried ginger possess a camphorhaceous and a coarser odor and is rich in both aroma and pungency factors. Chinese ginger is low pungency and mainly exported as preserves in sugar syrup or sugar candy (Govindarajan, 1982a, 1982b; Vasala, 2004; Kafer and Milner, 2008)

Ginger root and its main phenolic compounds such as gingerols and zerumbone have anticarcinogenic activity, antioxidant and anti inflammatory activity. Specially, the constituents of ginger root (figure 1) can inhibition of activation of NF-kB induced by a variety of various factors (Shukla and Singh, 2006; Ahmad et al., 2001; Katiyar et al., 1996; Park and Pezzuto, 2002, Surh, 1999- 2008; Manju and Nalini, 2005; Baliga et al., 2011). Ginger candy, ginger bread, biscuits, pickles, and ginger flavoured carbonated drinks (Arctangder, 1960; Bakhru, 1999).

Ginger tea or masala chai is a special tea prepared in India. In India is also considered as one of the traditional cooking spice (Murray, 1995). It is typically consumed as a fresh paste, dried powder and is an indispensable component of curry powder and sauces. Study of the anticancer, antioxidant, and antimycobacterial activities were performed by using the extracts of rosemary (Rosmarinus officinalis L.), turmeric (Curcuma longa L.) and ginger (Zingiber officinale Roscoe). The anticancer activity was tested against nine different types of human cancers. The extract of ginger and turmeric showed anticancer activities (Leal et al., 2003).
Clinical Significance of Ginger

Many of the herbs and spices possess an array of biochemical and pharmacological activities including anti-inflammatory and antioxidant properties that are believed to contribute to their antimutagenic and anticarcinogenic activities (Awang, 1992; Bakhru, 1999; Chen et al., 2011; Aggarwal and Shishodia, 2006; Ahmed and Sharma, 1997). The spice ginger contains gingerol, a phenolic substance mainly and has diverse pharmacologic effects such as anti-inflammatory, antioxidant, and anti-apoptotic effects.

Since tumor promotion is closely linked to inflammation and oxidative stress, a compound that exhibits anti-inflammatory and/or antioxidant properties could act as an anti-carcinogenic agent (Grzanna et al., 2005; Rhode et al., 2007; Sang et al., 2009; Butt and Sultan, 2011). The ginger has significant role in treating some diseases including gastrointestinal complications, treat stomach upset, diarrhea, rheumatic disorders, nausea, common colds, fever, and dizziness. And also ginger possesses antineoplastic and chemopreventive properties (Pereira, 2011; Baliga et al., 2011).

Chemical Composition of Ginger

Ginger contains two distinct groups of chemicals and they are volatile and non-volatile compounds (Table 1). The volatile oil components consist mainly of sesquiterpene hydrocarbons, predominantly zingiberene (35%), curcumene (18%) and farnesene (10%), with lesser amounts of bisabolene and b-sesquiphellandrene. A smaller amount of at least 40 different monoterpene hydrocarbons are present with 1, 8-cineole, neral, borneol, linalool, and geraniol being the most abundant and many of these volatile oil components contribute to the distinct aroma and taste of ginger (Govindarajan, 1982). Ginger contains biologically active constituents including the non-volatile pungent principles, such as the gingerols, paradols, shogaols, and zingerone that produce a hot sensation (Shukla and Singh, 2007; WHO 2008).

The ginger contains zingiberene and 6- gingerol being the important constituents in stomachic medications. The gingerols were identified as the major active components in the fresh rhizome and are a series of chemical homologs differentiated by the length of their unbranched alkyl chains (Govindarajan, 1982). In addition, the shogaols, dehydrated form of the gingerols, are the predominant pungent constituents in dried ginger (Connell and Sutherland, 1969).

Paradol is similar to gingerol and is formed on hydrogenation of shogoal. In addition to the extractable oleoresins, ginger contains many fats, vitamins, carbohydrates, waxes, and minerals. Ginger rhizomes also contain zingibain a potent proteolytic enzyme (Shukla and Singh, 2007).
Anticancer Properties of Ginger

Ginger rich with many active components. The [6]-gingerol, a major pungent ingredient of ginger is a potent anti-angiogenic activity in vitro and in vivo. And [6]-gingerol may inhibit tumor growth and metastasis via its anti-angiogenic activity (Kim et al., 2005a,b). Topical application of [6]-gingerol inhibited COX-2 (cyclooxygenase-2) expression along with suppressed NF-κB DNA binding activity in mouse skin (Kim et al., 2004).

The proposed mechanisms of action of gingerol involved in anticancer and chemopreventive properties via multiple pathways that includes the inhibition of cyclooxygenase -2 (COX-2) expression by inhibiting p38 MAPK–NF-xB (mitogen activated protein kinase – necrosis factor kappa B) signaling pathway (Shukla and Singh, 2007). Ginger is a natural antioxidant and anticarcinogenic dietary component. The treatment with ginger on ovarian cancer cells in vitro revealed that inhibition in growth of cells effectively by 6- Shogaol and also inhibition of NF-κB activation and decreases VEGF (growth factor) and IL-8 secretion. Ginger components modulate secretion of angiogenic factors in ovarian cancer cells in vitro and act as potent chemopreventive dietary agent (Rhode et al, 2007).

A novel anticancer drug β- elemene is extracted from the ginger plant and it triggers apoptosis mediated through a mitochondrial release of the cytochrome c in non-small-cell lung cancer cells. The β-elemene induces caspase-3, -7 and -9 activities, decreases Bcl-2 expression, causes cytochrome c release and increases the levels of cleaved caspase-9 and poly (ADP-ribose) polymerase in cells (Wang et al., 2005). Enhanced enzyme activity of glutathione reductase (GR), glutathione peroxidase (GPX), glutathione -S- transferase (GST) leads to the suppression of colon carcinogenesis by ginger supplement. Ginger is very effectively reduces the colon cancer (Manju and Nalini, 2005).

Ginger and its component [6]- gingerol is effective against ovarian cancers in vivo. Ginger inhibits necrosis factor kappa -B (NF-kB) and also interleukin-8 (IL-8) inhibitions (Rhode et al., 2007). The [6]- gingerol is effective in suppressing growth of colon tumor in mice (Jeong et al., 2009); [6]- gingerol acts against skin cancer (Nigam et al., 2009); breast cancer (Lee et al., 2008); ovarian cancer (Rhode et al., 2007); [6]- gingerol and [6] shogals inhibits gastric cancer (Ishiguro et al., 2007). The ginger constituents including [6] - shogaol, [6] - gingerol, [8] – gingerol and

Table 1: The Chemical Composition of Ginger Rhizome and Uses of Ginger

<table>
<thead>
<tr>
<th>S No</th>
<th>Chemical Composition (in %)</th>
<th>Volatile Oil Consists: The Monoterpenes &amp; Sesquiterpenes</th>
<th>Non-Volatile Oil Contains</th>
<th>Other Constituents</th>
<th>Uses of Ginger</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Protein: 9%</td>
<td></td>
<td>A series of homologs with linear alkyl chains [3-6], [8]-[10],and [12]-gingerols; and having a side-chain with 7–10, 12, 14, or 16 carbon atoms.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Fatty oil: 3-6%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Crude fiber: 3- 8%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Ash: 8%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Water: 9-12%</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>7</td>
<td>Volatile oil : 2-3%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>And also contains:</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>Vasala, 2004;</td>
<td></td>
<td></td>
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</tbody>
</table>

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[10]-gingerol were examined on humans to study pharmacokinetic properties of anticancer agents. (Zick et al., 2008). Another ginger compound [6]-paradol displays anticancer activity against skin cancer (Surh et al., 1999).

Reduced the elevated expression of tumor necrosis factor - alfa (TNF-α) and NF-κB by extract ginger in liver cancer of rat (Habib et al., 2008). The supplementation of ginger reduced lipid peroxidation and acts as an antioxidant via which it suppressed liver carcinogenesis (Yasmin Anum Mohd Yusof et al., 2009). There are three ginger compounds include [6], [8], [10] - Shagaols are much stronger against tumor growth, observed in H-1299 human lung cancer cells and among these three [6]-Shagaol shows potential agent than [6]-gingerol (sang et al., 2009).

Growth of colon and lung cancer in mouse was suppressed and activates apoptosis by Zerumbone (Kim et al., 2008); Zerumbone inhibits NF-kB activation in osteoclastogenesis in mouse (Sung et al., 2009); Zerumbone induces apoptosis in colon cancer and inhibits gastric cancers (Yodkeeree et al., 2009). There are two important target specific mechanisms in cancer therapy and they are telomerase inhibition and c-Myc inhibition. The ginger extract might prove to be a potential agent in cancer prevention and maintenance therapy (Tuntiwechapikul et al., 2010).

Anti-metastasis activity of 6-Shogaol was observed in vitro and 6-Shogaol is active against breast cancer (Ling et al., 2010). Study on the pharmacokinetic properties of anticancer agents identified from some of the important medicinal herbs was performed (Chen et al., 2011). Two Bangladeshi ginger varieties (Fulbaria and Syedpuri) used to find out antioxidant and anticancer activities against MCF-7 and MDA-MB-231, two human breast cancer cell lines (Rahman et al., 2011).

Fresh ginger contains various phytochemicals with biological activities relevant in disease associated with reactive oxygen species (ROS). From the root bark of the fresh ginger, isolated about 29 phenolic compounds and their structures were fully characterized. They have examined the effect of these compounds against nine human tumor cell lines to study about their anticancer activity. The cytotoxic property in cell lines exhibited by three compounds, 6-shogaol, 10- gingerol and enone- diarylehtanoids analog of curcumin (Peng et al., 2012). Terpenoids of ginger induces apoptosis by activation of p53 in an endometrial cancer cells (Yang Liu et al., 2012). Ginger root effective on COX-1 in Colon cancer (Yan Jiang et al., 2013). The major compound of ginger [6]-Shogaol are active in cancer cells (Yingdong Zhu et al., 2013).

### Table 2: Anticancer Activity of Ginger and Compounds of Ginger against Cancer

<table>
<thead>
<tr>
<th>S. No</th>
<th>Compound Name</th>
<th>Cancer</th>
<th>Mechanism</th>
<th>Cell Lines/System</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>β-Elemene</td>
<td>non-small-cell lung cancer cells</td>
<td>release of cytochrome c</td>
<td>In vitro</td>
<td>Wang et al., 2005</td>
</tr>
<tr>
<td>2</td>
<td>Ginger – whole and [6]-gingerol.</td>
<td>Ovarian cancer</td>
<td>Inhibiton NF-κB ; tumor growth</td>
<td>In vitro</td>
<td>Rhode et al., 2007</td>
</tr>
<tr>
<td>3</td>
<td>Ginger extract</td>
<td>Liver cancer</td>
<td>Reduced the elevated expression of TNF-αand NF-κB</td>
<td>rats.</td>
<td>Habib et al., 2008</td>
</tr>
<tr>
<td>4</td>
<td>[6]-gingerol</td>
<td>Breast cancer</td>
<td>Inhibits cell adhesion invasion motility</td>
<td>In vitro</td>
<td>Lee et al., 2008</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Skin cancer.</td>
<td>Enhances apoptosis</td>
<td>Mouse</td>
<td>Nigam et al., 2009</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Colon cancer</td>
<td>Inhibition of leukotriene activity</td>
<td>mice</td>
<td>Jeong et al., 2009</td>
</tr>
<tr>
<td>5</td>
<td>Zerumbone</td>
<td>Lung and colon cancer</td>
<td>Suppresses modulatory mechanisms of growth and induce apoptosis. Reduces expression of NF-κB.</td>
<td>mouse</td>
<td>Kim et al., 2008</td>
</tr>
</tbody>
</table>
CONCLUSIONS

Earlier research results conclude that ginger is an essential spice with many active principles. Ginger compounds involved in neutralizing many functions of a cell in unfavorable conditions, disease and cancer. The mechanism involved in the chemopreventive effects of ginger are contribute by free radical scavenging, antioxidant pathways, alteration of gene expressions and induction of apoptosis and thus cause decrease in tumor initiation, promotion and progression.

ACKNOWLEDGEMENTS

I thank UGC, New Delhi for providing financial assistance and was supported by the UGC Major Research Project. I thank BADRI KAMESHWAR RAO, USA, Prof. D.V.R. Sai Gopal, Head Department of Virology, S.V.University and Prof. S.D.S. Murthy, Head, Department of Biochemistry, S.V.University, Tirupati, AP, India.

Note: I thank all the authors quoted in this article for their contribution and their research on novel anticancer drug development.

REFERENCES


