



GINGER MEDICINAL USES AND BENEFITS

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ABSTRACT

Ginger is a spice that has traditionally been treated as medicine in both Traditional Chinese Medicine (/supplements/traditional-chinese-medicine/) and Ayurveda (/supplements/ayurveda/), doses of 1-3g can reduce nausea and ease digestion quite effectively; superloading the powdered rhizome (vertical root) at 10-15g daily might increase Testosterone (/topics/testosterone/). The metabolic syndrome is associated with an increased risk of development and progression of chronic kidney disease. Renal inflammation is well known to play an important role in the initiation and progression of tubulointerstitial injury of the kidneys. Ginger, one of the most commonly used spices and medicinal plants, has been demonstrated to improve diet-induced metabolic abnormalities. However, the efficacy of ginger on the metabolic syndrome-associated kidney injury remains unknown.

KEYWORDS: Ginger, Anti inflammatory, Anticancer, Anticoagulant.

INTRODUCTION

Ginger (*Zingiber officinale* Roscoe, Zingiberaceae) is widely used around the world in foods as a spice. Native to tropical Asia, ginger is a perennial cultivated in the tropical climates of Australia, Brazil, China, India, Jamaica, West Africa, and parts of the United States (Langner E et al 1998). Ginger rhizome has a long history of use in Chinese and Ayurvedic medicine as an antiemetic, antipyretic, and anti-inflammatory agent. Here, the aim was to summarize the more recent and common actions and therapeutic application of ginger and its active constituents (Leung AY et al). The modern times have witnessed advancement in the treatment of Rheumatoid Arthritis. The DMRAD's are therapeutic agents which rapidly reduce the severity of inflammation. Today the goal of the treatment is complete remission (Emery P et al 2005). Ayurveda is also a time-tested Health Science serving the mankind since ages. The sages of Ayurveda invented many remedies to combat this disease. Chakrapani was the pioneer to lay down the line of treatment of Amavata (in the book titled Chakra Duttam, Amavata Rogadhikara, authorized by him) (Chakradutta Amavatadhikara et al 2007). It has been known from ancient times that essential oils from aromatic and medicinal plants possess biological activity, antibacterial, antifungal and antioxidant properties. Due to the growing interest in the use of essential oils in both the food and the pharmaceutical industries, a systematic study on these plant extracts have become very important. Spices were used from ancient times for different purposes viz

flavouring, keeping away the pests, and in perfumery. Ginger is a rhizomatous plant grown throughout South-eastern Asia, China and in parts of Japan, Austria, Latin America, Jamaica and Africa. Ginger has been used as a spice and medicine in India and China since ancient times. Ginger plants were grown in pots and carried to abroad on sea long voyages to prevent scurvy. The spice was known in Germany and France in the ninth century and in England in 10th century for its medicinal properties. Many oils exhibit antimicrobial properties due to the presence of components such as thymol, eugenol, 1,8- cineole, α - and β - pinenes, linalool, α - terpineol etc (Srivastava A et al 2000, Sinha GK 1990). Since these compounds and their relative concentration vary from oil to oil and from different oils which accounts for a varied antimicrobial activity (Santos FA et al 1997).

CAUTION

Castor oil should not be used indiscriminately by patients suffering from infections of the kidney, bladder, bile duct, and intestines, or by those suffering from Jaundice. It should not be used by pregnant or lactating women. No health hazards or side effects have been noticed if this oil is administered properly in prescribed doses. Long-term use of this oil can lead to loss of electrolytes, in particular, Potassium ions. This can result in hyper aldosteronism, and inhibition of intestinal motility.

Phytoconstituents

The constituents of ginger are numerous and vary depending on the place of origin and whether the rhizomes are fresh or dry but to summarize the major components that have been implicated in the pharmacological activities of the crude drug. The primary pungent agents (phenylalkylketones or vanillyl ketones) of ginger are gingerol, with other gingerol analogues such as the shogaols, paradol and zingerone

also found in high levels in rhizome extracts. The major pharmacological activity of ginger appears to be due to gingerol and shogaol (Duke and Beckstrom 1999). Phenylalkylketones or vanillyl ketones of ginger include 6-gingerol 8- gingerol and 10-gingerol, 6-shogaol, 8-shogaol, 10-shogaol and zingerone. 6-paradol, 6- and 10-dehydrogingerdione and 6- and 10- gingerdione have also been identified (Chrubasik JE *et al* 2007).

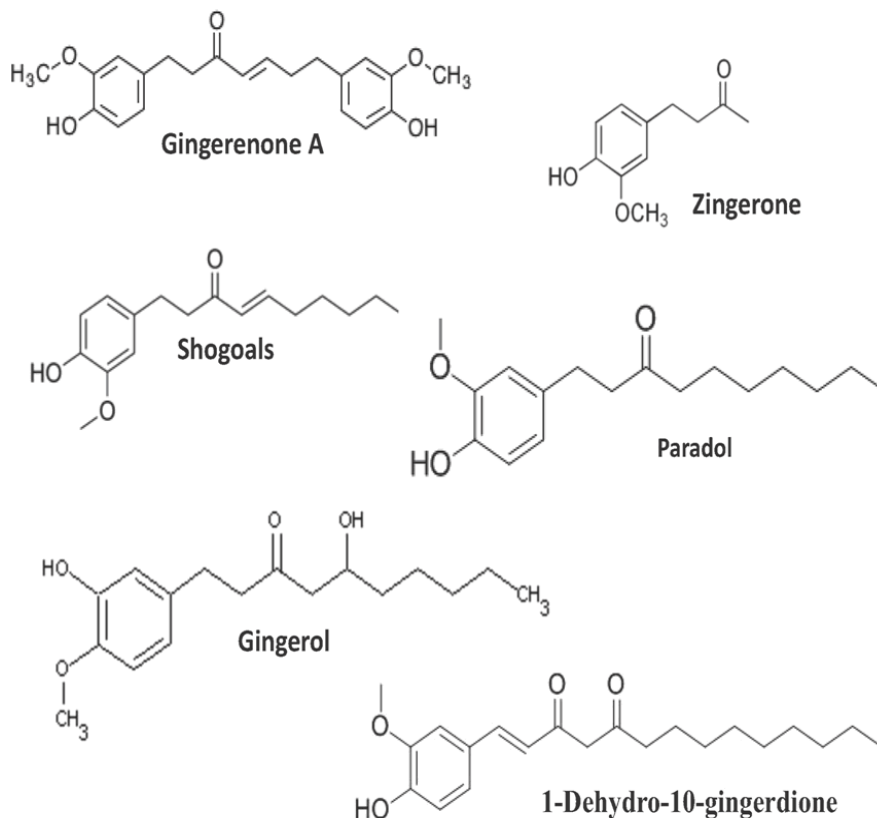


Fig.1: Chemical structure of active ingredient of ginger (Arshad H Rahmani *et al.*, 2014)

IR of Ginger oil

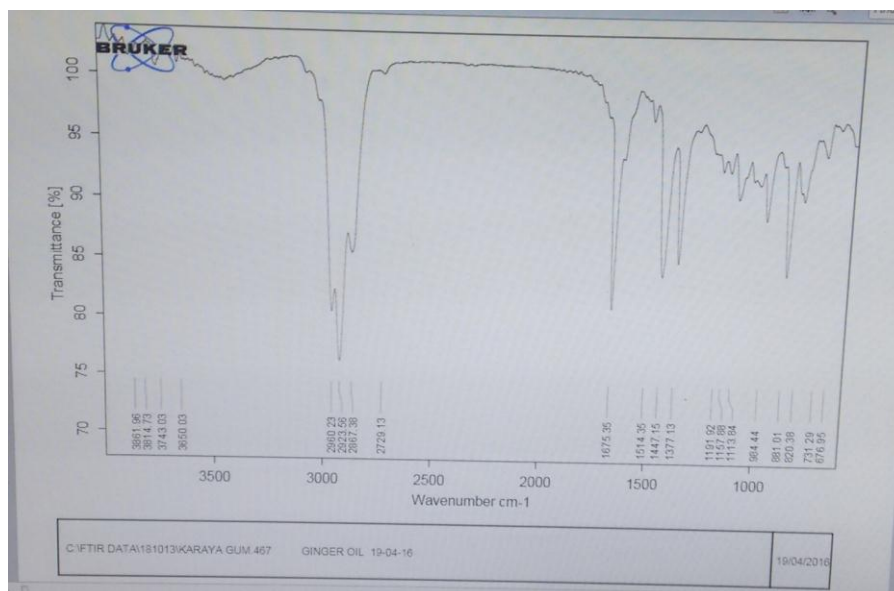


Fig 2: IR of Ginger oil

PHARMACOLOGY

Anti-inflammatory action of ginger

The anti-inflammatory properties of ginger have been known and valued for centuries. The original discovery of ginger's inhibitory effects on prostaglandin biosynthesis in the early 1970s has been repeatedly confirmed. This discovery identified ginger as an herbal medicinal product that shares pharmacological properties with nonsteroidal anti-inflammatory drugs. Ginger suppresses prostaglandin synthesis through inhibition of cyclooxygenase-1 and cyclooxygenase (Vanden BNR *et al* 2000). An important extension of this early work was the observation that ginger also suppresses leukotriene biosynthesis by inhibiting 5-lipoxygenase. This pharmacological property distinguishes ginger from nonsteroidal anti-inflammatory drugs. This discovery preceded the observation that dual inhibitors of cyclooxygenase and 5-lipoxygenase may have a better therapeutic profile and have fewer side effects than nonsteroidal anti-inflammatory drugs. The characterization of the pharmacological properties of ginger entered a new phase with the discovery that a ginger extract (EV.EXT.77) derived from *Zingiber officinale* (family Zingiberaceae) and *Alpinagalanga* (family Zingiberaceae) inhibits the induction of several genes involved in the inflammatory response. These include genes encoding cytokines, chemokines, and the inducible enzyme cyclooxygenase-2. This discovery provided the first evidence that ginger modulates biochemical pathways activated in chronic inflammation. The earlier report suggested that in Rheumatoid arthritis (RA) and Osteoarthritis (OA) patients, use of powdered ginger for 3-month to 2.5-year period, reduce pain and inflammation in 75% patients without any adverse effect and suggested ginger is an anti-inflammatory agent (Srivastava KC *et al* 1992). 6-gingerol acts as an anti-inflammatory compound that may be useful to treat inflammation without interfering with antigen presenting function of macrophages (Tripathi S *et al* 2007). It has been also recently observed that Synergistic effect of Ginger with anti-tuberculosis treatment were more beneficial effect rather than only ATT (anti-tuberculosis treatment) in anemic Pulmonary tuberculosis Patients and concluded that ginger supplementation in such patients not only increases absorption of iron but also significant decreases in CRP, Ferritin and significant increase in serum iron, total iron binding capacity, which in turn correct anemia (Subodh K *et al* 2013).

Anticancer Properties of Ginger

Ginger rich with many active components. The [6]-gingerol, a major pungent ingredient of ginger is a potent antiangiogenic 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- κ B 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- κ B (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- κ B 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- κ B) 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 14 Ranjani Ramakrishnan [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- κ B 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- κ B 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-diarylheptanoids 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).

Anticoagulant Effects

Ginger has been shown to inhibit platelet Aggregation (Wang CC *et al* 2003 Mahadev GB *et al* 2003, Nurthahja *et al* 2003) and to decrease platelet thromboxane production in vitro (Guh JH *et al* 1995, Srivastava KC *et al* 1986, Nurtjahja *et al* 2003). (8)- Gingerol, (8)-shogaol, (8)-paradol, and gingerol analogues (1 and 5) exhibited antiplatelet activities. (Nurtjahja *et al* 2003) However, its effects in vivo have not been well studied. Although Verma *et al.* found ginger to decrease platelet Aggregation (Verma SK *et al* 1993), Lumb found no effect of ginger on platelet count, bleeding time, or platelet aggregation (Lumb AB *et al* 1994). Similarly, Bordia *et al.* found ginger to have no effect on platelet aggregation, fibrinolytic activity, or fibrinogen levels. (Bordia A *et al* 1997) Janssen *et al.* showed no effect of oral ginger on platelet thromboxane B2 production (Janssen PL *et al* 1996), while Srivastava found thromboxane levels to be decreased by ginger ingestion in a small study (Srivastava KC *et al* 1989)

Antiemetic Effects

The mechanism of action of ginger's effect on nausea and vomiting remains uncertain.

However, there are several proposed mechanisms. The components in ginger that are responsible for the antiemetic effect are thought to be the gingerols, shogaols, and galanolactone, a diterpenoid of ginger (Bhattarai S *et al* 2001, Yamahara J *et al* 1989, Huang Q *et al* 1991). Recent animal models and in vitro studies have demonstrated that ginger extract possesses

antiserotonergic and 5-HT₃ receptor antagonism effects, which play an important role in the etiology of postoperative nausea and vomiting (Lumb AB *et al* 1993, Yamahara J *et al* 1989, Huang Q *et al* 1991). In a randomized, placebo-controlled, crossover trial of 16 healthy volunteers, ginger (1g orally) had no effect on gastric emptying. It appears unlikely that ginger's antiemetic or antinausea effects are mediated through increased gastro duodenal motility or through increased gastric emptying. Using gastro duodenal manometry, Micklefield *et al.* demonstrated that oral ginger increases antral motility during phase III of the migrating motor complex (MMC) and increases motor response to a test meal in the corpus. However, ginger had no significant effect in the antrum or corpus during other phases, except for a significant decrease in the amplitude of antral contractions during phase II of the MMC. Additionally, there was no effect of ginger on duodenal contractions or on the "motility index."

Antinociceptive Effects

(6)-shogaol has produced anti-nociception and inhibited the release of substance P in rats, seemingly via the same receptor to which capsaicin binds. However, it was observed to be 100 times less potent and to elicit half the maximal effect of capsaicin (Ma J *et al* 2004).

Antioxidant Effects

In vitro, ginger has been shown to exhibit antioxidant effects (Fuhrman B *et al* 2000). (6)-gingerol appears to be the antioxidant constituent present in ginger, as it was shown to protect HL-60 cells from oxidative stress (Wang CC *et al* 2003). Ginger oil has dominative protective effects on DNA damage induced by H₂O₂. Ginger oil might act as a scavenger of oxygen radical and might be used as an antioxidant (Ma J *et al* 2004).

Cardiovascular Effects

In vitro research indicates that gingerols and the related shogaols exhibit cardio depressant activity at low doses and cardiotonic properties at higher doses (Wang CC *et al* 2003). Both (6)-shogaol and (6)- gingerol, and the gingerdiones, are reportedly potent enzymatic inhibitors of prostaglandin, thromboxane, and leukotriene biosynthesis (Rajesh Kumar Mishra *et al* 2012).

Gastrointestinal Effects

There is evidence that ginger rhizome (root) increases stomach acid production. If so, it may interfere with antacids, sucralfate (Carafate), H₂ antagonists, or proton pump inhibitors. In contrast, other in vitro and animal studies have revealed gastro protective properties (Thomson M *et al* 2002, Al Yahya *et al* 1989) in addition, (6) shogaol, generally more potent than (6)-gingerol, has inhibited intestinal motility in intravenous preparations and facilitated gastrointestinal motility in oral preparations. Ginger extract has also been reported to inhibit the growth of *Helicobacter pylori* in vitro (Srivastava KC *et al* 1984) However, Desai *et al.* observed a significant increase in the exfoliation of

gastric surface epithelial cells following the consumption of 6g or more of ginger (after examining gastric aspirates in 10 healthy volunteers) (Desai HG *et al* 1990).

Antitussive Effects

(6)-shogaol, generally more potent than (6)-gingerol, has exhibited antitussive effects (Suekawa M *et al* 1984).

Immunomodulatory Effects

In vitro evidence indicates that ginger has immunomodulatory effects and is an effective antimicrobial and antiviral agent (Miri P *et al* 2008).

Lipid Effects

Oral ingestion of ginger extract has been shown to have hypocholesterolemic, hypolipidemic, and antiatherosclerotic effects in cholesterol-fed rabbits¹⁴ and in rats¹⁶. Inhibition of LDL oxidation and attenuated development of atherosclerosis has also been observed in apolipoprotein E-deficient mice (Fuhrman B *et al* 2000).

Weight Loss Effects

Spiced foods or herbal drinks, such as those that contain ginger, have the potential to produce significant effects on metabolic targets, such as satiety, thermogenesis, and fat oxidation (Westerterp Platenga *et al* 2006). A significant clinical outcomes sometime may appear straightforwardly but also depends too strongly on full compliance of subjects. Thermogenic ingredients, such as ginger, may be considered as functional agents that could help restore a "positive energy balance" and prevent obesity (Rajesh Kumar Mishra *et al* 2012).

Antiarthritic Effect

A study investigated the antiarthritic effects of ginger and its bioactive constituents. A wellcharacterized crude ginger extract was compared with a fraction containing [6]- gingerol and their derivatives to inhibit joint swelling in an animal model of rheumatoid arthritis, streptococcal cell wall-induced arthritis. Both extracts demonstrated anti-inflammatory activity. The crude dichloromethane extract, containing essential oils and more polar compounds, was more efficacious, when normalized to [6]-gingerol content, in preventing, both joint inflammation and destruction. Non-gingerol components enhance the antiarthritic effects of the more widely studied [6]-gingerol (Funk JL *et al* 2009).

Antimicrobial Activities

Ingenol and [6]-shogaol, isolated from ginger rhizome, demonstrated antiviral activity (Bordia A *et al* 1997). [10]-gingerol has been reported as active inhibitor of *M. avium* and *M. tuberculosis* *in vitro*. Gingerol and related compounds have been investigated for antimicrobial activities. [6]- gingerol and [12]-gingerol, isolated from ginger rhizome, demonstrated antibacterial activity against periodontal bacteria (Miri p *et al* 2008).

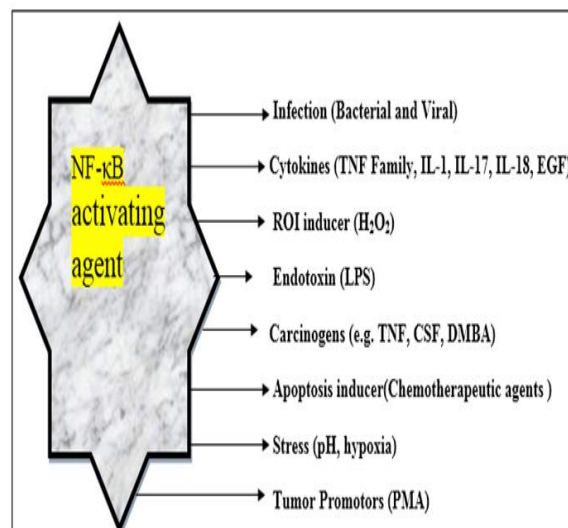


Fig 3: NF-κB activating agent (Subodh Kumar *et al.*, 2013).

Radio Protective Activity

In vitro, pre-treatment with [6]-gingerol reduced UVB-induced intracellular reactive oxygen species levels, activation of caspase- 3, -8, -9, and Fas expression. It also reduced UVB-induced expression and transactivation of COX-2. Translocation of NF-κB from cytosol to nucleus in HaCaT cells was inhibited by [6]-gingerol via suppression of IκBα phosphorylation (ser-32). Examination by EMSAs and immunohistochemistry showed that topical application of [6]-gingerol (30 μM) prior to UVB irradiation (5 kJ/m²) of hairless mice, also inhibited the induction of COX-2 mRNA and protein, as well as NF-κB translocation (Kim JK *et al* 2007).

Antigenotoxic Activity

Norethandrolone and oxandrolone were investigated for their genotoxic effect on human lymphocyte chromosomes using chromosomal aberrations and sister chromatid exchanges as parameters and subsequently Genistein and [6]-gingerol were used as antigenotoxic agents to ameliorate the genotoxicity induced by the steroids. Norethandrolone and oxandrolone were studied at 5, 10, 20, 30 and 40 μM, respectively and were found to be significantly genotoxic at 30 and 40 μM. Genistein and [6]- gingerol proved to be equally effective in reducing genotoxic damage at appropriate doses (Beg T *et al* 2008).

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