

## Review Article

**Pharmacological Activity of *Zingiber officinale***Rajesh Kumar Mishra<sup>\*</sup>, Anil Kumar and Ashok Kumar

Pharmacy College, Itaura, Chandeshwar, Azamgarh, Uttar Pradesh, India.

**ABSTRACT**

Ginger is a medicinal plant that has been widely used in Chinese, Ayurvedic and Tibb-Unani herbal medicines all over the world and has a long history of use in traditional systems of medicine. The primary pungent agents are due to the presence of phenylalkylketones or vanillyl ketones. Gingerol and shogaol are two most active constituents of ginger based preparations. They are reported to demonstrate antiemetic, antipyretic, analgesic, antiarthritic, and anti-inflammatory activities. Ginger, the rhizome of *Zingiber officinale*, is one of the most widely used species of the ginger family (*Zingiberaceae*) and is a common condiment for various foods and beverages. Ginger has a long history of medicinal use dating back 2,500 years in China and India for conditions such as headaches, nausea, rheumatism, and colds. Characterized in traditional Chinese medicine as spicy and hot, ginger is claimed to warm the body and treat cold extremities, improve a weak and tardy pulse, address a pale complexion, and strengthen the body after blood loss. The review article focuses on experimental advances in pharmacology of gingerol and its analogues.

**Keywords:** Ginger, phenylalkylketones, pharmacology, gingerol.

**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.<sup>1</sup> 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.<sup>2</sup>

**Botanical Description**

Ginger is herbaceous rhizomatous perennial, reaching up to 90 cm in height under cultivation. Rhizomes are aromatic, thick lobed, pale yellowish, bearing simple alternate distichous narrow oblong lanceolate leaves. The herb develops several lateral shoots in clumps, which begin to dry when the plant matures. Leaves are long and 2 - 3 cm broad with sheathing bases, the blade gradually tapering to a point. Inflorescence solitary, lateral radical pedunculate oblong cylindrical spikes. Flowers are rare, rather small, calyx superior, gamosepalous, three toothed; open splitting on one side, corolla of three sub equal

oblong to lanceolate connate greenish segments (Kawai, 1994).

**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<sup>3</sup>.

**Pharmacology****Anti-cancer effects:**

The anticancer effects of ginger are thought to be attributed to various constituents including vallinoids, viz. (6)-gingerol and (6)-paradol,

shogaols, zingerone, and Galanals A and B.<sup>21,20,27</sup> Galanals A and B have been found to be potent apoptosis inducers of human T lymphoma Jurkat cells.<sup>20</sup>

#### Anticoagulant Effects

Ginger has been shown to inhibit platelet aggregation<sup>7,8,13</sup> and to decrease platelet thromboxane production *in vitro*<sup>28,29,13</sup>. (8)-Gingerol, (8)-shogaol, (8)-paradol, and gingerol analogues (1 and 5) exhibited anti-platelet activities.<sup>13</sup> However, its effects *in vivo* have not been well studied. Although Verma et al. found ginger to decrease platelet aggregation<sup>30</sup>, Lumb found no effect of ginger on platelet count, bleeding time, or platelet aggregation<sup>31</sup>. Similarly, Bordia et al. found ginger to have no effect on platelet aggregation, fibrinolytic activity, or fibrinogen levels.<sup>32</sup> Janssen et al. showed no effect of oral ginger on platelet thromboxane B2 production<sup>33</sup>, while Srivastava found thromboxane levels to be decreased by ginger ingestion in a small study<sup>34</sup>.

#### 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.<sup>35,36,37</sup> 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 post-operative nausea and vomiting.<sup>38,37,36</sup> In a randomized, placebo-controlled, crossover trial of 16 healthy volunteers, ginger (1g orally) had no effect on gastric emptying.<sup>40</sup> It appears unlikely that ginger's anti-emetic or anti-nausea 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.<sup>41</sup> 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."

#### Anti-Inflammatory Effects

Ginger has a long history of use as an anti-inflammatory and many of its constituents have been identified as having anti-inflammatory properties.<sup>9</sup> Ginger has been found to inhibit prostaglandin biosynthesis<sup>19</sup> and interfere with the inflammatory cascade and the vanilloid nociceptor<sup>12</sup>. Ginger has been shown to share pharmacological properties with non-steroidal anti-inflammatory drugs (NSAIDs) because it suppresses prostaglandin synthesis through the inhibition of cyclooxygenase-1 and cyclooxygenase-2. However, ginger can be distinguished from NSAIDs based on its ability to suppress leukotriene biosynthesis by inhibiting 5-lipoxygenase. 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 NSAIDs. It was also discovered that a ginger extract (EV.EXT.77) derived from *Zingiber officinale* (and *Alpinia galanga*) inhibits the induction of several genes involved in the inflammatory response, including 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. Identification of the molecular targets of individual ginger constituents provides an opportunity to optimize and standardize ginger products with respect to their effects on specific biomarkers of inflammation.

#### 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.<sup>24</sup>

#### Antioxidant Effects

*In vitro*, ginger has been shown to exhibit antioxidant effects.<sup>15</sup> (6)-gingerol appears to be the antioxidant constituent present in ginger, as it was shown to protect HL-60 cells from oxidative stress.<sup>7</sup> Ginger oil has dominative protective effects on DNA damage induced by H<sub>2</sub>O<sub>2</sub>. Ginger oil might act as a scavenger of oxygen radical and might be used as an antioxidant.<sup>24</sup>

#### Cardiovascular Effects

*In vitro* research indicates that gingerols and the related shogaols exhibit cardio depressant activity at low doses and cardiotoxic properties

at higher doses.<sup>7</sup> Both (6)-shogaol and (6)-gingerol, and the gingerdiones, are reportedly potent enzymatic inhibitors of prostaglandin, thromboxane, and leukotriene biosynthesis.

### Gastrointestinal Effects

There is evidence that ginger rhizome (root) increases stomach acid production. If so, it may interfere with antacids, sucralfate (Carafate), H<sub>2</sub> antagonists, or proton pump inhibitors. In contrast, other *in vitro* and animal studies have revealed gastro protective properties.<sup>16, 17</sup> 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*.<sup>5</sup> 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).<sup>23</sup>

### Antitussive Effects

(6)-shogaol, generally more potent than (6)-gingerol, has exhibited antitussive effects.<sup>22</sup>

### Immunomodulatory Effects

*In vitro* evidence indicates that ginger has immunomodulatory effects and is an effective antimicrobial and antiviral agent.<sup>44</sup>

### Lipid Effects

Oral ingestion of ginger extract has been shown to have hypocholesterolemic, hypolipidemic, and antiatherosclerotic effects in cholesterol-fed rabbits<sup>14</sup> and in rats<sup>16</sup>. Inhibition of LDL oxidation and attenuated development of atherosclerosis has also been observed in apolipoprotein E-deficient mice.<sup>15</sup>

### 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.<sup>11</sup> 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.

### Antiarthritic Effect

A study investigated the antiarthritic effects of ginger and its bioactive constituents. A well-characterized 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.<sup>43</sup>

### Antimicrobial Activities

Ingenol and [6]-shogaol, isolated from ginger rhizome, demonstrated antiviral activity.<sup>32</sup> [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.<sup>44</sup>

### 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- $\kappa$ B from cytosol to nucleus in HaCaT cells was inhibited by [6]-gingerol via suppression of I $\kappa$ B $\alpha$  phosphorylation (ser-32). Examination by EMSAs and immunohistochemistry showed that topical application of [6]-gingerol (30  $\mu$ M) prior to UVB irradiation (5 kJ/m<sup>2</sup>) of hairless mice, also inhibited the induction of COX-2 mRNA and protein, as well as NF- $\kappa$ B translocation.<sup>45</sup>

### 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  $\mu$ M, respectively and were found to be significantly genotoxic at 30 and 40  $\mu$ M. Genistein and [6]-gingerol proved to be equally effective in reducing genotoxic damage at appropriate doses.<sup>46</sup>

### Mutagenicity

A study was performed to discover the active part in mutagenesis of [6]-gingerol and [6]-shogaol. [6]-Shogaol was much less mutagenic ( $1 \times 10^3$  revertants/108 viable cells/700  $\mu$ M) than [6]-gingerol ( $1 \times 10^7$  of the same units). Mutation frequencies of their related compounds were  $4 \times 10^1$  for zingerone,  $1 \times 10^7$  for 3-hydroxymyristic acid and  $3 \times 10^2$  for 12-hydroxystearic acid.<sup>47</sup>

### CONCLUSION

This article has outlined some of the current thinking with regard to the experimental advances in gingerol and analogues. So far, reveals the empirical use of ginger in several ayurvedic medicinal products.



*Zingiber officinale* rhizome

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