

## Review

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# Ginger and its Effects on Inflammatory Diseases

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## ABSTRACT

Today, Ginger is used as a spice all around the world. In the past, Ginger was consumed for the treatment of various diseases, including osteo-arthritis, neurological diseases, vomiting, asthma, and so on. It seems that Ginger can reduce inflammation in those diseases. We searched the following keywords in PubMed, Google scholar, and Scopus database until 2015: inflammation and Ginger, Ginger and diseases. Clinical trials, animal studies, and human studies were included in the results of this search. Ginger extract with the antioxidant and anti-inflammatory ingredients such as 6 Gingerols, 6-Shogoals, Zhingerol, etc can reduce inflammatory mediators such as inflammatory cytokines and chemokines due to their effects on NF-κB activation, cyclooxygenase 2 reduction and serotonin receptors inhibition. It increases reducing antioxidant enzymes so it can be useful in inflammatory diseases improvement and their complications prevention. In conclusion, Ginger can help in the treatment of inflammatory chronic diseases such as Fatty Liver, Asthma, Cancer and Arthritis through anti-inflammatory, immunoregulatory and antioxidative mechanisms.

**KEYWORDS:** Ginger; *Zingiber officinale*; Inflammation; Diseases.

**ABBREVIATIONS:** NF-κB: Nuclear factor κB; BMI: Body mass index; SLM: Soft Lean Mass; IgE: Immunoglobulin E; COX-2: Cyclooxygenase2; AchE: Acetylcholinesterase; PPARδ: Peroxisome proliferator-activated receptor δ.

## INTRODUCTION

Today, Ginger, in both fresh and dried forms, is used as a spice all around the world. In the past, Ginger was consumed in the treatment of various diseases, including arthritis, neurological diseases, vomiting, and so on. More than 50 types of antioxidants have been extracted from Ginger rhizome. The major pharmacological activity of Ginger, with scientific name of "*Zingiber officinale*", is related to its active ingredients such as 2 and 6-Gingerol.<sup>1</sup> Shogoals, Gingerol, and similar compounds in Ginger. These ingredients prevent the biosynthesis of Leukotrienes and Prostaglandins by inhibiting 5-lipoxygenase and prostaglandin synthesizer.<sup>2</sup> Seemingly that Ginger can inhibit NF-κB (Nuclear factor κB) activation, TNFα expression and CRP production,<sup>3</sup> we reviewed the articles that discuss Ginger's anti-inflammatory effects.

## MATERIALS AND METHODS

We searched in PubMed, Google scholar, and Scopus database until 2015 and the key words, inflammation and Ginger, Clinical trials, animal studies, and human studies were included in our search.

## RESULTS

Our review of recent studies showed that Ginger, due to its anti-inflammatory, anti-carcinogenic, and antioxidative properties, can reduce inflammation in the body and improve related diseases. Below important effects are mentioned:

### Ginger and Body Composition

Ginger may reduce the rate of weight gain, Body Mass Index (BMI). It can improve body composition by decreasing body fat levels and increasing Soft Lean Mass (SLM). In addition, some enzymes such as Acetyl-coenzyme A, acyltransferase 1 and enoyl-CoA hydratase, which participate in the  $\beta$ -oxidation of fatty acids, have increased by consumption of Ginger.<sup>4</sup> Moreover Ginger extract prevents high-fat diet-induced obesity in mice *via* activation of the Peroxisome proliferator-activated receptor  $\delta$  (PPAR $\delta$ ) pathway.<sup>5</sup>

Besides, ginger tends to reduce lipid metabolism related-proteins mRNA expression levels in liver and visceral fat in hyperlipidemia and may also improve lipid metabolism.<sup>6</sup> The aqueous extract of *Z. officinale* Roscoe might inhibit the intestinal absorption of dietary fat by inhibiting its hydrolysis.<sup>7</sup>

Therefore, Ginger seems to improve body composition *via* its effects on liver enzymes, by reducing fat absorption, by increasing beta-oxidation of fats and energy expenditure.

### Ginger and Reduction of Airway Inflammation

Ginger can reduce airway inflammation in mice by enhancing the Th1 response and ameliorates ovalbumin-induced Th2 responses,<sup>8,9</sup> and by reducing level of IL4, IL5, eotaxin, and Immunoglobulin E (IgE).<sup>10</sup> It can also improve the symptoms of asthma by relaxing the airway smooth muscle due to the regulation of calcium channels function.<sup>11</sup>

### Ginger and Kidney Function

Gingerol fraction from *Zingiber officinale* prevents gentamicin-induced nephrotoxicity. It improves kidney functions, reduces lipid peroxidation, and decreases nitrosative stress.<sup>12</sup> In addition, Ginger extract diminishes chronic fructose consumption-induced kidney injury by suppression of renal over expression of pro inflammatory cytokines in rats.<sup>13</sup>

### Ginger and Liver Function

Dried Ginger (*Zingiber officinale*) inhibits inflammation in a mouse model, improves Pathological changes, and reduces level of INF $\gamma$  and IL6. It can also decrease liver Pro-inflammatory responses, TNF $\alpha$ , IL-6, and other inflammatory cytokines levels *via* inhibition of NF $\kappa$ B activation.<sup>14</sup>

### Ginger and Improvement of the Neurological Degenerative Diseases

6-Shogaol, an active constituent of Ginger, attenuates neuro-inflammation and cognitive deficits in animal models of dementia. Consequently, it plays an important role in the improvement of symptoms in patients who suffer from Alzheimer and other neurological diseases. It improves memory by inhibiting the activity of glial cells in animal models of dementia and also by reducing memory corruption.<sup>15</sup> Besides, Ginger decreases activity of NF- $\kappa$ B,<sup>16,17</sup> iNOS, and Cyclooxygenase2 (COX-2).<sup>18</sup> It protects HaCaT cells and C57BL/6 mice from ultraviolet B-induced inflammation.<sup>19</sup> Ginger also has an inhibitory effect on melanogenesis in B16F10 melanoma cells and as a result can protect skin from darkening.<sup>20</sup>

### Ginger and Diabetes

Ginger consumption in patients who suffer from type 2 diabetes mellitus affects glycemic status,<sup>21-24</sup> insulin sensitivity, lipid profiles,<sup>20,24</sup> and other metabolic disorders. It improves them by decreasing inflammatory factors like CRP, IL6, TNF $\alpha$ ,<sup>25-27</sup> It shows antagonistic activity against serotonin receptors.<sup>22,28</sup> Moreover, it inhibits the activity of intestinal glucosidase and amylase, resulting in the reduction of glucose absorption.<sup>29-31</sup> Neuroprotective effect of Ginger on the brain of streptozotocin-induced diabetic rats, may also be due to adjustment of astrocyte damage response, decreasing the expression of Acetylcholinesterase (AChE), and improving the construction of neurons.<sup>32</sup>

### Ginger and Rheumatic Disorders

Ginger has protective effects on joint inflammation, arthritis, and musculoskeletal disorders *via* its anti-inflammatory, antioxidant, and anti-serotonin influences. It inhibits Cyclooxygenase-2 and 5-Lipoxygenase pathways. Ginger induces T-helper-2, and anti-inflammatory cytokines such as IL-4 and IL-10 production,<sup>33,34</sup> increases glutathione level, and activity of the antioxidant enzyme like superoxide dismutase,<sup>35</sup> inhibits the release of substance P (mediator of inflammation and pain),<sup>36</sup> and decreases TNF $\alpha$ , IL1 $\beta$ , IL6, IL2, and prostaglandins levels. One Study shows Ginger is more effective than indomethacin in reducing the pain associated with inflammation and oxidative stress.<sup>37</sup> Moreover, Ginger can decrease muscle pain caused by sever exercise.<sup>31,38</sup>

### Ginger and Chemo-preventive Effects

Some active constituent of Ginger like [6]-Gingerol, and [6]-paradol have chemo-preventive and anti-tumor effects.<sup>39</sup> Ginger extract is effective in decreasing the gastric inflammation. Besides, it prevents gastric, colon, and lung carcinogenesis through bacterial reduction load. It also suppresses acute and chronic inflammation. In addition, Ginger can inhibit COX-2, NF $\kappa$ B, IL1 $\beta$ , IL8, and IL6 pathways.<sup>40,41</sup> Shogaol can suppress

cancer cell invasion and inflammation, and displays cytoprotective effects through modulation of NF- $\kappa$ B and Nrf2-Keap1 signaling pathways. Moreover, it induces NAD(P)H, heme-oxigenase, and oxidoreductase genes.<sup>42</sup> 6-Gingerol exerts anti-cancer activities *via* its effects on cell cycle regulation, cytotoxic activity, and angiogenesis inhibition.<sup>43</sup>

## DISCUSSION

Briefly, Ginger can be useful in the treatment of patients who suffer from inflammatory chronic diseases, due to its anti-inflammatory and anti-oxidative properties. The anti-inflammatory effects of Ginger are caused by its inhibitory influence on COX-2, lipoxigenase, NF $\kappa$ B and TNF $\alpha$  activity, likewise they are caused by reduction of inflammatory factors such as IL1 $\beta$ , IL6, and IL2. The inhibitory effects of 6-Gingerol on the arachidonic acid metabolites include reduction of Platelet aggregation, formation of Thromboxan B2, and Prostaglandin 2D. Ginger's anti-oxidative effects are due to SOD activity induction, glutathione enhancement, and ROS reduction. Moreover, Ginger has an inhibitory effect on xanthine oxidase system which is responsible for the production of reactive oxygen species like superoxide anion.<sup>44-47</sup> Besides, Ginger is a serotonin blocker and inhibits the release of substance of P. Several compounds have found in Ginger may act as a blocker of serotonin receptors.<sup>48,49</sup> Laboratory studies have also shown the inhibition of serotonin receptors which is associated with the reduction of TNF $\alpha$ , IL1 $\beta$ , IL6, IL2, and prostaglandins.<sup>37</sup> In addition Ginger have thermogenic properties and increases energy expenditure by enhancing the thermic effect of food.<sup>50,51</sup>

## CONCLUSIONS

To conclude, It seems Ginger has anti-inflammatory effects. It can improve the symptoms of inflammatory disease. However, more clinical trial studies are needed to approve its effects and mechanisms of such effects.

## CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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