

Ginger and its active constituents as therapeutic agents: Recent perspectives with molecular evidences

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Ginger (*Zingiber officinale*) is a plant that originated mainly from Southeast Asia. It is now considered as one of the most healthiest and most delicious spices all over the globe.^[1] The rhizome is an underground part of the stem known as ginger root or simply called ginger. Ginger can be used in a variety of ways like as dried powder, oil, juice and can also be use freshly and it is one of the most common agents for the preparation of spicy foods. Ginger has a number of bioactive phenolic compounds such as gingerols, gingerenone A, zingerone, shogaols, paradols, quercetin, 6-dehydrogingerdione, and so on.^[2] Besides these, ginger also has several terpene compounds such as β -bisabolene, α -curcumene, zingiberene, α -farnesene, and β -sesquiphellandrene. Not only have these but it also contains polysaccharides, lipids, organic acids, and raw fibers.^[2] All these active compounds make ginger as a powerful antioxidant and anti-inflammatory agent.^[1,2] Recently, Joe Leech has reviewed several health benefits of ginger and its most active polyphenolic fraction gingerol as it showed commanding potentials against several human disorders.^[3] Numerous studies showed that gingerol reduces the risk of both bacterial and viral infections.^[4,5] Specifically, it was found to be highly effective against the oral bacteria associated with the gingivitis and periodontitis^[4] and effective against the respiratory syncytial viral infection.^[5] For these reasons, ginger has been regularly used for the improvement of digestion, reduction of nausea, and also to aid in fighting against the flu and common cold.^[1-5] Although at this moment, the World Health Organization said that ginger can have a “positive impact on your health, but it has no means of a medically proven treatment against coronavirus disease-19” although further investigations are still needed to be confirmed.^[6]

Osteoarthritis (OA) is the most common disease of joints, afflicting millions of people all over the globe, but still none of the compound(s) discovered that inhibit the progressive degradation of the joints. In recent years, I with colleagues investigated some novel therapeutic targets at molecular levels,^[7-9] which might be useful for drug designers for OA patients. In addition, my colleagues and I also have

successfully tested the therapeutic potential of several natural dietary products on the OA knee cells as anti-osteoarthritic agents against the joints degradation.^[10-12] Similarly, studies on ginger testing for OA patients showed that ginger and its active constituents have modestly efficacious and reasonably safe for treatment of patients with joints disorders,^[13-15] but still further studies are needed on a larger group of OA patients to warrant their efficacy as a useful treatment for joint pain and disability. Not only for OA patients, ginger and its active constituents have also been successfully tested as important therapeutic agents for the treatment of cancer patients. Numerous cellular-based studies showed that ginger and its active ingredients particularly gingerol perform anti-cancer activities by modulating the expression of cancer associated genes and their associated cell signaling pathways such as inhibition of transforming growth factor (TGF)- β , interferon- γ , tumor necrosis factor (TNF)- α , cyclooxygenase (COX)-2, B-cell lymphoma (Bcl₂), survivin, vascular endothelial growth factor, genes and suppression of nuclear transcription factor (NF)- κ B, signal transducer and activator of transcription (STAT)-3, and Akt activities, in different cancer cell types.^[16-19] Furthermore, the consumption of ginger has also been well known as an anti-diabetic agent as several studies on humans and animals showed that it reduces the blood glucose levels and hemoglobin A1c.^[20-23] Not only have these but it also reduces the chances for the onset of heart associated disorders as it significantly decreases apolipoprotein B/apolipoprotein A-I ratio and also decreases the levels of oxidative by-product malondialdehyde.^[23,24] Moreover, ginger has also potential to reduce body weight and now is also known as weight-reducing agents.^[25-27] Recently, Maharlouei *et al.* performed meta-analysis for analyzing the potential of ginger on overweight and obese individuals and concluded that intake of ginger not only reduces body weight, waist-to-hip ratio, and hip ratio but also reduces glucose levels and increases high-density lipoprotein-cholesterol levels.^[25] Another recent study performed by Sayed *et al.* demonstrated in obese animal model concluded that intake of ginger water reduces not only bodyweight but also improves expenditure of energy.^[26] These data have also been

supported by Ebrahimzadeh *et al.* systematic review performed on 27 research articles, out of them 17 were performed on animal models, six were cellular-based studies, and whereas four were directly performed on humans.^[27] Most of the animal and cellular-based studies supported the ginger intake reduces the body weight, but the findings from the clinical trials showed non-significant changes of anthropometric measurements and body composition in obese humans.^[27] Therefore, further studies on humans on a large scale are recommended to prove the potential of ginger as a weight-reducing agent. Intake of ginger is also beneficial for patients with chronic dyspepsia as it induces stomach gastric emptying and antral contractions.^[28] Importantly, intake of ginger is also very effective for females having menstrual pain if they have started taking it at the start of their menstrual period.^[29] Most importantly, it is also suggested that intake of ginger by menstrual females is equally or even more effective as general painkillers such as novafen and mefenamic acid.^[30,31] Furthermore, consumption of ginger also found to be effective in improving the brain functions and declining the neural ageing process.^[32,33] Numerous animal and cellular-based studies concluded that active ingredients of ginger perform anti-inflammatory activities in the brain which directly or indirectly protect age-associated decline of brain functions.^[32-35] In short, the ongoing mode of treatment for disorders such as OA, cardiovascular, cancer, diabetes is based on the synthetic drugs such as non-steroidal anti-inflammatory drugs, anti-diabetic synthetic drugs, chemo/radiotherapeutic agents which are somewhat effective, but causes adverse side effects and are expensive too. Therefore, a safe, effective, and inexpensive mode of treatment is always needed to control the onset/progression of diseases. Ginger and its constituents have potential to inhibit number of potent disease-associated genes TGF- β , COX2, TNF- α , INF- γ , BCL₂, NF- κ B, STAT-3, Akt, and so on. Therefore, ginger and its active constituent are recommended as novel therapeutic agents, but further confirmatory studies are still required, particularly at the level of human clinical trials.

Ethics Approval and Consent to Participate

Not applicable.

Availability of Data and Material

Not applicable.

Competing Interest

None.

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