Antiarthritic Activity of *Zingiber officinale* (Ginger): A Review

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Abstract

Arthritis is an inflammatory, chronic, and progressive autoimmune disease of joints. It is characterized by swelling, pain, and inflammation of different joints of human body. Almost half of the people of this world are suffering from arthritis, from there the woman are more prone to affect by arthritis than man. In the 21st century, the medical field develop different types of drugs and therapy to prevent arthritis. However, until now, there is no effective drug or therapy which can cure arthritis, so in this developing era, scientists are doing research on the herbs which can cure arthritis. There are many herbs which carry the antiarthritic activity, among those *Zingiber officinale* is the most prevalent and prior herbs which contain many constituents that can cure the arthritis. Hence, in this review, we are discussing about the antiarthritic activities of *Z. officinale* (Ginger).

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INTRODUCTION

Immunity is the main part of human body system, due to immunity our body can prevent many disease from occurring. However, sometime due to overactive immune system, our immune cells fails to determine the foreign particle and body's own particle, and they attack body's own cells leading to different types of disease, this type of disease is called autoimmune disease. Arthritis is a major autoimmune disease and it is chronic, progressive, and inflammatory also. It mainly affects on the body's joints. It is characterized by swelling and pain.

Half of the people of this world are suffering from arthritis, among them woman and old-aged people are more prone to suffer from arthritis. Arthritis is mainly two types – rheumatoid arthritis (RA) and osteoarthritis. RA is a type of autoimmune disorder characterized by chronic inflammation due to synovial hyperplasia which further progresses with massive irreversible bone destruction.^[1-5]

It is characterized by pain, swelling, loss of the ability of movement, etc. Recent epidemiological study shows that about 1% of people all over the world are now affected with RA, which exerts significant impact on the quality of life.^[6,7] The pathophysiology of RA is reported to be due to release of certain free radicals such as superoxide and nitrous oxide that generated as cellular metabolism by-products.^[8] These free radicals released can trigger the production of tumor necrosis factor (TNF- α) and interleukins (IL) from T-cells which altered the production of cytokines, growth factors, and adhesive molecules on immune cells, resulting with tissue destruction and inflammation.^[9]

Out of all the type of arthritis osteoarthritis is one of the most common types. It mainly seems in old-aged people as they losses the strength of bones due to old age. It occurs when protective cartilages of the ends of bones were down over times. It affects mainly joints in hands, knees, hips, and spine. The joints which are effected by osteoarthritis cannot be recovered. The osteoarthritis is characterized by pain, loss of flexibility, tenderness, stiffness, swelling, etc.

For both RA and osteoarthritis scientist have developed many drugs and therapies to prevent and to relief from these disease. The

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goals of RA treatment are to stop pain and inflammation, relieve symptoms, and prevent joint and organ damage.^[10] To these ends, non-steroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, and disease-modifying anti-rheumatic drugs (DMARDs) are prescribed.^[10]

Presently for the treatment of RA, strategies have changed from traditionally used NSAIDs or DMARDs to novel biological agents, like TNF monoclonal antibody.^[11] Immunosuppressive and cytotoxic drugs such as cyclosporine, azathioprine, and cyclophosphamide are used for the treatment of chronic patients.^[12-14] These type of drugs can reduce the join pain and little swelling, but they are lack of permanent curing capacity. The long-term use of these drugs also has other side effects such as – gastrointestinal irritation, allergy, and headache.

The new type of NSAIDs, the cyclooxygenase (COX)-2 inhibitors, has been found in numerous trials to increase the risk of adverse cardiovascular events, while traditional NSAIDs have been reported to increase the risk of adverse gastrointestinal events.^[15] Moreover, the more commonly prescribed NSAIDs, such as Naproxen, Indomethacin, and Ibuprofen, have been found to inhibit the synthesis of human cartilage matrix *in vitro*,^[16] which is likely to accelerate the rate of degeneration of articular cartilage in OA clinical effectiveness.

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From these drugs of arthritis, it is clearly seen that there are no effective drugs against arthritis which can completely cure arthritis. For that reason, scientist are doing research on herbs which have medicinal properties that carry anti-arthritic properties. Many herbs contain antiarthritic activity, among them ginger is one of the most important herbs which have the capacity to prevent arthritis. The brief discussion about ginger and its anti-arthritic activity is describe below.

GINGER AND ITS ROLE IN PREVENTING ARTHRITIS

Ginger (*Zingiber officinale*) or ginger root is the rhizome of the plant *Z. officinale*, ate up as a delicacy, remedy, or spice. It lends its name to its genus and family (*Zingiberaceae*).^[17]

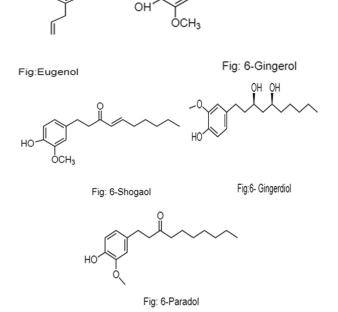
Rhizome of *Z. officinale* or ginger is widely used in both medicinal and culinary purposes in globally due to its ethno medicinal property and nutritious value. Most of the traditional and complementary systems of medicine such as Ayurveda, Siddha, Unani, Homeopathy, Tibetan, and Chinese prescribe *Z. officinale* individually or as a combination in both of infective and non-communicable diseases.^[18] In RA and osteoarthritis, ginger is used as a natural pain reliever and an anti-inflammatory agent.^[17] The main phytochemical constituents of ginger are categorized into volatile and non-volatile phytochemical constituents.

Classification of Ginger

- Kingdom Plantae
- Order Zingiberales
- Family Zingiberaceae
- Genus Zingiber
- Species Z. officinale.

The fresh and dried Z. officinale extracts have been reported to possess gingerols, 1,7-bis-(40-Hydroxy-30-methoxyphenyl)-3,5-heptadione, adenine, 1-Dehydro-3-dihydro-gingerdione, Acetoxy-6-dihydroparadol, Isogingerol, Beta-sitosterol palmitate, isovanillin, glycol monopalmitate, hexacosanoic acid 2,3-dihydroxypropyl ester 5-Methoxy-gingerol, Methyl diacetoxy-gingerdiol, Methyl diacetoxy-gingerdiol, 1-Dehydrogingerdione, Acetoxy-gingerol, Shogaol, Paradol, 1-(40 Hydroxy-30-methoxyphenyl)- 7-octen-3-one, 1-(40- Hydroxy-30-methoxyphenyl)-7-decen-3-one,1-(40-Hydroxy-30methoxyphenyl)-7-dodecen-3-one, maleimide-5oxime, p-hydroxybenzaldehyde, and 1-(omega-ferulyloxyceratyl) glycerol's.[19-21] These all are the chemical constituents of ginger. The pungency of ginger is due to the gingerols and shogaols.[22] Ginger oil contains monoterpene, hydrocarbons, sesquiterpene hydrocarbons, and oxygenated mono- and sesquiterpene.[23]

Some of the study reported that fresh ginger contains protein, fat, minerals, fibers, carbohydrates, lipids (including glycerides, phosphatidic acid, lecithins, and fatty acids), protease, iron, calcium, magnesium, potassium, and phosphorous.^[17] It also contains vitamins such as thiamine, riboflavin, niacin, and vitamin C.^[24,25] Some important structures of ginger constituents which carry the antiarthritic activities are as below.



ANTIARTHRITIC ACTIVITY OF GINGER

A study investigated the antiarthritic results of ginger and its bioactive ingredients, a properly characterized crude ginger extract changed into in comparison with a fraction containing. ^[6] gingerol and their derivatives to inhibit joint swelling in an animal version of rheumatoid arthritis, streptococcal cellular wall-prompted arthritis.^[17] Ginger's anti-inflammatory effects may be due in part to its inhibition of COX, inducible nitric oxide synthase, and lipoxygenase activities, as well as suppression of inflammatory prostaglandin synthesis and interference n cytokine signaling.^[18,26-28] A number of ginger constituents including gingerols, shogaols, and diarylheptanoids may contribute to these actions.^[26,28]

Crude ginger extract and (6)-gingerol to reduce joint swelling in animals induced with RA and exhibited potent antiinflammatory action.^[29] Van Breemen et al. reported the mechanism of anti-inflammatory effect of ginger constituents. They found that 10-gingerol, 8-shogaol, and 10-shogaol strongly inhibited COX-2 and thereby significantly reduced inflammation.[30] Although most papers show that ginger reveals its anti-inflammatory effect by blocking COX-2 enzymes, Grzanna has reported blocking the activities of both COX-1 and COX-2.^[18] Eun et al. (2009) evaluated the pharmacological effects of 14 phytochemicals isolated from Z. officinale, using the RAW 264.7 cell line.[31] They observed that 6-shogaol, 1-dehydro-10-gingerdione, and 10-gingerdione significantly decreased LPS-induced nitric oxide production, while the first two remarkably reduced iNOS expression, during development of RA high level of nitric oxide and iNOS which play pivotal role in cartilage damage and inflammation.^[1] Hence, these compounds may have beneficial effect to reduce the inflammation in RA.^[1] Lee et al. demonstrated that 6-gingerol remotes from Z. officinale which exhibited anti-inflammatory effect by blocking NF- $\kappa\beta$ and protein kinase C (PKC) signaling pathways.^[32] 6-Gingerol significantly suppressed $Ik\beta\alpha$ phosphorylation, NF- $\kappa\beta$ nuclear activation, and PKC- α translocation which, in turn, inhibited Ca2+

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mobilization and disrupted mitochondrial membrane potential in LPS stimulated macrophages; therefore, inducible nitric oxide synthase and TNF- α expression were significantly inhibited and reduced inflammation.^[1]

CONCLUSION

Arthritis is now a major disease among the wide population of the world. It is seen that the drugs which are developed for arthritis are not totally effective, that is, those drugs can only reduce the pain and inflammation, they are unable to cure arthritis completely. Hence, in this new developing era of science drug, developers found that many herbs contain the antiarthritic activity which can cure arthritis. Hence, among different types of herbs, they found that ginger is the most effective herb which contains different constituents that have strong antiarthritic activity. In this review, we have discussed briefly about the action of ginger constituents again arthritis. From this, we can conclude that ginger is most effective herb in medical field which gives the hope to cure arthritis completely.

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