Review Article

Pharmacological and biochemical properties of *Zingiber zerumbet* (L.) Roscoe ex Sm. and its therapeutic efficacy on osteoarthritis of knee

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Abstract

Osteoarthritis (OA) as the most frequent form of knee arthritis is one of the most annoying complications amongst old peoples. There are different pharmacological and non-pharmacological remedies which could be applied for treatment of knee OA. It's while, significant side effects mostly in patients who are older are the dangerous limiting factors. Integrative, supplementary, traditional remedies have been applied from long time ago in treatment of such chronic diseases like OA. Various topical and oral remedies have been presented in treatment of OA worldwide. In spite of the fact there are multiple remedies for reduction symptoms of patients who suffer from disorders and related inabilities which could enhance their life quality. Remedies which have been applied for a long time for treatment of OA have newly discovered to induce injury to some patients. On the other side, additional knowledge about alternative and supplementary remedies is a main way for enhancing health of patients who suffer from OA disorders. Zingiber zerumbet (Z. zerumbeton) is a kind of herb of the ginger family and is a natural compound with various biomedical characteristics like anti-proliferative, anti-inflammatory, and antioxidant effect. However, Z. zerumbet could be applied for reduction of OA symptoms because of its circulatory stimulant and anti-inflammatory effects. Anyway, up to now there is not any methodical literature review for evaluating the Z. zerumbet clinical effectiveness productiveness in treatment of OA. The main aim of the current study is to review scientific resources around therapeutic effectiveness of Zingiber zerumbet in treatment of adverse symptoms of OA disorder.

Keywords: Anti-inflammatory remedy, ginger, herbal medicine, osteoarthritis (OA), Zingiber zerumbet

Introduction

One of the most frequent forms of arthritis that could affect a lot of people worldwide is osteoarthritis which would be increasing with age and is a kind of chronic disease that would be specified by steady degeneration of the smooth articular cartilage with response of subchondral bone.[1] This disorder could damage health of people worldwide and on the other hand osteoarthritis (OA) would affects human beings with significant disability and morbidity.[2] The novel World Health

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Organization (WHO) survey uncover that about ten percent of world population with average age of 60 are suffering from OA disorder.[3]

Formerly, it was supposed that OA would be considered as a consequence of both biological and mechanical events which could cause disruption of the normal balance mechanism that could be happen amongst anabolic and catabolic processes within the articular cartilage. Chondrocyte cell within the mature smooth, white tissue of articular cartilage is the unique type of cell which is efficient for maintenance and production of extracellular matrix. Consequently, any decrement in density of chondrocyte cell will cause OA development.[4] Biomechanical estimations specified that the surface zone damage of the smooth, white tissue of articular cartilage could increase the cartilage matrix loading which would be resulting in higher stress on the underlying cartilage tissue and further subchondral reaction (Stoop *et al*., 2001). On the other hand, various factors like obesity, immobilization of joints and increased age could also cause the development of this disease.[5]

At the present time, there are not any commercially suitable remedies which could be applied for modifying the OA development. However, non-steroidal anti-inflammatory (NSAID) remedies are broadly specified for the OA pain treatment. Anyway, the application of such remedies in long periods of time would cause erosions, platelet aggregation elimination, and ulcers in upper gastrointestinal tract consists of the mouth.[6] As a matter of fact, novel remedies are beneficial for controlling some symptoms like pain. On the other hand, some detrimental side effects would be improved by the application of alternatives of botanical extracts. Plants extracts with pharmaceutical properties have been applied from a long time ago for management of various health disorders. The investigation of various compounds or plant extracts has been popular in several fields of the medicinal and biological sciences.[7]

Various extracts collected from different medicinal plants could have therapeutic effects like anti-cancer, anti-inflammatory, and anti-oxidants which Z. zerumbet is one of this effective plants.[8-10] For instance, zerumbone as a crystalline sesquiterpene which is derived from Z. zerumbet is one of these effective extracts. However, rhizomes of Z. zerumbet have large amount of zerumbone in. Additionally, antioxidant and anticancer actions of zerumbone would be main incentive for investigating if it has chondroprotective properties against OA.[11]

Materials and Method

A general research of the literature, containing English studies which were published or/and unpublished was administered by application of special study keywords. The liability of publications of foreign languages was included in English language and studies was with adequate details for determining if suitability criteria were met. An extensive research was conducted on some electronic databases including AMED, BioMed central gateway, AARP's AgeLine Database, MEDLINE, DARE, Cochrane library, EMBASE, Dissertations Abstract International, CINAHL Nursing Journal Databases, Cochrane library, Health Source Nursing/Academic edition, International Pharmaceutical Abstract and PubMed. Additionally, some clinical scientific review was investigated for evaluating the productiveness of homeopathic medicinal extracts of ginger amongst patients who suffer from OA disorders. The collected articles were categorized within four main groups including osteoarthritis disorder, Ginger herbalism, Z. zerumbet herbalism and therapeutic effect of Z. zerumbet in treatment of OA symptoms. After elimination of some of unrelated articles, finally 82 related articles were conducted within this comprehensive study. The schematic diagram in which demonstrates various steps of the selection way of this study has shown in Figure 1 that evidently presents specific domain of the current study.

OA development

The progression of OA is approximately a prolonged procedure and consist of two main stages. The first one is a parser stage where the cartilage erosion would hasten via the creation of matrix digesting enzymes and concurrent reduction in the matrix synthesis. The second one is a multi-step biosynthetic stage which chondrocyte cells attempt for repairing the defective extracellular matrix.[12] In comparison with the ordinary chondrocyte cells, the synthesis-depreciation balance of the matrix is modified in osteoarthritis chondrocyte cells mainly because of:

I: The increment of inflammatory cytokine such as IL-1, TNF-a, IL-6, IL-11 and IL-8.
II: The increment of proteolytic enzymes of metalloproteinases as matrix degrading enzymes (MMPs 1, 2, 3, 7, 8, 13, and 14), cysteine proteinases, serine and extracellular proteolytic enzymes of aggrecanase 1 and 2.
III: free radical's generation such as reactive nitrogen species (RNS) and reactive oxygen species (ROS)
IV: Programmed cell death of apoptosis induction
V: Decrement of synthesis of matrix metalloproteinases (MMP) enzyme inhibitors which known as tissue inhibitor of metalloproteinase (TIMPs)
VI: Decrement of the anabolic factors productions like proteins of bone morphogenetic, naturally growth factors and cytokines.[5,13]

Ahmed *et al*.[14] showed that the inferior inflammatory response discovered within OA is because of the increment of natural dinoprostone which successively cause degradative and inflammatory processes via participating within the collagen synthesis.[14] Therapeutic management using pharmaceutical drugs play a great role in OA and paracetamol, conventional non-steroidal anti-inflammatory drugs (NSAIDs), cyclooxygenase-2 inhibitors as a NSAI drug and narcotic analgesics remedies are proved to be able in reduction of pain in OA. Anyway, prolonged application of aspirin is proved to raise the risk of Cardiovascular disease (CVD); the usage of cyclooxygenase-2 inhibitors would increase stroke and myocardial infarction risk; using of NSAIDs could cause edema, ulcer disease, nausea, dyspepsia,

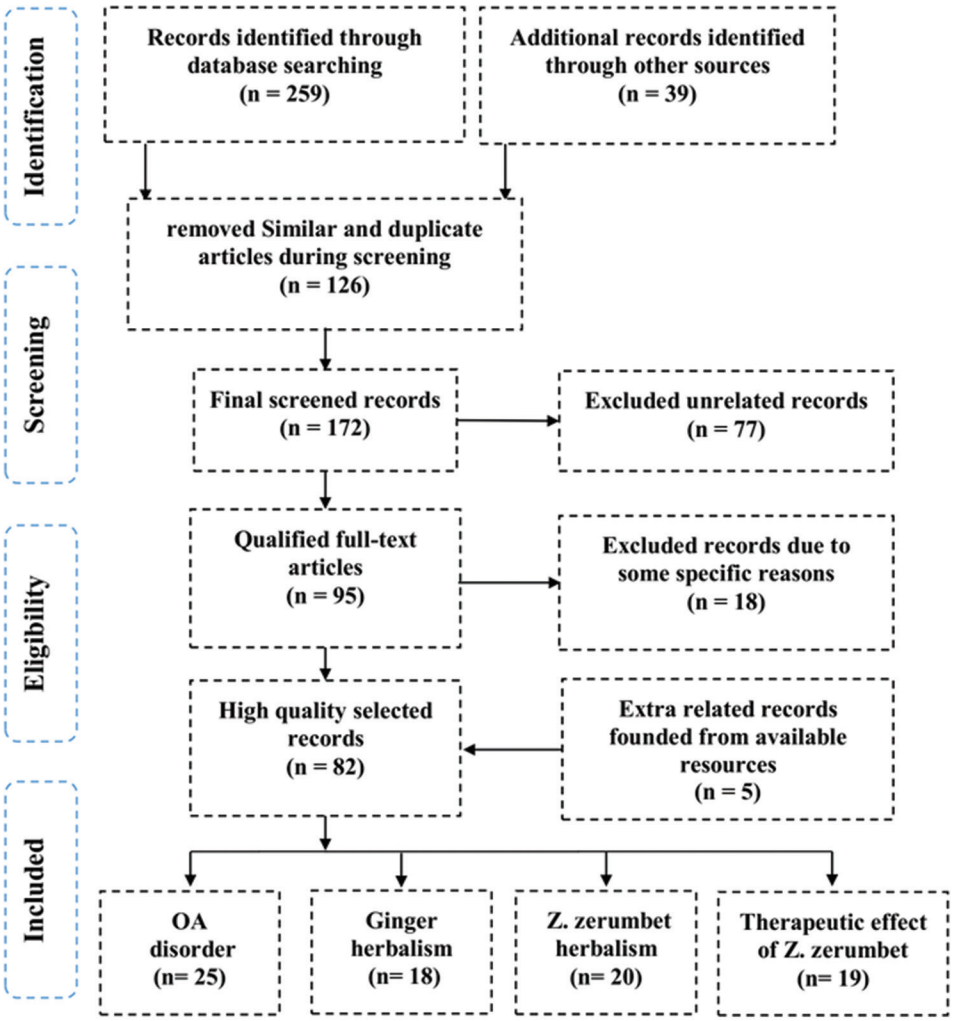

Figure 1: The chart of procedure of choosing related articles in current study in accordance with PRISMA method

gastrointestinal bleeding, bloating, hypertension aggravation, renal insufficiency and interstitial nephritis; and additionally narcotic analgesics drugs could cause giddiness, constipation, nausea, mouth dryness, sedation, and so on.[15,16]

Ginger effects

Overall humankind awareness publicly and within medical community is increasing about the application of alternative or unconventional treatment methods by patients.[17] Patients who suffer from chronic painful disease frequently are searching for alternative remedies and nowadays ginger and its derived extracts are such materials which could be used for treatment of rheumatic disorders.[18] From the ancient time, ginger has been applied for pharmaceutical purposes and particularly it had played an important role in traditional Indian and Chinese medical profession. However, Naheed *et al*.[19] have shown that ginger could treat rheumatic disorders and also its extracts could be applied for preventing metabolism of arachidonic acid and could affect as antirheumatic or anti-inflammatory agents.[19]

Nowadays such available drugs for treatment of osteoarthritis (OA) are just analgesia agents. The simple analgesics prescription like acetaminophen for reduction of pain commonly, applied before being treated with nonsteroidal anti-inflammatory drugs (NSAIDs). The application of NSAIDs is restricted due to the risk of extra side effects, exclusively renal and gastrointestinal perniciousness.[20]

Ginger clinical advantages

The higher rates of prevalence of chronic OA could have considerable impact on any society economy. On the other hand, the increment of pain frequency could force the patients to use analgesic or anti-inflammatory agents or go under orthopedic surgical procedure. Bookwala *et al*.[21] reported that patients who suffer from OA disorder will experience depression due to their inappropriate social and physical functioning. However, the depression rate amongst younger people who suffer from arthritis higher than older patients.[21]

In accordance with detrimental psychosocial and physiological consequences of OA disorder and their relative impact on life

quality of patients, the proper management of OA could impose a broad range of initiative and healthcare services.[22] Due to the fact that, there is not any universal cure for OA disorder a few number of supplementary, pharmaceutical and surgical remedies are existing which could diminish the OA disorder symptoms. Anyway, the concern about the effectiveness of some of this remedies would increase the mortality and morbidity of patients. Elizabeth *et al*.[23] reported that non-steroidal anti-inflammatory drugs (NSAIDs), such as cyclooxygenase-2 inhibitors could enhance the risk of damaging cardiovascular events. It's while, traditional NSAIDs have been shown to enhance the risk of damaging gastrointestinal events.

Furthermore, the most frequent NSAIDs including Ibuprofen, Naproxen and Indomethacin could prevent the release and synthesis of human cartilage matrix proteoglycans *in vitro* which could speed up the articular cartilage degeneration rate in OA.[24] Anyway, recently there is not any methodical documented review on the efficacy and safety of NSAIDS in OA. However, most of patients have become progressively attentive about the safety of these medical agents and afterwards tried for applying alternative and supplementary treatments for alternative solutions. In accordance with the newest trials, one of the most effective remedies which not proved scientifically but traditionally is prescribed by herb doctors is ginger and its extracts.[25]

One of the most important capabilities of ginger and its extracts is the circulatory stimulant and anti-inflammatory effect which could be effectively used in treatment of OA. Additionally, one of the most important plants in the family of ginger is Zingiber zerumbet that known as bitter ginger which has the same remedial effects on OA disorder like ginger. In accordance with such related experimental studies Z. zerumbet could prevent the intermediary of the pro-inflammatory synthesis including nitric oxide and Prostaglandin-E4 within Leukotriene-B4 and porcine chondrocyte cells *in vitro* could decrease inflammation and pain level in patients with OA disorder.[26]

The effect of ginger extracts on OA patients

The findings of Al-Saffar *et al*.[27] study demonstrated that the effectiveness of ibuprofen and ginger extract is higher than placebo in reduction of pain amongst patients who suffer from OA. On the other hand, they reported that the application of NSAIDs in treatment of osteoarthritis would not be without any side effects, but unfortunately the fact is that a lot of patients and medics approve these remedies for various treatment term application.[27] Anyway, the remedial productivity of these remedies would often be restricted due to their side effect development, mainly complications of gastrointestinal ulceration. Complications of peptic ulcer like perforation and bleeding corresponding with NSAID medication mostly happen without any previous warning and could be great threatening for life. The properties of ginger extracts are not known certainly, but investigations around the extracts of lipophilic rhizome have proved that shogaols, gingerols and some possible active components could be achieved.[26]

Inflammation could increase arachidonic acid oxygenation which would be metabolized via 5-lipoxygenase and cyclooxygenase and could be outstanding to leukotriene B4 and prostaglandin E2 which two of them are strong inflammation mediators.[21] However, ginger possess chemical substances with potential of antiinflammatory effect which would be able to have the effects of shogaols, dialdehyd diterpens, diphenylheptanoids and gingerols which could prevent physiologically active lipid compounds inflammation.[28] These agents could prevent of synthesis of signaling molecules which could make the extracted materials more efficient in the rheumatology field. Therefore, the ginger anti-inflammatory efficacy would be because of the decrement of the leukotrienes and prostaglandins formation.[28,29]

Alternative and supplementary remedies within the arthritis therapy

OA is a prolonged intense disorder and involves frequent application of therapeutic managements that would have various side effects and invalidate the favorable effects on extended use. Consequently, there is a great demand for effective and safe alternative remedies which would be free of any side effects. On the other hand, Ahmet *et al*.[30] suggested that the application of alternative and supplementary therapeutic strategies such as traditional medicines (TM), alternative medicine like acupressure and acupuncture, homeopathy, vitamin completion and dietary limitation and also prayer and spiritual healing has been growing between patients who suffer from rheumatic diseases. Additionally, they reported that approximately 48% of adults aged 60 and over who suffer from osteoarthritis use alternative supplementary medicine.[30]

In accordance with reliable sources, the application of herbal remedies like some folk and traditional systems of medication is widely spread. This is due to that plenty of plants have registered details of their application within traditional systems from the ancient past and also are easily obtainable and inexpensive.[30] Z. zerumbet is a kind of plant belonged to the ginger family, has leafy stems and growing to a height of 1.2 m. It arises from Asia originally, but occasionally could be discovered in many tropical countries. Some other ordinary names are including shampoo ginger, bitter ginger, pinecone ginger, and awapuhi. The leaves grow from its branched rhizome and also the flowers that which are similar to orchids, colorless, and would take place within a dense spike-primrose including of multiple overlapping scales upon an extended stalk. Additionally, as reported by Baliga *et al*.[31] it has been farmed more than thousands of years for pharmaceutical reasons and also as a popular spice.[31]

Ginger phytochemicals properties

Investigation of phytochemical properties of ginger have demonstrated that it's rhizome have a broad range of biologically active compounds. quantitative researches represent that the rhizome has protein, fatty oil, volatile oil, vitamins, ash, water, crude fiber, and various minerals.[32]

Ginger anti-inflammatory effect

Inflammation is a complex procedure which affects both molecular and cellular components and also could actuate extensive variations within the physiological systems. The main characteristics of inflammation are include inactivating mutations, swelling, heat, redness, and pain.[33] Based on the onset and time duration of inflammation, it could be signified as chronic or acute and additionally would be detrimental or beneficial. The time duration of acute inflammation is not long, occur rapidly and is decisive for deflecting infection. On the other hand, chronic inflammation would last longer and frequently is damaging. Inflammation of stratum synoviale would cause multiplication of articular mucosa, cartilage destruction, interpenetrate bone, tendons and ligament tears and could causes in destruction of joints.[33,34] The ginger anti-inflammatory characteristics have been investigated and evaluated more than hundred years ago. Ojewole *et al*.[35] have reported that intraperitoneal performance of dried ginger ethanolic extract could interdict the inflammation caused via carrageenans and also induced inflammation of egg albumin.[35] Newly, a specified raw extract of gringer and a small fraction of gingerols in combination with its derivatives have been developed for controlling anti-inflammatory effects upon the genus of gram-positive coccus of rheumatoid arthritis.[27]

Biochemical analytical studies have proved that ginger pacifies synthesis of prostaglandin via prohibition of prostaglandin G/H synthase 1, Prostaglandin-endoperoxide synthase 1, and biosynthesis of leukotriene through preventing arachidonate 5-lipoxygenase.[36] Ginger extract could prevent synthase of prostaglandin-endoperoxide, somehow 8-shogaol and 8-paradol as the main components of ginger could have strong repressive effects on activity of COX-2 enzyme *in vitro*.[37] The repressive activity of COX-1 enzyme of 8-paradol was shown to be more powerful than within the anti-biofilm agents of gingerol analogs.[37] On the other hand, it has been demonstrated that 8-paradol as the main active flavor element of the seeds of ginger could effectively suppress COX-1, while diphenylheptanoids with groups of 1,2-dihydroxybenzene could be the most active against arachidonate 5-lipoxygenase.[38]

Z. zerumbet various aspects

Ginger family consist of a wide range of species and genres which are distributed mostly in Asia.[39] Various members of this family including ginger, turmeric, Z. zerumbet, and true cardamom are mostly applied in traditional medicine, food flavoring, agriculture, and/or ornamental plants.[40,41] In accordance with Marlina[42] reports, plants of the genus zingiber includes nearly 80 species. The major species of genus ginger (Zingiber) is Zingiber officinale Roscoe which biological active compounds include anti-inflammatory properties, pungent constituents of ginger, gingerol, characteristic aroma and flavor. Consequently, this plant mostly would be applied in medical profession and also other purposes related to cooking.[41] Remedial potential of Z. zerumbet maked it possible to investigate its chemical composition. Therefore, Z. zerumbet could produce a combination of large and varied species of organic compounds known as terpenes with a prevalence of sesquiterpenes.[43] Commercially, Z. zerumbet would be used as a pharmaceutical plant with excellent potential of being cultivated without extra prices.

Traditional uses

It's extensively proved that a prevalent comprehension about the application of medicinal herbs in medical care of various disease that require to be acknowledged. The traditional application of medicinal herbs would spread the knowledge and could be employed by scientists for investigation around it's pharmacological activities.[44] Norulaini *et al*.[45] suggested that the rhizome of Z. zerumbet could be used for pharmaceutical purposes. These traditional remedies are commonly produced via fresh rhizome infusion or/and maceration and additionally poultices, tinctures and also various herbals are other remedial applications. On the other hand, Z. zerumbet has a broad range of traditional applications in addition to pharmacological and biological properties.[46]

The rhizome of Z. zerumbet has been broadly applied with significant remedial effects for the remedy of stomach pains, diarrhea, inflammation, flatulence, fever, poisoning, allergies, and bacterial infections.[47] The powder form of rhizome could be applied for treatment of toothache, infections of ear and additionally in form of herbal tea for treating stomach disease.[48] Manpreet *et al*.[49] have investigated about Z. zerumbet cultivation and reported that it's leaves could be used in treatment of joint inflammation and pain. On the other hand, the cooked rhizome juice is an effective material for preventing worms in children. Additionally, Yu *et al*.[43] reported that the smooth sticky substance existing within the mature inflorescence, is full of surfactants and could be used as a natural shampoo.

Herbal biology description

Z. zerumbet is a perennial of the nature of a tuber herb which could be discovered naturally like spread plants within shady and damp parts of mountain slopes or lowlands. This plant could be discovered near water sources, rivers, and waterfalls.[50] However, it could be characterized via it's stems which are nearly 1.5 m high that are round, straight, and are coated with flat leaves sheaths. The cluster and leaves grow up from an underground stem or a thick rhizome. The clusters of flowers are green when they are young would become red when grew up and became old and their height will reach about 10 cm.[51] As one of the main botanical characteristics of Z. zerumbet it could be noted that it's yarn is linked with a long beak which is curved. Additionally, as Yob *et al*.[51] mentioned the seeds of this herb are black and ellipsoids, it's rhizome is thick, yellow, aromatic, and perennial.

Z. zerumbet chemical mixture

Z. zerumbet is combined from various compounds which belong to a broad range of chemical metabolites like terpenes, polyphenols and alkaloids.[52] Terpenes are a broad and various category of organic compounds which could be produced via plenty of plants particularly coniferophyta. One of the main compounds of Z. zerumbet is zerumbone which could be

derived from urgent Z. zerumbet oil and also certify its structure. Zerumbone is a sesquiterpene with one ring of atoms in its molecule which has three double bonds[53] [Figure 2].

Pharmacological activities

The remedial characteristics of the active compositions derived from the rhizome have been applied for treatment of such major disorders like stomach disease.[54] On the other hand, it has been proved that they would have antiinflammatory, antibacterial, antitumoral, antiviral, painkiller, and antioxidant properties.[55-57] Specific biochemical interactions which could point out the characteristics of genuine zerumbone and rhizome derived juice with various dissolvent are mentioned in Table 1.

In accordance with Zakaria *et al*.[66] Z. zerumbet could prevent the prostaglandin-endoperoxide synthase (PTGS) activity within both central nervous and peripheral system and also the inflammatory mediator's synthesis. On the other hand, Somchit *et al*.[71] during their study have worked around two different models of anti-inflammatory constituents of Z. zerumbet consist of macrophage cell culture and paw edema. The remedial management of RAW 264.7 macrophages cells with zerumbone combinations and isolated 3-O-methyl quercetin and kaempfero would offer the most effective prevention of the inflammatory mediator's production. Additionally, Adriana *et al*.[72] have investigated anti-inflammatory and anti-hypersensitive activities of water extract of Z. zerumbet for recognizing its anti-inflammatory effect within vivo and vitro. Peritoneal cells of macrophages picked up from albino BALB/c mice and applied for evaluating the cytokines of IL-4 and tumor necrosis factor of TNFα.

Z. zerumbet biomedical applications

Various parts of plants have been applied within human diet from thousands of years ago. Different parts of plant including flowers, stems and leaves are applied for improving the odor, taste, color, and also the food quality.[73] Additionally, recent methodical experiments and researches have demonstrated the supernatural characteristics of herb extracts and also their derived spices and seasoning as antimicrobial, anti-oxidative, and/or preservative agents.[74] Due to the increment of such disorders like cancer, patients, and specialists would try for finding alternative and supplementary remedies for treating the disorder.[75] Pharmaceutic plants that are contained within group of alternative and complementary medicine because of their content of active different biologically active compounds have the potential of curing some special disorders.[76] In accordance with Shanmugam *et al*.[77] research, a diet which is full of fruits, herbs and seeds which contain essential pharmaceutical compounds would not have any damaging side effects and optimistically could help in prevention and also treatment of cancer. One of these rich plant which has a lot of pharmaceutical effects is Z. zerumbet and its extracts that could be achieved from its rhizome.[77] Sosmitha *et al*.[78] within their study around biomedical characteristics of Z. zerumbet treatment of cancer reported that this plant has been applied for treatment of arthritis and muscular pain due to the fact that it has anti-inflammatory compounds. On the other hand, it would be beneficial for treating severe headaches, ulcers, and high cholesterol.[77]

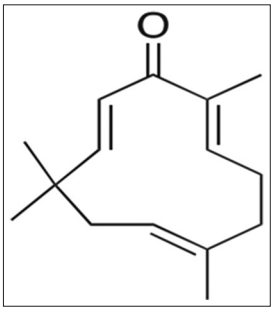

Figure 2: Chemical composition of zerumbone. Derived in accordance with Adriana *et al*.[54]

Anti-inflammatory effects of Z. zerumbet

Somchit *et al*.[72] during their study by studing around the effects of Z. Zerumbone derived from Zingiber zerumbet on reduction

Table 1: Several pharmacological activities of Z. zerumbet. Derived in accordance with Adriana *et al*.[54]

Source	Bioactive extraction compound	Pharmacological activity	Investigation source
Commercial	Zerumbone	Anti-inflammatory and antiproliferative effects	[58]
		Preventive activity versus cells of breast cancer	[59]
		prevention of progression of new blood vessels	[60]
Rhizome	Chloroform	Anti-bacterial activity	[61]
		Anti-bacterial activity against methicillin-resistant staphylococcus aureus	[62]
	Ethanol	Antipyretic and painkiller effect	[63]
		Antimalarials effect	[64]
	Methanol	Analgesic and anti-inflammatory effect	[65]
	Water	Juicy extract does not have toxic effect within the test concentrations	[66]
	Zerumbone	Treatment of alzheimer's disorders	[67]
		Systemic anticoagulant effect	[68]
		Preventing cervical and ovarian cancer	[69]
		Controlling hepatic cancer	[70]
		Effect on digestive system	[47]

of pain and inflammation reported that Z. Zerumbone have great anti-inflammatory capabilities.[72] Akkaya *et al*.[79] have worked on the effect of Z. zerumbet on tissue compatibility type II cells in osteoarthritic joint synovial stratum and reported that Z. zerumbet could prevent antigen-presenting cells (APCs) of immune and also decrease the osteoarthritis inflammatory process.[79] Somchit *et al*.[72] and Hosseinpour *et al*.[80] have worked on the application of Z. zerumbet due to its anti-inflammatory and analgesic characteristics and reported that, Z. zerumbet powerfully could prevent inflammation via lambda carrageenan and dinoprostone which was comparable to the nonsteroidal anti-inflammatory drug of the oxicam class. Additionally, they demonstrated that Z. zerumbet could prevent pain just alike to the NSAIDs.[80] Zakaria *et al*.[66] have investigated anti-inflammatory and antinociceptive of Z. zerumbet on arthritis. The reported that Z. zerumbet has the capability of prevention of prostaglandin-endoperoxide synthase (PTGS) and nitric oxide synthase (iNOS) in addition with dinoprostone.

The application of Z. zerumbet could increase the proliferation and polarization of T cell via endotoxin motivated the soft gelatinous tissue inside some bones derived dendritic cells within an allogeneic test of mixed lymphocyte reaction. Additionally, Shieh *et al*.[81] reported that Z. zerumbet could acts as anti-allergic agents upon viamodulation of cytokines of T-cell subsets. Al-saffar *et al*.[82] have worked around the productiveness of Z. zerumbet on increment of the immune reaction caused by an antigen within the synovial membrane in the monosodium iodoacetate model of osteoarthritis pain. Their outcomes proved that the application of Z. zerumbet could decrease the OA symptoms and improve the reaction of immune.[82]

Z. zerumbet clinical applications for treatment of OA

Al-Saffar *et al*.[27] have worked around the remedial effects of Z. zerumbet on patients who suffer from osteoarthritis. They reported that, Z. zerumbet could be applied for reduction of rheumatological pain and also attempted to confirm the Z. zerumbet role in reduction of joint pain such as OA. Additionally, at their study Al-Saffar *et al*.[27] demonstrated that the application of Z. zerumbet was obviously more advantageous than response of placebo in treatment of such disorder. Ganabadi *et al*.[29] have investigated around the effects of zerumbones as the main extract of Z. zerumbet on the treatment of osteoarthritis and reported that, the application of this remedy does not have any serious side effects. Additionally, they noted that this plant could easily mitigate edema and pain in patients who suffer from rheumatoid arthritis (RA) and OA disorder without having any adverse side effects during the period on application.[29]

Conclusion

Osteoarthritis (OA) is a degenerative joint disease, which is associated with increased pain and disability, and a simultaneous decline in the quality of life of sufferers. Various number of scientific experiments have investigated the application of the best knowledge of productiveness of Z. zerumbet in OA disorder, although the findings of these studies are not compatible. In accordance with the last researches, not any special cure is existing for OA. It's while there are multiple remedies for reduction symptoms of patients who suffer from disorders and related inabilities which could enhance their life quality. Remedies which have been applied for a long time for treatment of OA have newly discovered to induce injury to some patients. On the other side, additional knowledge about alternative and supplementary remedies is a main way for enhancing health of patients who suffer from OA disorders. Nonsteroidal anti-inflammatory drugs (NSAIDs) frequently are applied for symptomatic treatment of the disease and are linked with various side effects which would increase the attention to alternative remedy options. Z. zerumbet is a plant which could be frequently applied for reduction of OA symptoms because of its circulatory stimulant and anti-inflammatory effects.

Zingiber zerumb*et al*.so known as bitter ginger is an aromatic, tuberose plant which is perennial and grows within humid climates. Z. zerumbet traditionally could be discovered all over Asia where it is broadly applied within drink, foods and also as ornamental plants. The sticky liquid existing in the clusters of this plant is containing surfactants which could be applied as a hair shampoo.

The chemical composition of Z. zerumbet is mainly composed of polyphenols and terpenes. Zerumbone is a sesquiterpenoid with biological effects and broadly being investigated for its pharmaceutical properties. The substances and liquids extracted from Z. zerumbet are having such properties including antiviral, antimicrobial, anti-inflammatory, antidiabetic, analgesic, anticancer, and antioxidant. Additionally, Z. zerumbet could be applied as advantageous and safe remedies for decreasing the pain intensity and consequently could improve functional capacity of patients who suffer from OA disorder. Due to the fact that the prevalent documents around the effectiveness of this herbal remedies is not convincing enough, additional researches are required for determining if Z. zerumbet is more impressive than any other remedies.

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Conflicts of interest

There are no conflicts of interest.

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