An Overview Of Recent Research On The Pharmacological, Toxicological, And Phytochemical Properties Of Ginger (Zingiber Officinale Roscoe)

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Abstract
Since ancient times, ginger (Zingiber officinale Roscoe, Zingiberaceae) has been used in Chinese, Ayurvedic, and Tibb-Unani herbal medicines all over the world for a variety of unrelated illnesses. Rheumatism, arthritis, sprains, sore throats, cramps, constipation, indigestion, vomiting, fever, infectious diseases, and helminthiasis are a few of these conditions. Ginger is currently experiencing a resurgence in popularity, and a large number of scientific studies are being carried out to determine the active ingredients of the plant, validate its pharmacological actions and constituents, and provide evidence for the plant's application in treating a range of diseases. This article's objective is to review the most notable recent reports on these investigations. Ginger and the compounds extracted from it have a multitude of pharmacological properties, including anti-inflammatory, anti-tumorigenic, anti-apoptotic, anti-hyperglycaemic, anti-lipidemic, and anti-emetic effects. Strong antioxidants like ginger have the power to reduce or even stop the production of free radicals. It's believed to be a safe herbal remedy with very minor negative effects. Further studies on the kinetics of ginger and its components, as well as the long-term effects of consumption in humans and animals are required.

Keywords: anti-oxidant, anti-emetic, anti-tumorigenic, anti-inflammatory, and ginger and gingerols

1. Introduction

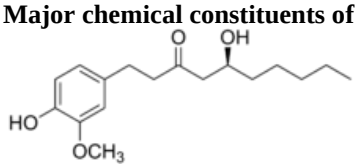
The spice ginger (Zingiber officinale Roscoe, Zingiberaceae) is used in cuisines worldwide. It's been a key ingredient in Chinese, Ayurvedic, and Tibb-Unani herbal medicines for centuries. These medicines are used to treat a variety of ailments, including diabetes, constipation, rheumatism, gingivitis, toothaches, asthma, and neurological disorders (Awang et al., 1992); (Wang et al., 2005); (Tapsell et al., 2006). This plant's widespread use as a spice and medicinal plant may be the reason it has been the focus of numerous reviews in the literature (Afzal et al., 2001); (Chrubasik et al., 2005). Many reviews have highlighted specific aspects of ginger's behavior. The review by Grzanna et al. is one such example. While the 2005 study looked at ginger's potential to prevent cancer, study concentrated on the substance's possible anti-inflammatory properties (Shukla et al.,2007). Examined ginger's effects as a post-operative anti-emetic medication. The aim of this synopsis was to highlight the traditional and modern medicinal applications of ginger and its active components (Chaiyakunapruk et al.,2006).

2. Chemistry

The composition of ginger varies greatly depending on where it comes from and whether the rhizomes are fresh or dry. Rather than covering all the many compounds that have been reported for ginger, our aim in this review is to give a summary of the primary ingredients that have been connected to the pharmacological actions of the unrefined drug.
The volatile oil in ginger, which has a yield ranging from 1% to 3%, is the main component that determines its smell. Sesquiterpenoids [a-zingiberene (30–70%), b-sesquiphellandrene (15–20%), b-bisabolene (10–15%), (E–E)-a-farnesene, curcumene, zingiberol] and monoterpenoids [b-phellandrene, (+)-camphene, cineole, geraniol, curcumene, citral, terpineol, borneol] make up the majority of the oil's components. Certain components of oil change into substances that become less indicative of an odor after drying (Langner et al., 1998); (Evanse et al., 2002). The strong flavour of fresh ginger is mostly attributed to the homologous class of phenols called gingerols. The most common gingerol is [6]-gingerol, though other gingerols with different chain lengths are also present in smaller amounts. Shogaols, or dehydrated gingerols {e.g., [6]-shogaol, are the primary source of pungency in dry ginger. Shogaols are produced by heat processing corresponding gingerols (Wohlmuth et al., 2005). Additionally, it was found that the rates of [6]-gingerol to [6]-shogaol degradation varied with pH, exhibiting the fastest reversible degradation at pH 1 and 100 C and the maximum stability at pH 4. (Bhattarai et al., 2001). The thermal degradation of gingerols to ginger-one, shogaols, and related compounds was demonstrated by (Jolad et al.,2004). In fresh, organically grown ginger, discovered 63 compounds, 20 of which had never

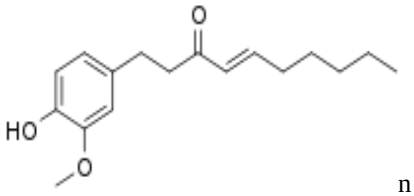
been previously identified and 31 of which had been previously reported as ginger constituents. Gingerols, shogaols, 3-dihydroshogaols, paradols, dihydroparadols, gingerol acetyl derivatives, gingerdiols, mono-and di-acetyl derivatives, 1-dehydrogingerdiones, diarylheptanoids, and certain methyl ether derivatives of these compounds were among the components that were identified (Jolad et al.,2004). Other forms of the compound were identified as and gingerol except gingerol in addition to methyl and methyl gingerol. In addition to the compounds and shogaol, the following compounds were characterized: methyl methyl and methyl shogaol. Examined commercially processed dry ginger using the same techniques as their 2004 study. Eighty-eight of the 115 compounds they found were published (Jolad et al.,2005). According, 45 of these had already been identified as fresh ginger. The remaining thirty-one compounds were new and included [6]-isoshogaol (13), methyl [8]-paradol, and methyl [6]-isogingerol. The remaining 12 components had been isolated earlier by other staff members. It was observed that fresh white and yellow gingers contained [6]-(14), [8]-, [10]-, and [12]-gingerdiones, which had not previously been identified in gingers. The dried ginger had slightly lower concentrations of gingerols than fresh ginger, but higher concentrations of shogaols to (Melad et al.,2004).

Fig. 1. Major chemical constituents of ginger.

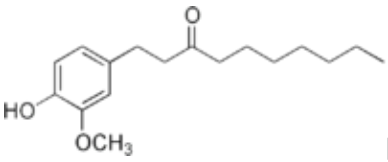


n = 4 [6] - gingerol 1

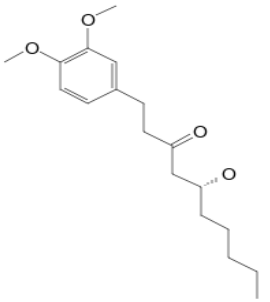
n = 2 [4] - gingerol 3
n = 5 [7] - gingerol 4
n = 6 [8] - gingerol 5
n = 8 [10] - gingerol 6



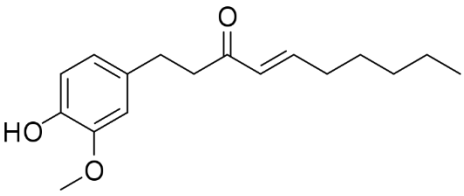
n = 4 [6] - shogaol 2
n = 2 [4] - shogaol 7
n = 6 [8] - shogaol 8
n = 8 [10] - shogaol 9
n = 10 [12] - shogaol 10



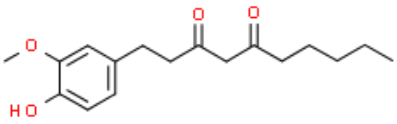
[6] - paradol 11



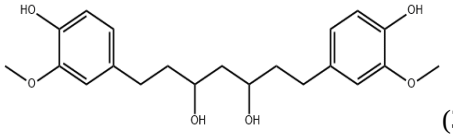
methyl [6] - isogingerol 12



[6] - isoshogaol 13



[6] - gingerdione 14



(3S,5S) - 3,5 - diacetoxy - 1,7 - bis (4-hydroxy-3-methoxy) - heptane 15

Dialylheptanoids have been reported to be present in both fresh and dry ginger (Jolad et al., 2004), (Ma et al., 2004) reported the isolation of seven previously unidentified diarylheptanoids from the ethanol extract of Chinese ginger, in addition to 25 known compounds, including 8 diarylheptanoids. (3S, 5S)1,7-bis(4-hydroxy-3-methoxyphenyl)-3,5-diacetoxyOne example of a novel compound that has been reported is heptane (Ma et al. 2004). In a subsequent paper by several constituents of ginger, including some diarylheptanoids and compounds related to gingerol, showed significant cytotoxic and apoptotic activities against human promyelocytic leukaemia cells. It has been shown that the following features of the structure significantly increase activity: A high-performance liquid chromatographic method for analysing the primary components of ginger ([6]-, [8]-, [10]-gingerol and [6]-shogaol) in dietary supplements, spices, teas, and drinks that contain the crude drug were recently published by Schwertner and Rios (in press) (Wei et al., 2005).

3. Pharmacological properties of ginger

3.1. Kinetics

Though a great deal of research has been done on ginger in both humans and an animal, relatively little is known about how it impacts patients who are undergoing treatment. After a three milligram/kg bolus intravenous injection of [6]-gingerol (1), the plasma concentration–time curve was described by a two-compartment open model. Gingerol was extracted from plasma quickly, with a terminal half-life of 7.23 minutes and a total body clearance of 16.8 ml/min/kg. [6]-gingerol had a 92.4% binding percentage to serum proteins (Ding et al., 1991). When the same group looked at the kinetics in rats with experimental acute hepatic or renal failure, they found that there were no appreciable differences in any pharmacokinetic parameter or plasma concentration–time curve between the control and nephrectomised rats (Naora et al., 1992)**.** Thus, the theory states that renal excretion plays no part at all in the removal of [6]-gingerol from rat plasma. However, because of hepatic toxicity, [6]-gingerol's plasma concentration rose during the terminal phase. Its elimination half-life increased from 8.5 to 11.0 min in rats with hepatic damage. Serum protein bound less than 90% of the [6]-gingerol (1), and the toxicity had no effect at all. These elements imply that the liver contributes to the partial removal of [6]-gingerol**.** 10,000 · g of supernatant from rat liver treated with phenobarbital was used to study the main pungent component of ginger, S-(+)- [6]-gingerol (1), in vitro (Surh et al.,1994). The mechanism for producing NADPH was present in this system. The stereospecificity of the reduction was shown. The ethyl acetate-extractable products were separated using gas chromatography/mass spectrometry, and it was discovered that two metabolites were diastereomers of [6]-ginger diol. The same authors have shown that the pungent principle of ginger, [6]-shogaol (2), can be reduced in vitro in rat liver. The creation of Shogaol's ethyl acetate-extractable metabolites involved combining this alpha, beta-unsaturated ketone with a rat liver cytosolic fraction fortified with either a NADPH- or a NADPH-generating system; two major metabolites were identified as 1-(4-hydroxy-3-methoxyphenyl)-decan-3-one {[6]-paradol (11)} and 1-(4-hydroxy-3-methoxy)-decan-3-ol (reduced [6]-par-adol. Under similar incubation conditions, 1-(4-Hydroxy-3-methoxyphenyl)-deca-1-ene-3-one (dihydroparadol), a non-pungent analogue of shogaol, formed the same metabolites as [6]-shogaol. It appears that paradol mediates the reductive metabolism of alpha. through shogaol's corresponding saturated alcohol, the beta-unsaturated ketone moiety (Surh et al.,1994). These isolated metabolites' pharmacological properties have not yet been documented. The diastereomers of two aliphatic hydroxylation products, the diastereomers of [6]-ginger diol, and two aromatic hydroxylation products were tentatively identified by means of gas chromatographic–mass spectrometric (GC–MS)

analysis. This was observed after rat hepatic microsomes fortified with NADPH were incubated with [6]-gingerol, producing eight metabolites. Liquid chromatography-mass spectrometry/mass spectrometry (LC-MS/MS) analysis revealed that hepatic microsomes from rats and humans, fortified with UDPGA, glucuronidated [6]-gingerol primarily at the phenolic hydroxyl group. However, there were also traces of a different monoglucuronide that had an aliphatic hydroxyl group present. Only the phenolic glucuronide was formed by human intestinal microsomes. While UGT1A9 catalysed the specific formation of the alcoholic glucuronide and UGT2B7 the predominant, highly active formation of the phenolic glucuronide, supersomes containing human UGT1A1 and 1A3 exclusively generated the phenolic glucuronide, albeit with very low activities. According to given the compound's wide range of biological activities, it is important to take into account the relatively complex metabolism of [6]-gingerol, which this study demonstrates (Pfeiffer et al., 2006). Investigated the metabolic fate of [6]-gingerol in rats. S)-[6]-gingerol-40 - O-b-glucuronide was found to be a major metabolite in the bile of rats that had received oral [6]-gingerol, according to high-performance liquid chromatographic (HPLC) analysis. Following enzymatic hydrolysis, the urine's ethyl acetate extract revealed the presence of six minor metabolites: 9-hydroxy [6]-gingerol, ferulic acid (S)-(+)-4-hydroxy-6-oxo-8-(4-hydroxy-3-methoxyphenyl)-octanoic acid, 4-(4-hydroxy-3-methoxyphenyl) butanoic acid and vanillic acid (Nakazawa et al., 2002). Urine did not contain any of the [6]-gingerol metabolites. The total cumulative amount of the major metabolite excreted in the bile and the six minor metabolites in the urine within 60 hours of oral [6]-gingerol administration were approximately 48% and 16% of the dose, respectively. The excretion of the six minor metabolites in the urine decreased after gut sterilization, suggesting that the gut flora may be involved in metabolism. On the other hand, when [6]-gingerol was incubated with rat liver, 9-hydroxy- [6]-gingerol, ginger diol, and (S)- [6]-gingol-40-O-b-glucuronide were discovered. These findings suggest that gut microbiota and hepatic enzymes are important components in the metabolism of [6]-gingerol.

3.2. Effect on lipid and glucose concentrations in blood

It has been observed that treatment with a methanolic extract of dried ginger rhizomes significantly reduces the elevation of body weight, lipid levels, hyperglycaemia, and hyperinsulinemia brought on by fructose. After being treated with an ethyl acetate extract of ginger, neither of the final two parameters showed any discernible changes. However, the end result was elevated lipid levels and a significant reduction in body weight. The concentration of [6]-gingerol in the methanol extract was found to be higher than that of the ethyl acetate extract. The results suggest that the methanolic extract of ginger has greater beneficial effects than the ethyl acetate extract in fructose-induced hyperlipidemia associated with insulin resistance. The amount of [6]-gingerol in the extracts appears to be related to their level of activity (Kadnur et al., 2005). For eight weeks, mice were given extracts of ginger (methanol and ethyl acetate) by the same authors (Goyal et al., 2006). They saw that the treatment reduced the elevated levels of insulin and glucose in the treated mice as well as the obesity brought on by goldthioglucose. It was suggested that ginger had greatly improved the animals' sensitivity to insulin. Tested the hypoglycemic potential of raw ginger in diabetic rats induced with streptozotocin (STZ). For seven weeks, the rats received 500 mg/kg of an aqueous extract of raw ginger intraperitoneally every day. Tests were conducted on fasting animals' blood serum to measure triacylglycerol, cholesterol, and glucose levels. The rats that were given STZ injections showed signs of hyperglycaemia and weight loss. When compared to the control group, the diabetic rats given 500 mg/kg of ginger showed a noteworthy reduction in their levels of triacylglycerol, cholesterol, and serum glucose. Urine protein levels were also significantly reduced by the ginger treatment. Furthermore, the diabetic rats that were fed ginger kept their starting weights throughout the course of the treatment. Furthermore, in the STZ-induced diabetic rats, ginger reduced the amount of water consumed as well as urine produced. These findings supported previous research that postulated the hypoglycemic, hypocholesterolaemia, and hypolipidemic benefits of raw ginger. It also demonstrated the effectiveness of raw ginger in halting the proteinuria and weight loss of the diabetic rats. Ginger may therefore assist in reducing the consequences of diabetes complications in people. Without raising the risk of hypoglycaemia, aldose reductase inhibitors are thought to hold great promise in the treatment of diabetes mellitus and its complications (Giannoukakis et al.,2006). According to a recent report, five active compounds, including 2-(4-hydroxy-3-methoxyphenyl) ethanol and 2-(4-hydroxy-3-methoxyphenyl) ethanoic acid, were isolated from ginger during the aldose reductase inhibitor assay. These two compounds, with IC50 values of 19.2 ± 1.9 and 18.5 ± 1.1 lM, respectively, demonstrated good inhibitory effects against recombinant human aldose reductase. Moreover, these substances greatly decreased the quantity of lens galactitol that accumulated in 30% of cataract rats fed galactose and the quantity of sorbitol that accumulated in human erythrocytes. According to, these results imply that ginger or its extract containing aldose reductase inhibitors may be taken as a dietary supplement to prevent or treat diabetic complications (Kato et al.,2006). But given what is known about the long-term effects of ingesting ginger in humans, more research is necessary in addition to the limited amount of experimental data (Tapsell et al., 2006).

3.3. Effect on blood clotting

We looked at the effects of giving rats an oral or intraperitoneal (IP) raw aqueous extract of ginger for four weeks in terms of prostaglandin-E2 (PGE2) and platelet thromboxane-B2 (TBX2). A modest dosage of ginger (50 mg/kg), administered orally or intraperitoneally, did not significantly lower the levels of TBX2 in the serum. At this dosage, however, oral ginger administration dramatically altered serum PGE2. Ginger at high doses (500 mg/kg) administered orally or intraperitoneally was found to be significantly effective in reducing serum PGE2. TXB2 levels were considerably higher in rats given IP than in rats given 500 mg/kg of ginger orally. These results suggest that ginger may have applications as an anti-inflammatory and anti-thrombotic drug (Thompson et al., 2002).

3.4. Effect on blood pressure

Many pieces of evidence, primarily from rat studies, have demonstrated the diverse direct and indirect effects of ginger on blood pressure and heart rate (Afzal et al., 2001) [28]. More recently, discovered that when anesthetized rats were given a crude extract of ginger, their arterial blood pressure dropped in a dose-dependent manner (0.3–3 mg/kg) (Ghayur et al.,2005). In paired atria from Guinea pigs, the crude extract had a cardio depressant effect on the force and rate of spontaneous contractions. In the rabbit thoracic aorta preparation, the crude extract attenuated the phenylephrine-induced vascular contraction at a dose ten times higher than that required to prevent K-induced contraction. The Ca2+ channel-blocking activity of the crude extract was confirmed by its capacity to cause a shift to the right in the Ca2+ dose-response curves, similar to the effects of verapamil. Additionally, it demonstrated that it functions at both membrane-bound and intracellular Ca2+ channels by suppressing the phenylephrine control peaks in both Ca2+-containing and non-Ca2+-containing normal solutions. It was found to relax the K-induced contraction at a dose 14 times lower than that needed to relax the PE-induced contraction in rats with intact endothelium aortas. Because the vasodilator effect of the crude extract was replicated in the endothelium-denuded preparations within the same dose range and because it was unaffected by atropine or L-NAME, a non-selective inhibitor of nitric oxide synthase that is used experimentally to induce hypertension, it was concluded to be endothelium-independent. These results suggest that the mechanism by which ginger reduces blood pressure may involve the blocking of voltage-dependent calcium channels. In a different paper, the same group concluded that the dual inhibitory effect of the aqueous ginger extract, which lowered blood pressure, was mediated by both muscarinic receptor stimulation and Ca2+ channel blockade. It's interesting that they also brought up the possibility of contradictory effects on blood vessel reactivity from the different components of ginger. In contrast, [6]-shogaol showed a mild vasodilator effect. For example, the ginger phenolic constituents [6]-, [8]-, and [10]-gingerol were found to exhibit both an atropine-resistant and L-NAME-sensitive vasodilator activity (Ghayur et al., 2005).

3.5. Anti-inflammatory and analgesic activities of ginger

Ginger has long been known to have anti-inflammatory qualities (Afzal et al.,2001); (Grzanna et al., 2005). Numerous lines of evidence have been used to support the anti-inflammatory and anti-inflammatory mediator properties of ginger or its isolated compounds. Most of these lines of evidence relate to various animal models of inflammation and, to a lesser extent, to human or human cell models. Ginger was first demonstrated to have anti-inflammatory properties in the early 1980s due to its ability to inhibit prostaglandin synthesis (Kiuchi et al., 1982). Further studies have demonstrated that in intact human leukocytes cultured in vitro, components of ginger, such as gingerdiones (e.g., 14) and shogaols (e.g., 2, 7–10), have pharmacological properties reminiscent of dual-acting non-steroidal anti-inflammatory drugs (NSAIDs) (Flynn et al., 1968). Compared to conventional NSAIDs, these inhibitors are known to be less harmful and more effective (Charlier et al., 2003) ;(Martel-Pelletier et al., 2003). Furthermore, it has been shown that gingerols are very successful at preventing leukotriene and prostaglandin synthesis in RBL-1 cells. Furthermore, it has been discovered that gingerols with longer alkyl side chains are more efficient in inhibiting the synthesis of leukotrienes than prostaglandins (Kiuchi et al., 1992). More recently, research has shown that ginger (and some of its constituents) efficiently suppresses cytokine production and secretion at the sites of inflammation (Grzanna et al., 2005). At sites of inflammation, lymphocytes, macrophages, fibroblasts, and other cells release small proteins known as cytokines. They carry out the role of chemical messengers between immune system and inflammatory response cells. Ginger has been shown by to modulate specific biochemical pathways that are activated in chronic inflammation (Grzanna et al., 2005).

It was discovered that the induction of many genes associated with the inflammatory response was inhibited; these genes included those that encoded chemokines, cytokines, and the inducible enzyme cyclo-oxygenase-2 (COX-2). Demonstrated the effect of ginger extract on human monocyte cell activity using an experiment involving cultured THP-1 monocytes. They discovered that the extract can prevent the expression of chemokines and cytokines that are triggered by beta-amyloid peptide (Grzanna et al., 2004). In an in vitro investigation, the same group showed that Z. officinale extract inhibits pro-inflammatory cytokines and chemokines secreted by leukocytes, chondrocytes, and synoviocytes, thereby suppressing inflammation brought on by arthritis. Ginger extract was found to be an effective way to inhibit the expression of chemokines (Phan et al., 2005). The anti-inflammatory, analgesic, and antipyretic effects of an ethanolic ginger extract were tested on rats. The extract decreased carrageenan-induced paw swelling and yeast-induced fever, but it was unable to stop the writhing brought on by intraperitoneal acetic acid (Mascolo et al., 1989). Additionally, a dose-dependent inhibition of prostaglandin release was observed using rat peritoneal leucocytes. Confirmed the inhibitory effect of ginger on prostaglandins by observing that giving rats a raw aqueous extract of ginger (500 mg/kg) orally or intraperitoneally for four weeks was effective in significantly lowering serum prostaglandin-E2. A recent study in rats and mice demonstrated the anti-inflammatory, analgesic, and antipyretic effects of an ethanolic ginger extract (Ojewole et al., 2006) (Thomson et al., 2002).The mechanism of action of ginger, compounds containing gingerol, and their derivatives has been studied by many authors. Gingerols and their derivatives, especially [8]-par-adol, have been found to be more effective anti-platelet and cyclo-oxygenase-1 (COX-1) inhibitors than aspirin when tested in vitro using the Chrono Log whole blood plate-let aggregometer (Nurtjahja-Tjendraputra et al., 2003). These authors suggest that the carbonyl functional group at position C3 may be responsible for the potent anti-platelet action of paradol and the diarylheptanoid series, as well as their inhibition of COX-1. These phenolic compounds may function by suppressing the thromboxane synthase/COX-1/system, which in turn suppresses the cascade of AA metabolism. Compared aspirin's capacity to inhibit AA-induced human platelet serotonin release in vitro with that of gingerols and related analog. Gingerols and related analog were found to be, within the same dose range, approximately two to three times less potent than aspirin against the platelet release reaction induced by AA and two to four times less potent than aspirin at inhibiting AA-induced platelet aggregation. Gingerols

inhibited COX activity, as shown by measuring PGD2, a byproduct of COX's metabolism of AA. These results suggest that the inhibition of COX activity may be the underlying mechanism by which gingerols and related analog influence AA-induced platelet activation. In a different study, the same Australian group suggested that gingerols are agonists of the vanilloid receptor (VR1) (Koo et al., 2001) (Dedov et al., 2002). It has been shown that the VR1 receptor combines chemical and thermal nociceptive stimuli (Quirion et al., 2007). Therefore, direct activation/deactivation of the VR1 receptor at the site of pain generation during inflammation and other painful conditions represents a novel approach to the development of a new class of peripheral analgesics free from the well-known side effects of currently available analgesics and anti-inflammatory drugs. The production of nitric oxide (NO) by the pro-inflammatory enzyme inducible nitric oxide synthase (iNOS) has been associated with the pathogenesis of inflammatory diseases. studied the effects of a stable [6]-gingerol metabolite called RAC- [6]-dihydroparadol ([6]-DHP) and a closely related gingerol analog known as RAC-2-hydroxy-1-(4-hydroxy-3-methoxyphenyl) dodecan-3-one [a capsaicin/gingerol (capsarol) analog known as ZTX42] on the levels of protein expression in a murine macrophage cell line (Aktan et al.,2006). This was done because gingerols have been shown to have anti-inflammatory properties in vitro (Kiuchi et al., 1992); (Kim et al., 2005). [6]-DHP suppress NO production in murine macrophages by partially inhibiting iNOS enzymatic activity and reducing iNOS protein production, via attenuation of NF-kappa B-mediated iNOS gene expression, providing a possible mechanism of action for the anti-inflammatory activity reported for this class of compounds. More recently (in press) tested the hypothesis that whole ginger extract has a global inhibitory effect on macrophages function in vitro and that this accounts for its reputed anti-inflammatory effect in vivo. They also assumed a few things that the active component of ginger, [6]-gingerol, effectively reduces inflammation because it inhibits lipopolysaccharide-induced macrophage activation, or more accurately, by preventing these cells from presenting antigen and producing pro-inflammatory cytokines. It was found that although [6]-gingerol has no effect on antigen-presenting cells' (APCs) ability to function, it does specifically prevent macrophages from producing pro-inflammatory cytokines. Thus, [6]-gingerol, an anti-inflammatory compound, works and may be useful in treating inflammation without interfering with the macrophages' capacity to deliver antigens. Studies have indicated that the gastrointestinal side effects commonly associated with conventional NSAIDs due to prostaglandin inhibition are not caused by ginger or any of its constituents (Goldstein et al., 2004); (Konturek et al., 2005). In fact, research on rats has shown that ginger prevents ulcers (Yamahara et al., 1988); (Wu et al., 1990).

3.6. Effect of ginger on gastrointestinal (GIT) tract

Traditional medicine has long used powdered ginger rhizome to treat symptoms related to the gastrointestinal track diseases (Afzal et al., 2001). Research has shown that an acetone extract of ginger and its constituents to enhance the mice's gastric emptying of the charcoal meal (Yamahara et al., 1990). Ginger's effectiveness in treating vomiting associated with Fischer-Rasmussen hyperemesis gravidarum Additionally, cancer chemotherapy, motion sickness (Stewart et al., 1991), and (et al., 1990) have been declared (Sharma et al., 1997). Ginger has been shown to protect people from post-operative nausea and vomiting leaving the stomach's emptying process essentially unaffected (Phillips et al., 1993b) (Phillips et al., 1993a). Since ginger had no effect on the nystagmus response to optokinetic and vestibular stimuli, the authors conclude that ginger does not have a central anti-cholinergic effect. Although [6]-gingerol has been demonstrated to improve the GIT transit of charcoal meal in rats, the use of insufficient dosages was blamed for the lack of this effect in humans. Ginger extract has been shown to have a potential inhibitory effect on pre-synaptic muscarinic auto receptors, which is comparable to standard muscarinic antagonists, in addition to its direct cholinergic agonistic effect on post-synaptic M3 receptors (Yamahara et al., 1990) (Ghayur et al., 2007). In isolated Guinea pig ileum, it has been shown that ginseng compounds, including [6]-gingerol, [6]-shogaol, and galanolactone, have anti-serotonin (5-hydroxytryptamine) effects (Yamahara et al., 1989); (Huang et al., 1991). The anti-emetic effect of ginger or some of its constituents may be primarily mediated by these constituents because of their small molecular weights and ease of passage through the blood-brain barrier. Oral [6]-gingerol has been shown to completely prevent vomiting in response to cyclophosphamide in Suncus murinus (a house musk shrew), most likely via a central effect (Yamahara et al., 1989). The administration of cisplatin causes nausea and vomiting in both humans and animals. Ginger acetone and 50% ethanolic extracts significantly prevented cisplatin-induced emesis in dogs and rats when administered orally at doses of 25, 50, 100, and 200 mg/kg (Sharma et al., 1997) (Sharma et al., 1998). On the other hand, aqueous extract did not work at these dosages. Looked at the evidence from six clinical trials that suggested ginger could help with nausea and vomiting avoidance. Two of the three studies on post-operative nausea and vomiting showed that ginger had an effect similar to metoclopramide and was more effective than a placebo. Nonetheless, when ginger (1 g) was consumed before surgery, there was no statistically significant difference in the incidence of post-operative nausea between the ginger and placebo groups (absolute risk reduction: 0.052; 95% confidence interval: 0.082 to 0.186) (Ernst et al., 2000). For nausea brought on by chemotherapy, morning sickness, and seasickness, there is only one study available. These studies all seemed to point to ginger's superiority over placebo. The study found that opinions on how effective the crude medication is in treating this illness are still in dispute. More recently, looked at four carefully monitored, double-blind, randomized clinical trials that provide substantial evidence supporting ginger's effectiveness in treating nausea and vomiting associated with pregnancy. Additionally, it provides an updated dosage for each type of ginger. Conducted the first study to demonstrate the efficacy of gingerols, the active ingredients found in ginger, against Helicobacter pylori, the primary cause of peptic ulcer disease, dyspepsia, and the onset of gastric and colon cancer. The study was conducted in vitro (Mahady et al.,2003). Offered more evidence in support of this. O'(Mahony et al.,2005) investigated ginger's bactericidal and anti-adhesive properties along with several other culinary uses and medicinal herbs against H (Mahady et al.,2005)

and (Nostro et al.,2006). Pylori, finding that ginseng was particularly effective in getting rid of the infection but had less ability to stop these bacteria from sticking to the skin. Lately, discovered that H (Siddaraju et al., 2007). Pylori growth and gastric cell proton potassium ATPase activity were significantly inhibited by the phenolic fractions of ginger, both hydrolysed and ginger-free. These results suggested that the two fractions might function as inexpensive multistep ulcer prevention agents.

3.7. Tissue and radio-protective effects of ginger

Several fractions and extracts of Z. officinale have been shown to provide protection against chemical-induced tissue damage. For example, showed that pre-treating rats with an ethanol extracted oil and rhizome extract from Z (Yemitan et al., 2006). Officinal were effective in lowering the intensity of acute pain brought on by acetaminophen (paracetamol) and carbon tetra-chloride hepatotoxicity. The radioprotective effects of ginger rhizome hydroalcoholic extract (ZOE) were investigated in mice given the extract once daily for five consecutive days before the mice were exposed to 6–12 Gy of gamma radiation. After the radiation exposure, the mice were monitored every day for a maximum of 30 days in order to search for indications of radiation sickness and mortality (Jagetia et al.,2003). In a subsequent publication, the same authors confirmed that ginger provides a radiation lethality shield. Mice given ZOE prior to treatment showed reduced mortality and severity of radiation sickness, as well as protection against both gastrointestinal and bone marrow syndrome. ZOE was found to have a 1.15 dose reduction factor (Jagetia et al., 2004). The best protective dose at 10 mg/kg ZOE was 500 mg/kg, or 1/50 of the LD50.Ginger extract has been shown by to mitigate the neuro-behavioural effects of gamma radiation-induced conditioned taste aversion in Sprague-Dawley rats. Five post-treatment observational days were successfully blocked for the saccharin avoidance response by giving the extract one hour before 2-Gy gamma irradiation. The most effective dose for this effect was 200 mg/kg b.w.i.p, which was also observed to be dose- and time-dependent. In a more recent study, the same team examined the potential of a ginger hydroalcoholic extract as a gastroprotective agent, looking into how radiation caused rats to develop taste aversion (CTA) and begin vomiting. They discovered that the extract shielded the rats from CTA in the same way as the widely used anti-emetic medications onasterone and dexamethasone (Sharma et al.,2005). Numerous multifaceted mechanisms, such as neuromodulatory, antioxidant, and radioprotective mechanisms, have been proposed for gastro-protection. Ginger may be a medicinal ingredient that can safely and effectively reduce the early damage that ionizing radiation causes to cells and tissues, according to (Hassar et al.,2006).

3.8. Anti-oxidant actions of ginger

Many authors have shown ginger's strong antioxidant properties in vivo and in vitro. Ginger's antioxidant properties are one of the main theories explaining its protective effects against radiation toxicity and lethality, different toxic agents, and possible anti-ulcer drugs (Amin et al., 2006); (Yemitan et al, 2006) (Siddaraju et al.,2007) (Jaganetia et al., 2003) ;(Haksar et al., 2006). Recent research has shown that [6]-gingerol has strong anti-oxidant, anti-inflammatory, and anti-apoptotic effects in both vitro and in vivo settings (Kim et al., 2007). This makes it a very effective tool for reducing the production of reactive oxygen species and the expression of COX-2 that are brought on by ultraviolet B (UVB), and it may also be used as a treatment for skin conditions that are brought on by UVB.

3.9. Ginger–drug interactions

The literature doesn't contain many reported interactions between drugs and ginger. Ginger does not conflict with the anticoagulant drug warfarin in either rats or humans (Weidner et al., 2000); (Vaes et al., 2000). This was recently confirmed by in a randomized, open-label, three-way crossover study with 12 healthy volunteers. Ginger was taken orally for a week at a dose of 400 mg three times a day prior to starting warfarin. After that, it went on for a further week. Ginger was found to have no appreciable effect on the clotting status or the kinetics and dynamics of warfar in (Jiang et al., 2005). Researchers from Taiwan have looked at the combined effects of ginger and nifedipine on anti-platelet aggregation in both healthy human volunteers and hypertensive patients (Young et al., 2006). It was found that compared to healthy volunteers, a higher percentage of platelet aggregation caused by collagen, adenosine diphosphate (ADP), and adrenaline occurred in hypertensive patients. In individuals with hypertension and healthy volunteers, nifedipine's anti-platelet aggregation properties may be strengthened by aspirin or ginger. These results suggested that ginger and nifedipine had a synergistic effect on anti-platelet aggregation. It has been proposed that a combination of 1 gram of ginger and 10 milligrams of nifedipine taken once a day could be used as a potential treatment for heart and brain problems caused by platelet aggregation.

Table 1. The medicinal properties of ginger and its byproduct

Ginger and its Byproducts	Possible application	Employed assay(s)	Study model	Tested concentration(s)	Applicable extract	Country
Ginger extracts	Agent hepatoprotective	At 200 mg/kg i.p., thioacetamide yields	Rats living in the wild	250–500 mg/kg	Lawn	Philippines

Ginger	Agent hepatoprotective	Brought on by carbon acetaminophen-induced tetrachloride	Inside of living inside of living	200, 400, and 100 mg/kg, as well as 50 mg/kg when combined with 100 mg/kg of curcumin (singly)	NI Water containing ethanol	India and Egypt
Ginger	Antioxidant	Lipid peroxidation	Rats living in the wild	150 mm	Not in	India
Six Gerol And Six Shogaol	Repression of the stomach	Using hexobarbital causes	As it stands	70–140 mg/kg orally, 1.75–2.5 mg/kg intravenously	Not in	Japan
Ginger extracts	Anti-proliferative	G2 cells in the liver	Cell lines	Not in	Lawn	Malaysia
Six-gingerol is found in ginger.	Digestive protection	Ethanol-HCl produced	Inside a living	One thousand milligrams in a kilogram 100 milligrams to one kilogram	Acetonide	Japan
Gingerol comes in sixth.	Fighting oxidation and inflammation	UVB-induced intracellular reactive oxygen species	Both in vitro and in vivo (in mice)	NI stands for nanoliters.	Acetonide	South Korea
Ginger	Neuroprotective	Produced by glutamate monosodium	Within a living	One kilogramme at 100 milligrams	Diluted	Saudi Arabia
Ginger	Antioxidant and antidiabetic	FRAP-induced streptozotocin and MDA	Both in vitro and in vivo rats	Five percent ginger in everyday dishes	Not in	Iran
The essential oil of oleoresin	Antimicrobial (both antibacterial and antifungal)	Disks spreading out	Within living	NI (three uL)	Not in	Algeria
Oleoresin, 6-shogaol, 6-hydroshogaol,8-gingerol, and 10-gingerol	Anti-inflammatory, antimicrobial, and antioxidant	DPPH, disc diffusion, nitric oxide, and ABTS	Within living	Not in	Not in	India, Algeria
Ginger	Antimicrobial	Disks spreading out	Within living	In mg/ml, 1.0%, 0.125, 0.25, and 0.5 35.25, 75, 250, and 500 g/ml (20–40–60–80–100)	Aqueous n-hexane, ethanol, ethyl acetate, aqueous ethanol, ethanol	Nigeria Nigeria
Ginger	Anticancer (prostate and liver)	0.1% brought about by ethionine	In vitro and in vivo	One kilogramme at 100 milligrams	Not in	USA, Malaysia
Ginger	Reduction of cholesterol	Not in	Within a living	1,000, 1,000 mg/kg	Diluting	Kuwait

Extracts of ginger	Prevention of pancreatic cancer	Panc-1 cells	living cell lines	Not in	Lawn	Japan
6-, 8-, and 10-gingerol are found in ginger, but 6-shogaol is not.	Lowering the blood pressure	Resulting from pentothal	Inside a living	3–5 mg/kg	Diluted	Pakistan
	Analgesic, anti-inflammatory, hypoglycemic, and safe profile	Back paw	Rear paw	Between 50 and 800 mg/kg	Lawn	South Africa
Ginger	Anti-diabetic	Common spectrophotometric methods (glycation inhibition, glucose diffusion)	Within living	5, 10, 20, 40 g/L	Diluted	Pakistan
6. Gingerol	Insulin-producing	Causing streptozotocin to occur	Within a living	25, 50 milligrams per kilogram body weight	Diluted	Malaysia
Ginger powder	Anti-inflammatory and anti-arthritic	Back paw	Within a living	33 milligrams per kilogram	Not in	Malaysia
Ginger	Antidiuretic	Stimulating streptozotocin	Within a living	100, 300, and 500 mg/kg bw	Diluted	Malaysia

Table 2: The nutritional makeup of ginger (per 100g or 3.5oz) [13]

Participants	ground-grown ginger root	uncooked ginger root
Protein	8.98g	1.82g
Energy	71.6g	17.7 g
Fat	4.24g	0.75g
Carbohydrates	71.6g	17.7 g
Sugars	3.39g	1.7g
Dietary Fibre	14.1g	2.0g

3.10. Anti-microbial actions of ginger

Ginger extract (10 mg/kg) showed dose-dependent antimicrobial activity against Pseudomonas aeruginosa, Escherichia coli, Salmonella typhimurium, and Candida albicans when given intraperitoneally (Jagetia et al., 2003). According to in vitro research, ginger did not significantly inhibit the growth of *Aspergillus niger* and *Aspergillus flavus*. Based on the average diameter of the inhibition zones or the fungi inhibited found that ginger extract had the broadest spectrum of anti-fungal activity among 29 plant extracts. Ginger extract was the only plant extract that showed any activity against Rhizopus sp.; neither it nor the antifungal medications ketoconazole or berberine could inhibit this organism (Yin et al., 1998), (Ficker et al., 2003b). The same authors used bioassay-guided isolation and identification of anti-fungal compounds from ginger to report that the primary anti-fungal principles are [6], [8], and [10]-gingerols and [6]-ginger diol. The compounds showed activity against 13 human pathogens at concentrations below 1 mg/ml (Ficker et al., 2003a). The gingerol content of the African land race was at least three times higher than that of popular commercial cultivars. Consequently, these authors suggested that ginger extracts be used in therapeutic settings after they were standardized based on the compounds that were discovered to be anti-fungal agents. Investigated the anthelmintic activity of crude aqueous extract (CAE) (2–3 g/kg) and dried ginger powder (CP) in sheep that were naturally infected with mixed species of gastrointestinal nematodes (Iqbal et al., 2006). By day 10, both CP and CAE were exhibiting dose- and time-dependent anthelmintic effects, with maximum reductions in eggs per gram (EPG) of feces of 25.6% and 66.6%, respectively. Levamisole (7.5 mg/kg), a common anthelmintic, demonstrated a 99.2% decrease in EPG.

3.11. Miscellaneous effects

Investigated the components of ginger that aid in raising body temperature (Iwasaki et al., 2006). All gingerols and shogaols raised the intracellular calcium concentration during their interactions with rat transient receptor potential vanilloid subtype 1 (TRPV1)-expressing HEK293 cells. In this sense, the shogaols were more effective than the gingerols. Adverse reactions were induced in rats exposed to [6]- and [10]-gingerol and [6]-shogaol (5 mmol/l). However, no reaction was observed with [10]-shogaol (5 and 10 mmol/l). Rats' hind paws were subcutaneously injected with [10]-shogaol, which elicited nociceptive responses via TRPV1; [6]-shogaol and capsaicin (a caustic substance) were found to have similar effects. Similar effects on energy consumption were also observed for [6]- and [10]-gingerols and [6]- and [10]-

shogaols (1.6 lmol/kg, i.v.), which also stimulated the adrenal catecholamine secretion in rats. [10]-An inhibitor of the adrenaline secretion induced by shogaol, capsazepine, was given. TRPV1's adversary. It was determined that gingerols and Shogaols triggered TRPV1 and increased adrenaline secretion. Remarkably, [10]-shogaol is the only non-pungent substance. Compound that exists between the gingerols and shogaols, suggesting that it might be used as a functional food ingredient. Paraben are a class of chemicals that are widely used as preservatives in the cosmetic and pharmaceutical industries. These compounds' and their salts' primary applications are associated with their fungicidal and bactericidal properties. They can be found in store-bought moisturizers, shampoos, shaving gels, and toothpaste, parenteral and topical medications, cleansing gels, and personal lubricants. They also function as food. Additions claim that an aqueous ginger extract can reduce cytotoxicity. Caused in vitro by paraben (p-hydroxybenzoic acid) on healthy human erythrocytes. To RBC, paraben is added (Asnani et al., 2006). The sample was suspended, and this greatly increased the rate of haemolysis. However, a simultaneous 150 leg/ml addition of paraben and ginger extract dramatically decreased concentration-dependent bleeding in haemolysis caused by paraben. Additionally evaluated the effects of paraben (p-hydroxybenzoic acid) on the amounts of cholesterol, carbohydrates, and acidic, basic, and neutral proteins in the liver and kidney of mice (Verma et al., 2007). It was found that the liver and kidney's levels of all the protein types, carbohydrates, and cholesterol were significantly improved when Z. officinale aqueous extract (3 mg/animal/day) was given orally for thirty days along with paraben. In a recent paper, (Tripathi et al.,) presented preliminary findings indicating that ginger prolongs inhibits several macrophage functions in vitro and transplants mouse hearts into living organisms. The related compound 6-shogaol and the phenolic alanine 6-gingerol used different mechanisms to inhibit gastric cancer cells. Techniques (Ishiguro and associates, forthcoming). The latter compound significantly inhibits cancer cell viability by causing microtubule damage and mitotic arrest, while the former compound had no effect on cancer cell viability.

4. Toxicological properties of ginger

Ginger is a safe herbal remedy, according to the majority of people (Weidner et al., 2000). A unique extract of ginger EV.EXT 33 was given orally to three groups of 22 individuals at concentrations of 100, 333, and 1000 mg/kg. Rat females during gestation, from day 6 to day 15. As a comparison, a fourth group received sesame oil. Body weight and the amount of food and water consumed were recorded during the course of the treatment. The rats were killed on the twenty-first day of gestation, and standard parameters were used to evaluate the rats' reproductive performance. The foetuses were examined in order to markers of teratogenic and toxic effects.

The ginger preparation was warmly greeted. There were no documented deaths or adverse drug reactions. Food consumption and weight gain were similar in all groups during the gestation period. The effectiveness of reproduction was unaffected by the ginger treatment. Foetuses are checked for visceral, external, and changes to the skeleton demonstrated that the ginger preparation had no embryotoxic or teratogenic effects. Considering these findings, it was found that when given to pregnant rats during the organogenesis phase, the ginger preparation EV.EXT 33 did not cause maternal or developmental toxicity at daily doses of up to 1000 mg/kg body weight (Weidner et al., 2001). However, there have been some reported adverse effects of ginger in pregnant rats (Wilkinson et al, 2000). Ginger tea (15 g/l, 20 g/l, or 50 g/l) was given to pregnant Sprague-Dawley rats in drinking bottles from day 6 to day 15. The rats were then sacrificed after that on the twentieth day. The treatment groups lost twice as much embryonic tissue as the control groups did, despite the lack of maternal toxicity controls. The treated foetuses showed no overt morphologic abnormalities. The effect was more noticeable in female foetuses and did not correlate with larger placentas. Foetuses exposed to ginger tea were found to be noticeably heavier than controls. Additionally, treated foetuses had increased to determine advanced skeletal development; the sternal and metacarpal ossification centres were measured. The results of the study show that drinking ginger tea during pregnancy both increases the chance of early embryo loss and stimulates the growth of surviving foetuses (Wilkinson et al, 2000). Ginger has been proposed as a safe and effective alternative to conventional anti-emetic drugs however, until further research is done, it might be prudent for pregnant women to avoid using ginger or its extracts (Marcus et al, 2005). A few mild side effects have been associated with the use of ginger in humans. Twelve healthy participants were given an oral dose of ginger in a clinical trial. For two days, take 400 mg of ginger three times a day, one study subject had moderate diarrhoea for the first two days after starting the ginger pretreatment. Ginger could cause acid reflux; additionally, at doses higher than 6 g, they may a stomach irritant. Inhaling ginger dust may cause IGE-mediated allergies (Chrubasik et al., 2005).

5. Conclusions

The present review aimed to enumerate and analyze the literature that has been produced over the last ten or so years regarding ginger and its components. The papers that have been reviewed provide an additional example of how it could be able to Using terminology from traditional pharmacology and biochemistry; describe the action(s) of traditional medicines. Ginger as well as many others its chemical constituents have strong antioxidant capabilities. Further research on the potential anti-oxidant benefits of using ginger or any of its constituents as a means of combating oxidation is warranted, given the close correlation that exists between oxidative processes in the body and a number of metabolic diseases as well as age-related degenerative disorders. Because ginger is a raw material and some of its constituents have anti-cancer properties, it may be worthwhile to investigate the effect of ginger on vomiting during cancer chemotherapy. To fully comprehend the kinetics of ginger and its constituent parts, as well as the long-term consequences of ingesting them, more research is required. Considered a safe herbal remedy with minimal side effects, ginger can help with various health issues. More human trials are required to determine the efficacy of ginger (or any of its ingredients) and whether

any adverse effects are observed. However, conducting double blind clinical trials is difficult because ginger has a strong taste and smell.

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Conflicts of Interest

The authors declare no conflict of interest.

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