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Medicinal Effect of Ginger extract

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Abstract: **In this paper we have done survey about Gingerol which is derived from the rhizomes or subterranean stems of Zingiber officinale, a tropical herbaceous perennial plant in the family Zingiberaceae. The rhizome of Zingiber officinale (ginger), family Zingiberaceae, is grown in the majority of tropical areas of the world and is consumed as a spice and herbal cure worldwide. The chemical components of ginger rhizomes include volatiles (camphene, phellandrene, curcumene, cineole, geranyl acetate, terpineol, borneol, geraniol, linalool, zingiberol, phellandrene, sesquiphellandrene, bisabolene, zingiberenol, and farnesene) and non-volatile. 6-gingerol has been associated to a number of biological effects, such as anticancer,anti-diabetic, antioxidant, and anti-inflammation. Gingerol (BCS Class II) having so many properties but its therapeutic activity not able to get due to its poor solubility. Variuos approaches used like solid dispersion, microspheres and nanoparticles.Among all Liquisolid technology considered best as it converts drug solution into free flowing powder.**

Indexed Terms- Gingerol, Anticancer,Antidiabetic,Anti-inflammatory **(*Keywords*)**

I. INTRODUCTION

Phytochemicals are known to affect various diseases. Therefore, the chemical prevention of diseases using phytochemicals has become a successful field of research in the last decade(1).Most tropical areas of the world cultivate the rhizome of officinale (ginger), a member of the Zingiberaceae family that is consumed worldwide as a spice and herbal cure (2).

The chemical components of ginger rhizomes include volatiles (camphene, phellandrene, curcumene, cineole, geranyl acetate, terpineol, borneol, geraniol, linalool, zingiberol, phellandrene, sesquiphellandrene, bisabolene, zingiberenol, and farnesene) .

The phenolic compounds from medicinal plants, fruits, and vegetables in their diet may play a significant role in the protection, according to many population-based studies that found that people in South East Asian countries have a lower risk of colon, gastrointestinal, prostate, breast, and other cancers than their western counterparts(5). Gingerols are a group of strong-smelling phenolic compounds found in ginger.

The primary pharmacologically active component of ginger is one of these, 6-gingerol (1-[4'-hydroxy-3'-methoxyphenyl]-5-hydroxy-3-decanone)(6)(7). The active component of the molecule is the aliphatic chain moiety having a hydroxyl group(8).

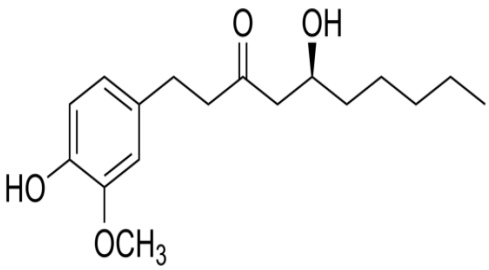

Fig. 1. Structure of Gingerol

Numerous biological characteristics, including anticancer, antioxidant, anti-inflammation, have been linked to 6-gingerol(9)(10)(11)

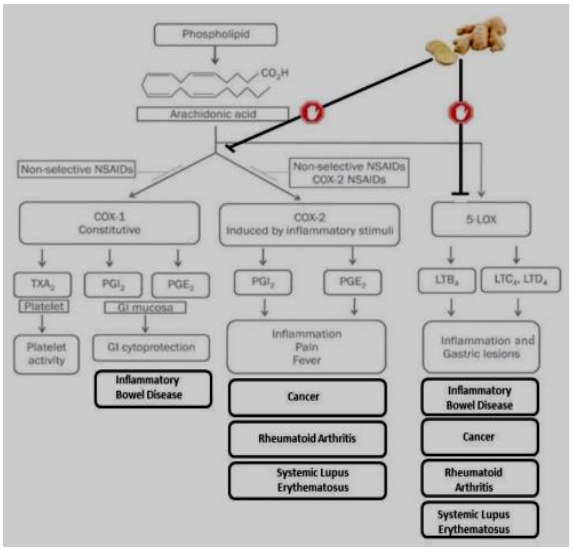

Fig. 2. Uses of Gingerol

II. LITERATURE REVIEW

Anti-oxidative

Free radical scavengers are present in ginger's complex phytochemistry, which is produced by biological processes. Some free radicals produced during the oxidation process are necessary for the generation of energy, Increased production of free radicals results in oxidative stress that can lead to DNA damage. (12). Supplementing the diet with extra antioxidants under such unbalanced conditions is crucial for the health of the organism. Many in vitro and in vivo studies have been conducted to examine the anti-oxidative capabilities of ginger and its constituents.

The body's defences can be strengthened by increasing antioxidant status, which will surely shield people from numerous chronic ailments(13). Humans will surely be protected from many chronic diseases by bolstering the body's defences by increasing antioxidant status(14). In one trial, Z. officinale ethanol extract, both by itself and in conjunction with vitamin E, partially reduced the nephrotoxicity brought on by cisplatin. The renal antioxidant defence system acts as a conduit for this protection(15). The protective effect of ginger extract

against CCl (4) and acetaminophen-induced liver damage was investigated in the other study, and the results suggested that Z. officinale may be helpful in preventing acute liver injury(16).By the inhibition of 5-lipoxygenase or prostaglandin synthetase, gingerol, shogaol, and other structurally similar compounds in ginger prevent the formation of prostaglandins and leukotrienes.

Antiinflammatory

They can also prevent the production of pro-inflammatory cytokines such IL-1, TNF-, and IL-8(17)(18). In a different study, Pan et al. demonstrated that shogaol can suppress the production of the inflammatory genes iNOS and COX-2 in macrophages(19). There is disagreement over the findings of studies examining ginger's efficacy in osteoarthritis sufferers. In a single trial, ginger extract was found to significantly lessen the symptoms of knee osteoarthritis. In a different trial, ginger's impact on osteoarthritis was only felt during the first few weeks of treatment(20 The immune system is strengthened by ginger and its products in many nations By the inhibition of 5-lipoxygenase or prostaglandin synthetase, gingerol, shogaol, and other structurally similar compounds in ginger prevent the formation of prostaglandins and leukotrienes. They can also prevent the production of pro-inflammatory cytokines such IL-1, TNF-, and IL-8 In a different study, Pan et al. demonstrated that shogaol can suppress the production of the inflammatory genes iNOS and COX-2 in macrophages(21). There is disagreement over the findings of studies examining ginger's efficacy in osteoarthritis sufferers. In a single trial, ginger extract was found to significantly lessen the symptoms of knee osteoarthritis. In a different trial, ginger's impact on osteoarthritis was only felt during the first few weeks of treatment(22). As a treatment for gouty arthritis, a rheumatic condition of the joints, [6]-shogaol possesses potent anti-inflammatory and antioxidant properties.Monosodium urate (MSU) crystal deposits in the articular fluid cause the acute inflammatory condition known as gouty arthritis, which is incredibly painful and severe. In addition to treating pain, treatment methods aim to reduce inflammation. In the current study, we assessed the effectiveness of 6-gingerol (25 mg/kg body weight) against inflammation caused by monosodium urate crystals in mice, an experimental model for gouty arthritis. Indomethacin (3 mg/kg body weight), a non-steroidal anti-inflammatory medicine, was utilised as a standard for comparison. Paw volume and lysosomal enzyme levels/activities in normal and monosodium urate crystal-induced mice were measured. In addition, the amounts of acid phosphatase and lactate dehydrogenase released by polymorphonuclear leucocytes (PMNL) that were incubated with monosodium urate crystals in vitro were measured. an increase in lysosomal enzyme levels, and paw volume were seen in mice given monosodium urate crystals. These biochemical changes were restored to nearly normal levels after treatment with 6-Gingerol, comparable to indomethacin. In vitro incubation of PMNL cells with monosodium urate crystals also resulted in a decrease in lactate dehydrogenase and acid phosphate release due to 6-gingerol. These findings firmly establish the viability of using 6-Gingerol as an anti-inflammatory treatment for gouty arthritis(23).

Anticancer

Researchers disagree on the exact mechanism through which ginger works as a spice to prevent cancer. Several components of ginger, including [6]-gingerol, [6]-shogaol, [6]-paradol, and zerumbone, have anti-inflammatory and antitumorigenic properties. Prostate, skin, breast, ovarian, gastric, gastrointestinal, ovarian, hepatic, and colorectal cancers can all be effectively controlled with ginger and its bioactive components(24). It has been proven that ginger and the biomolecules in it are effective at controlling ovarian cancer. Ginger reduced the secretion of VEGF and IL-8 and prevented NF-B activation, which helped treat ovarian cancer(25). The usefulness of ginger against diabetes and its consequences has been demonstrated in some research investigations(26). In an experimental investigation, Weidner and Sigwart found that ginger extract with high gingerol and shogaol concentrations did not significantly alter blood glucose, blood coagulation, blood pressure, or heart rate in rat models(27). In addition to lowering total and LDL cholesterol in high-fat diets, ginger's ethanolic extract also reduced levels of glucose, insulin, triglycerides, free fatty acids, and phospholipids(28). The physiological effects of gingerol on humans have not been extensively studied in clinical trials. A pre-clinical meta-analysis of gingerol compounds reported research in-vitro and in-vivo, as well as anticancer, anti-inflammatory, anti-fungal,antioxidant, neuroprotective(29). Although many of the molecular pathways behind gingerols' actions on cells have undergone extensive study, very few of them have done so in a therapeutic environment. This results from both the vast variety of natural phytochemicals and the ineffectiveness of studies. The African ginger was three times more effective than its commercial Indonesian counterpart when tested for its anti-fungal qualities against 13 human diseases(30). The phytochemicals shogaols, paradols, and zingerone, as well as the gingerol molecules, are hypothesised to cooperate. Two particular research utilising mice found that [6]-gingerol compounds triggered death in cancer cells by interfering with the mitochondrial membrane. This resulted from a meta analysis that examined the impact of numerous different phytochemicals on prostate cancer. Two particular research utilising mice found that [6]-gingerol compounds triggered death in cancer cells by interfering with the mitochondrial membrane. This resulted from a meta analysis that examined the impact of numerous different phytochemicals on prostate cancer. It appears that protein disruption is the primary method by which gingerol phytochemicals affect cancer cells. In a study looking at the molecular mechanisms underlying mouse skin cancer, the anti-carcinogenic efficacy of [6]-gingerol and [6]-paradol was examined, and it specifically targeted the activator proteins linked to tumour initiation. Because AP-1 proteins are blocked by gingerol molecules, normal cells cannot become cancerous. Paradol's cytotoxic action promoted apoptosis when cancer did occur . In cancer cells [6]-gingerol causes apoptosis, enzyme-coupled cell signalling receptor degradation, and cell cycle arrest. Through preventing the translation of Cyclin proteins required for replication during the G1 and G2 phases of cell division, gingerol has been seen to decrease proliferation(31).

Cytochrome C is expelled from the mitochondria to encourage apoptosis in cancer cells, which stops the generation of ATP and leaves the mitochondria dysfunctional. Apoptosis is induced when Cytochrome C forms an apoptosome, which then activates Caspase-9 and starts an executioner Caspase cascade, effectively converting DNA into histones. The anti-apoptotic Bcl-2 proteins on the surface of mitochondria are likewise inhibited by [6]-gingerol, which increases the ability of the pro-apoptotic Bcl-2 proteins to start cell death. Growth hormone activator proteins, which are expressed through enzyme-coupled signalling pathways, are found in abundance in cancer cells. The Akt protein cannot interact with its PH domain when PI-3-Kinase phosphorylation is stopped, effectively inhibiting the downstream signal. A double-negative biological signalling pathway to promote apoptosis is created by successively binding bad proteins to anti-apoptotic proteins, preventing them from stimulating cell growth. To ascertain the effects on living cells, different doses of [6]-gingerol were applied to cultured human breast cancer cells. According to these concentration-dependent findings, there was no effect at 5 M but a 16% reduction at 10 M(32). While adhesion remained mostly unaffected, [6]-gingerol specifically targeted three proteins in breast cancer cells that support metastasis. This prevented the cancer cells from spreading and growing larger, even while adherence was unaffected. While adhesion remained mostly unaffected, [6]-gingerol specifically targeted three proteins in breast cancer cells that support metastasis. This prevented the cancer cells from spreading and growing larger, even while adherence was unaffected. In-vitro testing on human cells revealed gingerol's effectiveness in reducing oxidative stress. Although shogaol demonstrated the anti-inflammatory effects of gingerol, the findings indicated that most promising results in the fight against free radicals (33). According to a different study, mice with improved glucose tolerance and decreased lipoprotein cholesterol also had higher enzyme activity (CAT) and glutathione production. These changes were connected with the physiological effects of gingerol phytochemicals. Cardio-arrhythmia is a frequent complication of diabetes, however gingerol's anti-inflammatory properties reduced the risks by lowering blood glucose levels in-vivo (34). [6]-Gingerol's antioxidant capabilities have been proposed as an Alzheimer's disease defence. According to a study, gingerol may help neuroprotection by observing the molecular pathways that keep cells from degrading their mitochondrial membrane potential and DNA integrity. ginger has anti-oxidative qualities that increase the production of glutathione in cells, including nerve cells, which lowers the risk of Alzheimer's disease in human neuroblastoma cells and mouse hippocampal cells(35).

III. BIOSYNTHESIS

Based on research on the production of 6-gingerol by Denniff and Whiting in 1970 and by Schröder in 1997, it had been assumed that both ginger (Zingiber officinale) and turmeric (Curcuma longa) used the phenylpropanoid pathway and produced putative type III polyketide synthase products. The main gingerol found in ginger rhizomes is 6-gingerol, which has some interesting pharmacological properties like analgesic effects. Although the production of 6-gingerol is not entirely understood, below are some likely mechanisms. The starting material for the proposed biosynthetic pathway, Scheme 1, is L-Phe (1). It is changed by the enzyme phenylalanine ammonia lyase into cinnamic acid. (PAL). Then, using cinnamate 4-hydroxylase, it is converted into p-coumaric acid. (C4H). After that, p-Coumaroyl-CoA is produced using 4-coumarate:CoA ligase (4CL) . The enzyme P-Coumaroyl Shikimate Transferase (CST) is in charge of the covalent interaction between p-Coumaroyl-CoA and shikimic acid. P-coumaryl 5-O-shikimate 3'-hydroxylase (CS3'H) then preferentially oxidises the complexed at C3 to alcohol. Shikimate is separated from this intermediate by a further action of CST, resulting in Caffeoyl-Co. The hydroxyl group at C3 is changed into methoxy by caffeoyl-CoA O-methyltransferase (CCOMT), resulting in the appropriate substitution pattern on the aromatic ring in Feruloyl-CoA [36-37]

IV. CHALLENGES

Major problem associated with gingerol is its solubility. As gingerol used in various perspectives but it therapeutic activity is limited due to poor solubility. Various techniques used to increase solubility are:

Table 1. Various techniques

S.No	Techniques
1	Solid dispersion
2	Micospheres
3	Nanotechnology
4	Liquisolid technology

As in solid dispersion stability issues, microspheres agglomeration and nanotechnology is costly and need sophisticated machinery

Among all Liquisolid technology is considered best as drug in liquid state converts into free flowing powder .Excipients plays important role in dissolution rate. As maximum solubility in solvent less amount of carrier is used. Carrier and coating material with high SSA is considered better.[38]

V. CONCLUSION

The ability of ginger to fight cancer has long been known, and its useful components, such as gingerols, shogaols, and paradols, are effective anticancer agents.Before declaring ginger's efficacy, further research is necessary due to various ambiguities that were present in this review.

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