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Ginger as a possible treatment for COVID-19

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SARS-CoV-2 is a novel strain of coronavirus that has not been previously identified in humans. The most common symptoms at onset of illness were fever, cough and myalgia or fatigue. Less common symptoms were sputum production; headache, haemoptysis and diarrhea patients had lymphopenia. All patients had pneumonia with abnormal findings on chest CT; Moreover Complications included acute respiratory distress syndrome, RNA aemia, acute cardiac injury .Until now there is no specific treatment available for SARS-CoV-2. In this review, we aimed to provide some information about clinical effects of Ginger to develop safe and effective therapeutic agents from Ginger derived compounds against SARS-CoV-2. Otherwise, Ginger is one of the most important medicinal agents in various alternative systems of medical scientific studies have shown that ginger use in treating colds, headache, nausea, stomach upset, and diarrhea. Moreover scientific studies have shown that ginger has anti-inflammatory, anti-oxidative, immunomodulatory and bronchodilator.

Keywords: SARS-CoV-2, Covid-19, Ginger

INTRODUCTION

Clinical symptoms of patients with COVID-19

On 31 December 2019 WHO reported that the Chinese authorities identified a new type of coronavirus (novel coronavirus, nCoV), which was isolated on 7 January 2020. Laboratory testing was conducted on all suspected cases identified through active case finding and retrospective review. Other respiratory pathogens such as influenza, avian influenza, adenovirus, severe Acute Respiratory Syndrome coronavirus (SARS-CoV), Middle East Respiratory Syndrome coronavirus (MERS-CoV) were ruled out as the cause (WHO, 2020a). In March 1, 2020 WHO reported that a majority of patients with COVID-19 are adults. Among 44 672 patients in China with confirmed infection, 2.1% were below the age of 20. The most commonly reported symptoms included fever, dry cough, and shortness of breath, and most patients (80%) experienced mild illness. Approximately 14% experienced severe disease and 5% were critically ill. Early reports suggest that illness severity is associated with age (>60 years old) and co-morbid disease (WHO, 2020b). Huang et al informed that the most common symptoms at onset of illness were fever, cough and myalgia or fatigue. Less common symptoms were sputum production, headache, haemoptysis and diarrhea patients had lymphopenia. All patients had pneumonia with abnormal findings on chest CT and Complications included acute respiratory distress syndrome, RNA aemia, acute cardiac injury, and

secondary infection. 32% patients were admitted to an ICU and six (15%) died (Chaolin et al. 2020). Whereas infected children may be asymptomatic or have fever, dry cough and fatigue; some patients experience gastrointestinal symptoms, including abdominal discomfort, nausea, vomiting, abdominal pain and diarrhea .Most infected children have mild clinical manifestations and usually have a good prognosis Usually they recover within1-2 weeks after the onset of the disease (Zhang et al. 2020; Wei et al. 2020; Chen et al. 2020; Zeng et al. 2020). Recently, Giacomelli et al (2020) reported that 20 of 59 (33.9%) of SARS-CoV-2–positive hospitalized patients had an olfactory or taste disorder.

SARS-CoV-2 can be transmitted in the asymptomatic or pauci symptomatic stages; therefore, olfactory and taste disorders can be significant signs for its early detection to control transmission (Giacomelli et al. 2020).Jang et al founded that olfactory and taste disorders can be the first and only signs of COVID-19 pneumonia (Jang et al. 2020).

Li et al. conducted that SARSCoV-2 infected patients showing the activation and reduction in CD4+ and CD8+ T cell counts (Li et al. 2020).

Zumla et al. (2020) reported that SARS-CoV-2 patients have acute respiratory distress syndrome (ARDS). ARDS is a cytokine storm syndrome (CSS) which is a lethal uncontrollable inflammatory response resulting from the release of large pro-inflammatory cytokines (IL-1β, IFN-α, IFN-γ, IL-12, IL-6, IL-18, TNF-α, IL-33, TGFβ, etc.).

2-Ginger

Ginger (Zingiber officinale Roscoe), a well-known herbaceous plant, has been widely used as a flavoring agent and herbal medicine for centuries. Chinese describe ginger as pungent and warm; and as a cold discutient, diaphoretic, antiemetic, mucolytic, antitussive, detoxicant, and anti-inflammatory. Fresh ginger is used in common cold due to pathogenic “wind-cold” (characterized by severe intolerance to cold, slight fever, headache, general aches, nasal congestion, runny nose, and floating and tense pulse), cough and vomiting caused by pathogenic cold in the stomach. Ginger is known to remove chills caused by common cold, and to warm body (Akbar, 2020).

2.1- Ginger anti -inflammatory

A research paper published by young et al reported that ginger extract and its constituents improved inflammatory responses by decreasing the levels of nitrite, PGE2, IL-6, and IL-8 via NF-κB inhibition (Yun et al. 2017). 6-gingerol active compound isolated from ginger has been studied by Tripathi et al, who concluded the 6-gingerol inhibited the production of proinflammatory cytokines from LPS-stimulated macrophages (Tripathi et al. 2017). Another study by Luettig et al (2016) has proven that Anti-inflammatory properties of the ginger-derived pungent component 6-SG had barrier-protective effects by affecting TNF-α-induced claudin-2 upregulation and claudin-1 disassembly via inhibition of phoshatidylinositol-3-kinase/Akt and nuclear factor kappa light chain enhancer of activated B-cell signaling. Therefore, 6-SG-containing food might be beneficial for barrier preservation during intestinal inflammation.

1-dehydro-[10]-gingerdione (D10G), one of the pungent constituents of ginger was tested by Lee et al. (2012) who suggested that D10G Inhibits IKKβ activity for NF-κB activation and suppresses NF-κB-regulated expression of inflammatory genes(Lee et al. 2012).

Deol et al. reported that Novel cobiotic (Coadministration of ginger extract–Lactobacillus acidophilus) exhibited significant beneficial effect by lowering this gut inflammation by activating various reversal pathways, which include reduction in oxidative stress and proinflammatory cytokines; strengthening the gut integrity; and downregulating COX-2 , iNOS , and c-Myc expression (Deol et al. 2018).

2.2- Ginger and lung damage

The anticancer effect of 6-shogaol (pungent constituents of ginger) in human non-small cell lung cancer A549 cells tested by Hung et al found that 6-Shogaol inhibited cell proliferation by inducing autophagic cell death, Hung et al suggested that 6-shogaol may be a promising chemo preventive agent against human non-small cell lung cancer. 6-shogaol may be a promising chemo preventive agent against human non-small cell lung cancer (Hung et al. 2009).

Xie et al. (2013) analyzed the role of the active components of ginger against RAW 264.7 cells and acute lung injury induced by lipopolysaccharide (LPS) in mice Xie et al found that zinger one significantly inhibited the production of LPS-induced proinflammatory cytokines in vitro and in vivo When pretreated with zinger pulmonary histopathology changes, as well as alveolar hemorrhage and neutrophil infiltration were substantially suppressed in lung tissues, with evidence of reduced myeloperoxidase (MPO) activity in murine acute lung injury model .

Another study by Cifci et al. (2018) reported that Ginger efficiently reduced the lung damage

and protected the lungs from severe damage due to hyperoxia and inflammation.

2.3- Efficacy of ginger for the treatment nausea and vomiting

Three studies compared the effectiveness of ginger and vitamin B6 for treatment of nausea and vomiting in pregnancy, these studies showed that both ginger and vitamin B6 were effective for the treatment of nausea and vomiting in pregnancy. Moreover, ginger was more effective than vitamin B6. Side effects from ginger were reported to be minor and did not need any treatment (Chittumma et al. 2007; Ensiyeh and Sakineh, 2007 ; Lete and Allué, 2016). In another two studies compared the effectiveness of ginger and placebo for treatment of nausea and vomiting in pregnancy (Basirat et al. 2009 ; Ozgoli et al. 2009a). The result of these studies was ginger significantly more effective than placebo in relieving nausea, and effective at reducing vomiting. A recent study by Soltani (Soltani et al. 2018) recommended that the administration of oral ginger 1 h before operation to control the severity of postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy.

2.4-Efficacy of ginger for the treatment of pain

Ozgoli reported that no significant difference between the use of Ginger *(Z. officinale*) ibuprofen, and mefenamic acid to treat the pain of dysmenorrhea (Ozgoli et al. 2009b).

Another study by Black et al. demonstrated that daily consumption of raw and heat-treated ginger resulted in moderate-to-large reductions in muscle pain following exercise-induced muscle injury (Black et al. 2010).

Rondanelli et al. (2020) proven that Ginger had a pain-reducing effect and it can modulate pain through various mechanisms: inhibition of prostaglandins via the COX and LOX-pathways, antioxidant activity, inhibition of the transcription factor nf–kB, or acting as agonist of vanilloid nociceptor.

2.5- Effect of ginger in acute respiratory distress syndrome

Shariatpanahi (Shariatpanahi et al. 2013) reported that an enteral diet supplemented with ginger in patients with acute respiratory distress syndrome may be beneficial for gas exchange and could decrease duration of mechanical ventilation and length of stay in intensive care unit.

Mao et al. indicated that ginger and its bioactive constituents including 6-gingerol, 8-gingerol, 6-shogaol, citral and eucalyptol, had protective effects against respiratory disorders, at least mediating them through the induction of relaxation in airway smooth muscle and the attenuation of airway resistance and inflammation (Mao et al. 2019).

2.6- Immunomodulatory activity of ginger

The immunomodulatory effects of the volatile oil of ginger(Zingiber officinale Roscoe) in vitro and in vivo in mice were studied by Zhou (Zhou et al. 2006) who suggested that the volatile oil of ginger influences both cell-mediated immune response and nonspecific proliferation of T lymphocyte, and may exert beneficial effects in a number of clinical conditions, such as chronic inflammation and autoimmune diseases.

Ginger bioactive compounds potentially increased cellular and humoral immune response increasing the Ratio of T-cell Surface Molecules of CD3+CD4+:CD3+CD8+ In-Vitro reported by Tejasari (Tejasari, 2007). Moreover, Carrasco et al reported that humoral and cell mediated immune response in immune suppressed mice was improve by ginger essential oil (Carrasco et al. 2009).

The main function of IL-12 is differentiation of naive T cells intoTh1 cells and TGF-β is a powerful immunoregulatory cytokine**.** Jafarzadeh et al evaluated the effects of ginger extract on the expression of IL-12 and TGF-β in a model of experimental autoimmune encephalomyelitis mice. These rustle indicated that ginger extract modulates the expression of IL-12 and TGF-β in CNS and serum of experimental autoimmune encephalomyelitis mice (Jafarzadeh et al. 2017).

Ginger can improve Rheumatoid Arthritis by decreasing disease manifestations via increasing FoxP3 genes expression and by decreasing RORγt and T-bet genes expression (Aryaeian et al. 2019).

2.7- anti-viral activity of ginger

Ginger (Zingiber officinale) was inhibited the viral replication inside the HCV-infected HepG2 cells (El-Wahab et al. 2009) by testing lyophilized juice extract from ginger (Zingiber officinale) at different concentrations in vitro as anti-HCV using the hepatocellular carcinoma HepG2 cell line infected with HCV. Moreover, fresh ginger was effective against HRSV (human respiratory syncytial virus) induced plaque formation on airway epithelium by blocking viral attachment and internalization after testing the effect of hot water extracts of fresh and dried gingers on HRSV by plaque reduction assay in both human upper (HEp-2) and low (A549) respiratory tract cell lines (Chang et al. 2013). The active compounds present in ginger are allicin and alliin showed effective inhibitory activity against H1N1 neuraminidase (a surface glycoprotein and is a suitable target for

H1N1) in binding condition (Sahoo et al. 2016).The anti-chikungunya activities of ginger in Vero cell-line (the animal cell culture model) were checked and his result revealed that the aquatic plant extract of *Ginger* showed anti-chikungunya activity (Kaushik et al., 2020).

2.8- Side Effects and Toxicity of Ginger:

Ginger is on the U. S. Food and Drug Administration's GRAS (generally recognized as safe) list. The British Herbal Compendium documents no adverse effects of ginger (Das et al. 2014).

CONCLUSION

The results from this study could be used to optimize the design of clinical studies to enhance the efficacy of ginger against SARS-CoV-2.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS

Noha ME has concepted and designed of the study. Khaled ME and Noor M M A acquisition of data and collected data from the literature. Noha ME and Ahmed AMM interpreted data and wrote final manuscript. Ahmed AMM revised final approval of the version to be submitted.

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