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Antiviral Properties and Potential of Ginger (Zingiber Officinale) and Its Derivatives: A Systematic Review

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Abstract

Antiviral Properties and Potential of Ginger (Zingiber Officinale) and Its Derivatives: A Systematic Review. *Ginger has long been valued in traditional medicine for its therapeutic benefits. Recently, its antiviral capabilities have attracted significant interest, highlighting its potential as a natural antiviral agent. This systematic review seeks to thoroughly evaluate the antiviral effects of ginger and its active compounds, providing valuable insights to support future research and clinical applications in natural antiviral therapies. A comprehensive electronic search was undertaken across PubMed, Embase, and Scopus databases, employing MeSH terms, Emtree, and relevant synonyms to capture studies on ginger and its antiviral effects. The initial search yielded 531 records, which were de-duplicated and subsequently screened by title and abstract using Rayyan software. Fourteen studies specifically addressing antiviral effects against human pathogens met the inclusion criteria. This systematic review was conducted in strict accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure rigorous reporting of findings. The majority of included studies were in vitro, revealing anti-viral effects of ginger against various viruses, including Influenza A, Chikungunya, Dengue, hRSV, HSV-2, and SARS-CoV-2 in different cell lines across various concentrations. In addition, Ginger extracts also demonstrated efficacy against Influenza A in both in vivo and in ovo studies, and a randomized controlled trial showcased encouraging antiviral effects targeting SARS-CoV-2. Ginger shows promising antiviral effects in most of the in vitro studies. Translating these findings to in vivo models is imperative for clinical relevance. Further in vivo research is essential before progressing to human studies to ascertain ginger's potential as an effective antiviral agent.*

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INTRODUCTION

Viral infections pose a persistent threat to global health, with the emergence and re-emergence of viruses like influenza, SARS-CoV-2, and hepatitis C causing significant morbidity and mortality worldwide, emphasizing the importance of antiviral drugs and vaccines. (Altindis & Kahraman Kilbas, 2023; Kawaoka, 2023). The continuous emergence of new viruses and the development of drug-resistant strains underscore the importance of sustained research into new antiviral treatments that can effectively tackle viral mutations.(Goncalves et al., 2021) It becomes crucial to explore alternatives, either as treatments or supplements to pharmacological therapy, and natural products represent one such promising avenue.

The therapeutic potential of natural products in preventing and treating viral infections has gained significant attention in contemporary medical research. Plant-based products containing phytochemicals like coumarins, alkaloids, and flavonoids show promise in combating viral infections due to their antiviral properties and lower likelihood of resistance.(Palai et al., 2023) Among these, ginger (*Zingiber officinale*), a widely used dietary spice and medicinal herb, has been explored for its broad spectrum of biological activities, including anti-oxidant (Ballester et al., 2022), anti-inflammatory (Kamankesh et al., 2023)And anti-diabetic and anti-obesity.(Yang et al., 2024) These effects are due to the different active compounds present in Ginger. An Australian study using HPLC quantitatively analyzed 98 ginger samples and demonstrated that the majority of active components in ginger extract are phenolic compounds such as gingerols, shogaols, and paradols.(Johnson et al., 2021)

Ginger has also shown antimicrobial and antiviral effects.(Edo et al., 2024) This systematic review specifically assesses evidence across a wide array of studies, from in vitro experiments to in vivo and clinical trials, to explore ginger's antiviral efficacy against various viruses, including influenza, herpes simplex, Chikungunya, Dengue, and emerging viruses like SARS-CoV-2. The review seeks to delineate ginger's antiviral potential, proposing it as a natural, accessible, and cost-effective adjunct or alternative to conventional antiviral medications. Through meticulous collection and examination of data from diverse studies, it aims to offer a thorough evaluation of the evidence supporting ginger's effectiveness against viral infections.

METHODS

Search Strategy And Data Sources:

Three prominent databases, i.e., PubMed, Embase, and Scopus, were searched for the review. The search term included MeSH terms, Emtree, and synonyms associated with ginger and antiviral activity. For Pubmed this search strategy was employed ("*Zingiber officinale*"[MeSH Terms] OR "*Zingiber officinale*"[Title/Abstract] OR "Ginger"[Title/Abstract] OR "Ginger extract"[Title/Abstract] OR "Gingerols"[Title/Abstract]) AND ("Antiviral agents"[MeSH Terms] OR "Virucidal"[Title/Abstract] OR "Antiviral activity"[Title/Abstract] OR "Antiviral properties"[Title/Abstract]). The search strategy for Embase and Scopus paralleled that of PubMed to maintain consistency across databases. The search encompassed all research articles available until 5 March 2024; only articles published in English were included.

Study Selection/Inclusion and Exclusion Criteria:

To ensure the rigor and focus of this systematic review, specific inclusion and exclusion criteria were applied. Only original manuscripts were included. To prioritize direct evidence from primary sources, review articles were not considered. Also, In-silico studies, which depend on computational modeling rather than empirical data, were excluded from the analysis. Furthermore, studies involving animal viruses were excluded, as the primary interest was in human viral infections.

Those studies that examined blends or concoctions of ingredients, particularly decoctions containing multiple medicinal plants, to isolate the antiviral properties of individual substances were also excluded. The review exclusively focused on antiviral activities, with studies addressing other antimicrobial effects not considered to maintain clarity and specificity.

Data Extraction:

Two reviewers (NA and HA) used the search strategy and extracted data meeting the eligibility criteria from the databases. The data was subsequently checked by a third reviewer (VS), who resolved any discrepancies or disagreements between the initial reviewers. Data were extracted and tabulated based on the types of studies, such as in vivo, in vitro, and Randomized Controlled Trials. The key data elements included study characteristics such as author and year of publication, parts or extracts of ginger used, cell types used in in vitro studies, animals used in in vivo studies, and the outcomes or mechanisms of action. In randomized controlled trials (RCTs), participant details such as sample size, age, health status, intervention specifics including type, dosage, and duration of the antiviral treatment, and outcomes measured were noted. Data extraction was made by the agreement of two independent authors of this study.

Risk of Bias Within Studies:

Several factors may have introduced bias in these studies. There's variability in experimental designs, including differences in cell lines used and viral strains targeted, which complicates direct comparisons between studies. The concentration and purity of ginger extracts, as well as the specific active components examined, varied widely among the studies, potentially influencing outcomes and introducing bias. Additionally, the methods of extract preparation (aqueous, methanol, essential oil) and the forms of ginger used (fresh rhizome, dried powder, specific compounds like 6-gingerol) further contribute to this inconsistency. Also, the lack of standardization in outcome measures, such as the assays used to assess viral replication and cell viability, poses a significant risk of bias. So, a formal quality appraisal tool, such as the Cochrane Risk of Bias Tool (RoB) or ROBIS, was not applied.

RESULTS AND DISCUSSION

Utilizing the adopted search strategy, a total of 531 records were identified from three databases: Embase, PubMed, and Scopus. 147 duplicates were removed using Rayyan. The remaining articles were read based on their titles and abstracts, leading to the exclusion of 333 articles. Subsequently, 51 studies were retrieved for full-text reading, resulting in the exclusion of 37 studies. The reasons for exclusion were 20 in-silico studies, one letter to the editor without much data, four studies on animal viruses, and 12 other non-conforming articles. Ultimately, 14 studies were included in the systematic review. This process is depicted in the standard PRIMSA flow diagram below (Fig. 1). (Page et al., 2021)

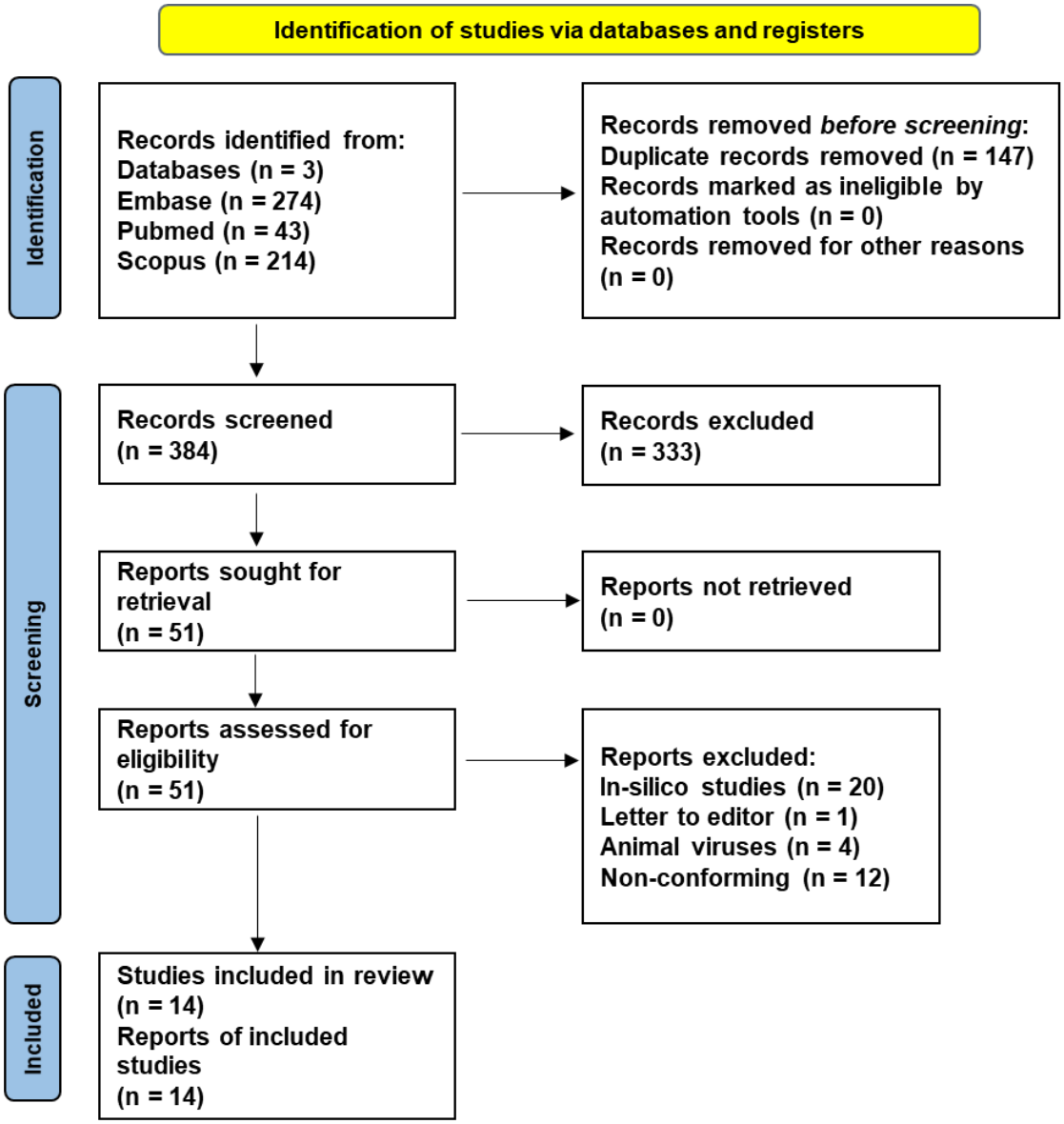

Figure 1. Flowchart Depicting The Process of Study Inclusion for This Review

Fourteen studies from the retrieved literature were critically read and analyzed. The articles were categorized based on their study design and type, resulting in four distinct categories: In vitro studies, in vivo studies, in ovo studies, and randomized controlled trials (RCTs). The results for each category are presented in the tables below: In vitro studies in Table 1, In vivo and ovo studies in Table 2, and RCTs in Table 3. Studies that assessed antiviral activity using more than one study design were categorized accordingly in each relevant category.

Extracts and active constituents isolated from ginger demonstrated antiviral activity against Influenza A, Chikungunya, Dengue, HSV-2, Rhino Virus, HRSV, Polio, Enterovirus, and SARS-CoV-2 across all included studies.

Study Characteristics

The selected publications included articles available up to March 5, 2024. They were categorized and analyzed based on their study types: In vitro, In vivo, In ovo, and clinical trials. All studies focused on human viruses, with the majority being in vitro in nature. Most in vitro

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Table 1. In-vitro studies

Study Reference	Extract/Part of Ginger used	Targeted Viral Pathogen	Cell Line Used	Mechanism of Action/Outcome
(Wang, Prinz, et al., 2020)	Gingerenone A from Ginger Root	Influenza A virus (IAV)	MDCK (Madin–Darby Canine Kidney) A549 (Human Lung Cancer) 293T (Human Embryonic Kidney) DF1 (Chicken Fibroblast)	Targeted inhibition of the JAK2 signaling pathway, essential for IAV replication, leads to reduced viral proliferation and enhanced cellular viability.
(Kaushik et al., 2020)	Aqueous extract from fresh rhizome	Chikungunya virus (CHIKV)	Vero cell lines	Decreased cytopathic effects and increased cell viability through the MTT assay
(Raghavendhar et al., 2019)	Water extract from dry powdered Rhizome	Chikungunya virus (CHIKV)	Vero cell lines (Monkey Kidney cells)	Proposed inhibition of viral replication, targeting RNA helicase activity, indicating that Ginger interferes with the virus's ability to unwind RNA during replication.
(Sharma et al., 2015)	*Z. Officinale* rhizomes aqueous extract (ZOA)	Dengue Virus 3 (strain SLMC-50)	Vero cells	Inhibited the activity and expression of MMP-2 and MMP-9, crucial in promoting vascular permeability associated with severe dengue complications. It also up-regulated the expression of TIMPs (TIMP-1 and TIMP-2), which regulate MMP activity.
(Koch et al., 2008)	Essential oil from Ginger	HSV-2 (HG52 Strain)	RC-37 cells	The essential oils from ginger primarily exhibit a virucidal effect before the HSV attaches to host cells. They may interfere with virion envelope structures or potentially mask viral compounds crucial for adsorption or entry into host cells. When added after the adsorption, virus titers were either not significantly reduced or only moderately affected.
(Imanishi et al., 2006)	*Zingiber officinale Rosc* (ZOR)	Influenza A virus (strain A/Aichi/2/1968 H3N2)	Madin–Darby Canine Kidney cells (MDCK cells)	Conditioned medium (CM) from ZOR-stimulated RAW cells exhibited an inhibitory effect by activating macrophages to produce TNF-α, which in turn reduced the viral yield in MDCK cells. The effect was

				absent when TNF-α was neutralized with antibodies.
(Dutta et al., 2023)	6-Gingerol	Influenza A virus (H1N1, PR8)	Madin–Darby Canine Kidney cells (MDCK cells)	6-Gingerol inhibits viral neuraminidase (NA). Neuraminidase activates transforming growth factor-beta (TGF-β), which is a cytokine known to suppress immune responses.
(José-Rita et al., 2022)	*Zingiber officinale* Essential oil (ZOEO)	Poliovirus type I and Enterovirus	L20B cells RD cells	ZOEO exhibited significant antiviral activity against poliovirus type I and enterovirus type I. This effect was achieved through the disruption of viral replication mechanisms, as indicated by reduced cytopathic effects in the cell cultures.
(Nugraha Halim et al., 2021)	6-Gingerol	Dengue Virus (DENV-1, -2, -3, -4)	Human alveolar epithelial carcinoma cells (A549)	6-Gingerol inhibited the growth of DENV. Strong inhibition was shown against DENV-1 and DENV-2 compared to DENV-3 and DENV-4.
(Hayati et al., 2021)	6-Gingerol	Chikungunya virus (CHIKV) JMB-192 strain	Human hepatocyte cell line (HepG2)	6-Gingerol significantly curtails CHIKV replication in post-infection and combined treatment assays.
(Chang et al., 2013)	Lyophilized powder from fresh ginger rhizome	Human respiratory syncytial virus (HRSV)	Human larynx epidermoid carcinoma cells (HEp-2) Human alveolar epithelial carcinoma cells (A549)	Fresh ginger inhibits HRSV infection by preventing viral attachment and internalization into host cells. Another possible mechanism is triggering the secretion of interferon-beta (IFN-β), contributing to an antiviral response.
(Denyer et al., 1994)	Methanol extracts of Ginger rhizome	Rhinovirus IB (RVIB)	M-Hela cells	A reduced number of viral plaques indicated diminished viral growth and spread within the culture cells in the Plaque reduction test. Ginger could have interfered with the viral replication cycle, although detailed mechanistic pathways were not delineated within the scope of this research.

Table 2. In-vivo and in-ovo studies

IN-OVO STUDIES

Study Reference	Extract/Part of Ginger used	Targeted Viral Pathogen	Embryo used	Mechanism of Action/Outcome
(Rasool et al., 2017)	Aqueous extract from the rhizome	Avian Influenza Virus H9N2	Chicken Embryo	Antiviral activity was inferred from the observed reduction in virus detectability and the decreased severity of lesions by studying the histopathological changes in the chorioallantoic membrane CAM.

IN-VIVO STUDIES

Study Reference	Extract/Part of Ginger used	Targeted Viral Pathogen	Animal model	Mechanism of Action/Outcome
(Wang, Prinz, et al., 2020)	Gingerenone A from Ginger Root	Influenza A virus (IAV)	Female C57BL/6 mice	Gingerenone A inhibited IAV replication by targeting JAK2, reducing viral protein levels and virus titers in female C57BL/6 mice
(Dutta et al., 2023)	6-gingerol	Influenza A virus (H1N1, PR8)	C57BL/10J mice	6-Gingerol inhibited the activation of TGF-β mediated by neuraminidase NA.

Table 3. Randomized controlled study with ginger capsule

Citation	Blinding/ Funding	Number of Patients	Virus	Dosage/ Duration	Mean Age	Intervention/ Comparator	Outcomes
(Li Jian et al., 2022)	Double blind randomization.	109	SARS-CoV-2	1500 mg/day OR 3000 mg/day for 2 weeks	52.7	Low-dose ginger capsule (1500 mg/day), Normal dose (3000 mg/day) vs Control (standard treatment)	Reduction in dehydration, improvement in oxygen levels, and an increase in consciousness levels post-treatment

Studies utilized MDCK (Madin-Darby Canine Kidney) and Vero cells, employing MTT assays or plaque reduction methods to evaluate antiviral properties. In vivo studies only involved mouse models, while one in ovo study utilized chicken embryos. A single randomized clinical trial (RCT) was included, conducted in a Chinese hospital, involving 109 patients with SARS-CoV-2 infection. The majority of the studies investigated the antiviral effects of aqueous extracts from ginger rhizomes, with a few also examining the compound 6-gingerol, an isolate of ginger.

In Vitro Studies

In vitro studies show evidence for ginger's diverse antiviral activities against various respiratory and mosquito-borne viruses. One prominent mechanism involves the inhibition of key viral enzymes. Gingerenone A (Gin A) demonstrates potent activity against Influenza A virus (IAV) by specifically targeting Janus Kinase 2 (JAK2) and its downstream signaling pathway involving STAT3 phosphorylation.(Wang, Prinz, et al., 2020) This effectively disrupts viral replication, offering a promising strategy against IAV infections. Similarly, 6-gingerol, a major bioactive component of ginger, exhibits antiviral activity against all four serotypes of Dengue virus (DENV) (Nugraha Halim et al., 2021), with the most potent effect observed against DENV-1 and DENV-2. Beyond enzyme inhibition, ginger compounds appear to target various stages of the viral lifecycle. Studies with Chikungunya virus (CHIKV) revealed that 6-gingerol significantly reduces viral replication in HepG2 cells without substantial cytotoxicity.(Hayati et al., 2021) The supposed mechanism focuses on inhibiting viral replication in post-infection rather than directly eliminating the virus. Fresh ginger extract demonstrated a remarkable ability to reduce Human respiratory syncytial virus (HRSV) plaque formation in a dose-dependent manner, with the antiviral effect potentially mediated by blocking viral entry into host cells by preventing viral attachment and internalization into host cells.(Chang et al., 2013) In another study, the administration of methanol extracts of Ginger rhizome reduced a number of viral plaques, indicated diminished viral growth and spread within the culture cells in the Plaque Reduction Test Rhinovirus IB (RVIB).(Denyer et al., 1994)

Other studies using MDCK cell lines demonstrated that 6-gingerol effectively inhibits the neuraminidase enzyme of the influenza virus, which is crucial for viral spread within the host.(Dutta et al., 2023) *Zingiber officinale* essential oil (ZOEO) exhibited antiviral effects against non-enveloped viruses like poliovirus type I and enterovirus type I, potentially disrupting viral replication processes.(José-Rita et al., 2022) An aqueous extract of *Zingiber officinale* Roscoe (ZOA) modulated the expression and activity of enzymes involved in vascular leakage during Dengue virus infection, potentially mitigating severe complications.(Sharma et al., 2015) Interestingly (Imanishi et al., 2006) Showed that while direct addition of *Zingiber officinale Rosc* (ZOR) to influenza A virus-infected cells has no effect, conditioned medium from ZOR-stimulated macrophages exhibited significant antiviral activity, suggesting an indirect mechanism through macrophage activation and cytokine production. These studies show the importance of building upon these findings to unlock the full potential of ginger as an agent against viral infections.

In Vivo and Ovo Studies

In vivo studies demonstrated the antiviral potential of ginger compounds against influenza A virus (IAV). Gingerenone A (Gin A) treatment in mice significantly suppressed

H5N1 virus replication in the lungs, reducing viral proteins and titers.(Wang, Prinz, et al., 2020) Similarly, 6-gingerol administration in mice reduced lung viral load, alleviated weight loss and mortality, and additionally inhibited the immunosuppressive cytokine TGF-β, potentially enhancing the Th1 and Th17 cell response.(Dutta et al., 2023) These findings highlight ginger compounds' dual antiviral and immunomodulatory effects, warranting further investigation into their potential as therapeutic agents for IAV infections.

The in ovo study investigated the antiviral potential using aqueous rhizome extract of ginger against Avian Influenza Virus (H9N2) in chick embryos. Through histopathological analysis, the researchers observed a reduction in detectable virus and a lessening of the severity of lesions on the chorioallantoic membrane (CAM).(Rasool et al., 2017) The findings suggest the extract possesses antiviral activity against the H9N2 influenza virus in chick embryos.

Human Trials

A randomized controlled trial (RCT) investigated ginger's effectiveness against severe COVID-19 symptoms (November-December 2021). 109 hospitalized patients were divided into three groups: a low-dose ginger group (1500mg/day), a normal-dose ginger group (3000mg/day), and a control group receiving standard treatment. The double-blind study, funded by a government grant, showed promising results against SARS-CoV-2. The outcomes measured were dehydration, level of oxygenation, and consciousness. Dehydration significantly decreased in the low-dose ginger group (72% to 42%, P=0.04). Both ginger groups had higher oxygen levels compared to the control group (P=0.01). Ginger groups also showed a higher frequency of conscious patients compared to the control group (P=0.02). The findings from this study suggest that, particularly at lower doses, ginger may be effective in reducing dehydration and improving oxygen levels, potentially helping in managing severe COVID-19 symptoms. The study adds to the growing evidence for ginger's therapeutic benefits in viral infections, potentially improving respiratory health in severe COVID-19 cases.(Li Jian et al., 2022)

All the studies in this review provided evidence for ginger's (*Zingiber officinale Roscoe*) diverse antiviral properties against a range of viruses. The review analyzed the findings, demonstrating ginger's potential as an antiviral agent through its diverse bioactive components acting via various mechanisms. Ginger showed to be a broad-spectrum antiviral agent as it showed activity against a range of viruses, including influenza A, Chikungunya, Dengue, hRSV, HSV-2, and SARS-CoV-2. However, the variability in study designs, concentrations, extracts, and cell lines used in these studies highlights the need for standardized methodologies to ensure replicability and comparability of results. For instance, one study did not show any antiviral effect of ginger extract against SARS-CoV-2, indicating that the efficacy of ginger might be context-dependent or influenced by specific experimental conditions.(Leka et al., 2022)

Ginger manifests its effect via different mechanisms. It inhibits JAK1 and JAK2 signaling pathways and curtails Influenza A replication.(Wang, Prinz, et al., 2020) Studies have shown that JAK 1 and JAK2 are involved in IAV and that it’s inhibition inhibits IAV replication.(Wang, Sun, et al., 2020) In another study, Ginger showed to inhibit the helicase activity and thus impede the virus's capacity to unwind RNA during replication.(Raghavendhar et al., 2019) Helicase inhibitors have been tested for their inhibitory effects on SARS-CoV, MERS-CoV, and SARS-CoV-2 helicases, showing potential as antiviral agents with good antiviral activity and moderate cytotoxicity.(Glitscher et al., 2018; Mehyar, 2023; Mukherjee et al., 2014)

Ginger's inhibition of MMP-2 and MMP-9, coupled with the upregulation of TIMP-1 and TIMP-2, mitigates vascular permeability, a critical factor in severe dengue complications.(Sharma et al., 2015) 6-gingerol exhibits potent inhibition of viral neuraminidase (NA), consequently suppressing TGF-β activation, a cytokine known to dampen

immune responses.(Dutta et al., 2023) Fresh ginger prevents HRSV infection by inhibiting viral attachment and internalization and potentially triggering IFN-β secretion, contributing to an enhanced antiviral response.(Chang et al., 2013) Other studies have also shown the significant antiviral effect of Interferon beta (IFN-β).(Acosta et al., 2020; Sheahan et al., 2020) Collectively, these mechanisms affirm ginger's robust antiviral properties, presenting it as a promising candidate for therapeutic intervention against various viral infections.

Researchers have employed computational studies utilizing molecular docking, molecular dynamics simulations, and other in silico methods to explore how ginger compounds interact with viral proteins and host cell receptors. In silico studies have identified potent compounds in ginger with antiviral activity against SARS-CoV-2 and shown affinity to different proteins in SARS-CoV-2 and inhibited the virus.(Ahkam et al., 2020; Al-Sanea et al., 2021; Rajagopal et al., 2020) In a separate computational study, ginger compounds were found to inhibit the spike protein in various SARS-CoV-2 variants, suggesting a broad-spectrum effect against different strains of the virus.(Hasan et al., 2023) Ginger has also been recognized for its potential antiviral effects against viruses such as the mumps virus in in-silico studies.(Kharisma et al., 2023)

Given the promising findings, ginger and its extracts present a significant potential for antiviral therapy. However, it is important to advance this research through well-designed clinical trials to validate the efficacy and safety of ginger in humans. Additionally, the exploration of synergistic effects between ginger compounds and existing antiviral drugs could pave the way for novel combination therapies. The development of standardized extraction methods and precise dosing guidelines will further enhance the therapeutic applicability of ginger. Future research should also investigate the pharmacokinetics and bioavailability of ginger compounds to optimize their delivery and effectiveness in clinical settings. Overall, while the current evidence underscores ginger's potential, rigorous and comprehensive studies are essential to fully establish its role in antiviral therapy.

LIMITATION

The systematic review was subject to several limitations that may have influenced the interpretation and generalizability of the findings. First, a formal quality appraisal using validated tools such as the Cochrane Risk of Bias Tool or ROBIS was not conducted, primarily due to the heterogeneity in study types, which included in vitro, in vivo, and limited clinical studies. Consequently, the risk of bias within individual studies remains unquantified. Second, the included studies displayed considerable variability in design, methodology, and outcome measures, ranging from different assays for viral replication to diverse endpoints for cytotoxicity and efficacy, making direct comparisons challenging. Furthermore, variations in ginger preparations (e.g., fresh root, dried powder, ethanolic extracts) and the concentration or dosage used add another layer of complexity, potentially contributing to inconsistent findings across studies.

Language restrictions may have further limited the scope of this review; only studies published in English were considered, potentially excluding relevant data from non-English language journals. Additionally, only one randomized controlled trial involving human subjects was identified, severely limiting the ability to draw firm conclusions regarding the clinical applicability of ginger’s antiviral properties. Lastly, the presence of other bioactive compounds within ginger preparations and variability in experimental conditions across studies may have introduced confounding factors, complicating the attribution of observed effects specifically to ginger or its primary constituents.

CONCLUSION

Ginger exhibits significant antiviral properties, particularly in in vitro studies against a range of human viruses. The promising results from these preliminary studies, including one randomized controlled trial targeting SARS-CoV-2, underscore the potential of ginger and its extracts as antiviral agents. However, to establish clinical relevance, further in vivo research is crucial. Eventually, progressing from in vitro findings to robust in vivo and, eventually, human studies will be essential in validating ginger's efficacy and safety as a natural antiviral therapeutic.

SUGGESTION

To fully unlock ginger's therapeutic potential, future research must prioritize standardized methodologies for extract preparation and dosing to ensure reproducibility across studies, alongside integrating multi-omics approaches (e.g., proteomics, metabolomics) to dissect its multi-target mechanisms, such as JAK-STAT inhibition and helicase interference. Rigorous clinical trials, including adaptive designs to evaluate dose-response relationships and synergistic effects with existing antivirals, are critical to validate findings.

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