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Research Article

An Overview of Warfarin Interactions with Common Dietary Supplements and Herbal Medicines Used in the Prevention and Treatment of COVID-19

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Abstract

Background: Dietary supplements and herbal medicines were widely used during the COVID-19 pandemic. Their concomitant use with warfarin, an anticoagulant with a narrow therapeutic index, may alter anticoagulation control. This review examined interactions and their clinical relevance.

Methods: A narrative review searched PubMed/MEDLINE, Scopus, Web of Science, Embase, and Google Scholar from inception to January 2026. Clinical, observational, pharmacokinetic, experimental, and review evidence was assessed for interaction mechanisms, international normalized ratio (INR) changes, and bleeding or thrombotic outcomes. English-language publications were screened by title and abstract, followed by full-text assessment when appropriate; duplicate records and reports without interaction data were excluded. Findings were synthesized narratively without meta-analysis.

Results: Evidence was limited and heterogeneous, often relying on case reports or experimental findings. High-dose vitamin E, excessive vitamin A, melatonin, garlic, ginger, and quercetin may increase anticoagulant or antiplatelet effects, although clinical confirmation is inconsistent. N-acetylcysteine has shown potential effects on hemostasis, but clinically significant interactions remain unestablished. Isolated reports associated high-dose vitamin C with reduced warfarin response. Findings for omega-3 fatty acids and coenzyme Q10 were conflicting, while clinically important interactions with vitamin D, B-complex vitamins, and echinacea have not been consistently demonstrated.

Conclusion: This review summarizes possible interactions between warfarin and dietary supplements or herbal products commonly used in the context of COVID-19, whether for prevention, symptom management, or treatment. Evidence on interactions between warfarin and dietary supplements or herbal products is limited; however, some of these interactions may be clinically significant. They may either potentiate anticoagulation, increasing the risk of bleeding, or reduce warfarin efficacy, potentially increasing the risk of venous thromboembolism or stroke.

To mitigate these risks, healthcare professionals should remain vigilant for potential supplement–warfarin and herb–warfarin interactions. Patients should also be counseled on the hazards of self-medication with these products during warfarin therapy.

Keywords: COVID-19, Dietary supplements, Herb–drug interaction, Herbal medicines, Warfarin

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Introduction

A novel coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), led to an unprecedented global health crisis. Although the World Health Organization (WHO) declared in May 2023 that COVID-19 is no longer a Public Health Emergency of International Concern, SARS-CoV-2 continues to circulate and remains a public health threat, particularly for individuals at higher risk of severe disease [1].

Although evidence-based antiviral and immunomodulatory therapies are now available for selected patients with COVID-19, no universally effective cure exists, and management depends on disease severity, timing of therapy, and patient risk factors [1]. Complementary and alternative approaches, including dietary supplements and herbal products, are commonly used alongside standard care for symptom relief. However, the clinical evidence supporting their effectiveness for COVID-19 is limited, indicating a need for more controlled clinical trials. Additionally, limited data are available on the safety of these therapies and their potential interactions with conventional drugs [2]. Early reports from China found that, like any other respiratory tract infection, preexisting cardiovascular risk factors and cardiovascular disease (CVD) increase susceptibility to COVID-19 [3, 4], which was confirmed in subsequent studies. The frequent use of multiple concomitant pharmacotherapies in patients with CVD increases their risk of clinically significant drug-drug interactions, which is particularly important for medications that have a narrow therapeutic index, such as warfarin [5]. Warfarin, as one of the most commonly prescribed anticoagulants, acts by inhibiting the synthesis of the vitamin K-dependent coagulation factors (II, VII, IX, X) [6]. It has been used clinically for more than 60 years to prevent and manage deep venous thrombosis. Additionally, it helps prevent thromboembolic events in patients with indwelling central venous catheters, prosthetic heart valves, atrial fibrillation, or a history of coronary artery disease [3]. Warfarin presents challenges for clinicians and patients due to its narrow therapeutic window, potential drug and dietary interactions, individual variability in response, and the risk of complications such as bleeding. Regular monitoring of the international normalized ratio (INR) and frequent dose adjustments are essential to avoid severe, sometimes life-threatening, adverse reactions [4]. Drugs and foods can interact with warfarin through either pharmacokinetic or pharmacodynamic mechanisms. Pharmacokinetic interactions may involve reduced absorption, which decreases the anticoagulant effect. Additionally, they can affect metabolism in two ways: enzyme inhibition, which increases the International Normalized Ratio (INR), or CYP2C9 induction, which enhances clearance and reduces the drug's effectiveness. Other factors may include changes in transport or plasma protein binding. For instance, if highly protein-bound agents displace warfarin from albumin, this can increase the free fraction of warfarin and enhance its antithrombotic activity [7]. In addition to such pharmacokinetic effects, warfarin is subject to pharmacodynamic interactions. These include synergistic increases in bleeding risk through impaired hemostasis and/or reduced synthesis of coagulation factors, alterations in the vitamin K regulatory cycle that may change warfarin sensitivity (including rare hereditary resistance), and competitive antagonism by vitamin K, which counteracts warfarin's anticoagulant action [8]. While the literature reports interactions between warfarin and herbal medicines, the clinical implications of these findings remain unclear [9]. During the COVID-19 pandemic in 2020, when evidence-based specific therapies were limited, especially in the early phases, the use of herbal medicines and dietary supplements increased worldwide. In this review, we focused on the potential interactions between warfarin and dietary supplements and herbal products commonly used in the prevention and treatment of COVID-19.

Methods

Literature Search Strategy

A narrative review was conducted to summarize the available evidence regarding interactions between warfarin and dietary supplements and herbal medicines commonly used for the prevention and management of COVID-19 and other viral respiratory infections.

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A comprehensive literature search was performed using the electronic databases PubMed/MEDLINE, Scopus, Web of Science, Embase, and Google Scholar from database inception to June 2026, without restriction on the year of publication. The search strategy combined Medical Subject Headings (MeSH) and free-text keywords including:
"Warfarin," "vitamin K antagonist," "drug interaction," "herb-drug interaction," "dietary supplement," "herbal medicine," "COVID-19," "SARS-CoV-2," "vitamin C," "vitamin D," "vitamin E," "vitamin A," "vitamin B complex," "melatonin," "N-acetylcysteine," "omega-3," "coenzyme Q10," "quercetin," "garlic," "ginger," and *"echinacea."*
Reference lists of eligible articles and relevant review papers were also manually screened to identify additional studies.

Eligibility Criteria

Original clinical studies, observational studies, randomized controlled trials, pharmacokinetic studies, case reports, systematic reviews, meta-analyses, and relevant experimental studies evaluating potential interactions between warfarin and dietary supplements or herbal medicines were considered eligible.
Articles were excluded if they:

- were not published in English;
- did not evaluate warfarin;
- lacked information regarding interaction mechanisms or clinical outcomes;
- were conference abstracts without sufficient data or duplicate publications.

Study Selection and Data Extraction

Studies were screened based on titles and abstracts, followed by full-text evaluation when appropriate. Information extracted from eligible studies included:

- supplement or herbal medicine;
- proposed mechanism of interaction;
- pharmacokinetic or pharmacodynamic effects;
- reported changes in INR;
- bleeding or thrombotic outcomes;
- level of available clinical evidence.

The findings were synthesized narratively according to each supplement or herbal medicine.

Evidence Synthesis

Considering the heterogeneity of study designs, interventions, and reported outcomes, quantitative meta-analysis was not performed. Instead, the available evidence was critically summarized, emphasizing the strength of evidence, biological plausibility, and clinical relevance of each reported interaction.

Vitamin C

Vitamin C (ascorbic acid) is an essential water-soluble vitamin with antioxidant, anti-inflammatory, and immunomodulatory properties. During the SARS-CoV-1 outbreak in 2003, the use of vitamin C was recommended as a nonspecific treatment for severe viral respiratory tract infections [10, 11]. Vitamin C is believed to provide beneficial effects for the prevention and management of COVID-19 in patients [12, 13]. It has been suggested that a low oral dose (1–2 g/d) of vitamin C may be useful as a preventive measure, while in cases of severe COVID-19, a high-dose intravenous regimen (6 to 12 g/d) could be beneficial [13]. Although several clinical studies have evaluated vitamin C supplementation in patients with COVID-19, current evidence does not support its routine use for the prevention or treatment of the disease, and its clinical benefits remain uncertain [13-20].
The potential interaction between vitamin C and warfarin appears to be minimal. To date, no well-designed clinical studies have demonstrated a clinically significant interaction between these agents. However, a limited number of case reports have described decreased anticoagulant response or warfarin resistance following high-dose vitamin C supplementation, with restoration of anticoagulant sensitivity after discontinuation of vitamin C [21-23]. The underlying mechanism has not been clearly established and remains speculative. Proposed mechanisms include reduced warfarin bioavailability or altered pharmacokinetics; however, these hypotheses have not been confirmed in clinical studies [8, 9].
Overall, the available evidence suggests that clinically important interactions between vitamin C and warfarin are uncommon and are supported

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primarily by isolated case reports rather than controlled clinical studies. Nevertheless, because high-dose vitamin C supplementation may influence anticoagulant response in susceptible individuals, clinicians should consider closer INR monitoring when initiating or discontinuing high-dose vitamin C in patients receiving warfarin. Warfarin dose adjustment should be guided by INR values and the patient's clinical status rather than routine empirical modification.

Vitamin D

Vitamin D is a fat-soluble prohormone primarily recognized for its role in calcium and phosphate homeostasis and bone health. In addition to its classical functions, vitamin D contributes to immune regulation through the actions of its biologically active form, 1,25-dihydroxyvitamin D, which modulates both innate and adaptive immune responses [22-24]. During the COVID-19 pandemic, vitamin D supplementation received considerable attention because observational studies suggested an association between vitamin D deficiency and an increased susceptibility to, and severity of, respiratory viral infections, including COVID-19 [25-27]. The majority of researchers and commentators recommend vitamin D3 supplementation of 1,000 IU to 4,000 IU during the COVID-19 pandemic, aiming to achieve 25(OH) D levels of 30 ng/ml [26]. They strongly advise against taking doses exceeding the upper limit of daily vitamin D supplementation, which should not exceed a total of 4000 IU per day from both dietary sources and supplements [26]. Some reports suggest that higher doses of vitamin D may be beneficial in preventing and treating COVID-19. A review by Grant et al. recommended an initial dose of 10,000 IU per day for one month, followed by a maintenance dose of 5,000 IU per day. The goal is to achieve a 25(OH)D level of 40–60 ng/ml to help reduce the risk of COVID-19 [25]. Ebadi and Montano-Loza proposed higher vitamin D doses for COVID-19 patients: a loading dose of 1,000,000 IU in the first week, followed by 50,000 IU in weeks two and three [27].

However, despite extensive clinical investigation, current evidence does not support the routine use of vitamin D supplementation for the prevention or treatment of COVID-19 beyond correction of vitamin D deficiency according to established clinical recommendations [25-27].

Evidence regarding the interaction between vitamin D and warfarin remains limited. Experimental studies have suggested that vitamin D may influence coagulation-related pathways, while other investigations have reported effects on xenobiotic-metabolizing enzymes, including cytochrome P450 isoforms [7, 28]. Nevertheless, available evidence does not demonstrate a clinically established pharmacokinetic or pharmacodynamic interaction between vitamin D supplementation and warfarin. Therefore, the clinical significance of these findings for patients receiving warfarin remains uncertain and warrants further investigation [7]. Routine INR monitoring should continue according to standard warfarin management, particularly following the initiation of high-dose vitamin D supplementation or substantial changes in supplementation status.

Vitamin A

Vitamin A is a fat-soluble vitamin whose primary biological functions include the maintenance of normal vision, growth, epithelial integrity, and immune function [29, 30]. Vitamin A plays a fundamental role in both innate and adaptive immune responses and contributes to host defense against a wide range of infectious diseases [29]. Epidemiological and clinical studies have demonstrated that vitamin A deficiency is associated with increased susceptibility to respiratory and other infectious diseases, whereas adequate vitamin A status supports normal immune function [31]. During the COVID-19 pandemic, vitamin A attracted considerable interest because of its immunomodulatory properties and its potential role in reducing the severity of viral infections. Recent studies have also reported reduced serum retinol levels in patients with COVID-19, particularly in those with more severe disease [32-34]. However, current clinical evidence remains insufficient to support the routine use of vitamin A supplementation for the prevention or treatment of COVID-19 beyond correction of vitamin A deficiency.

Regarding the potential interaction between vitamin A and warfarin, available evidence suggests that

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excessive vitamin A intake may enhance the anticoagulant effect of warfarin and increase the risk of bleeding [41]. The mechanism underlying the reported interaction between vitamin A and warfarin remains unclear, and no clinical studies have demonstrated a clinically significant effect of vitamin A on warfarin pharmacokinetics or metabolism [9]. However, direct clinical evidence supporting a clinically significant interaction remains limited. Therefore, patients receiving warfarin who initiate high-dose vitamin A supplementation should undergo routine INR monitoring, and warfarin dosage should be adjusted according to the patient's anticoagulant response.

Vitamin E

Vitamin E is a fat-soluble antioxidant that plays an essential role in protecting cell membranes against oxidative damage and maintaining immune function. It is highly concentrated in the membranes of immune cells and contributes to the regulation of both innate and adaptive immune responses [36, 37]. Vitamin E deficiency has been associated with impaired immune function and an increased susceptibility to infectious diseases, whereas supplementation has been shown to improve immune responses, particularly in older adults and individuals with inadequate vitamin E status [36-38]. Several clinical studies have also suggested that vitamin E supplementation may reduce the incidence or severity of respiratory tract infections in selected populations [38, 39]. During the COVID-19 pandemic, vitamin E attracted interest because of its antioxidant and immunomodulatory properties. However, although it has been proposed as a potential adjunctive therapy, current clinical evidence remains insufficient to support the routine use of vitamin E supplementation for the prevention or treatment of COVID-19 beyond correction of nutritional deficiency [12].

Regarding potential interactions with warfarin, available evidence suggests that high-dose vitamin E supplementation may enhance the anticoagulant effect of warfarin and increase the risk of bleeding [43, 44]. Although the exact mechanism remains uncertain, proposed mechanisms include interference with vitamin K-dependent coagulation pathways and inhibition of platelet aggregation [9, 35]. High-dose vitamin E supplementation, especially at doses of 400–800 IU/day, may prolong prothrombin time in patients taking warfarin. However, clinical findings regarding this effect have been inconsistent [9, 35]. Therefore, patients receiving warfarin should be advised to avoid excessive vitamin E supplementation without medical supervision. Routine INR monitoring is recommended following the initiation of high-dose vitamin E supplementation or substantial changes in vitamin E intake, and warfarin dosage should be adjusted according to the patient's anticoagulant response.

Vitamin B complex

B-complex vitamins (vitamins B1, B2, B3, B5, B6, B9, and B12) are water-soluble vitamins, each of which plays an essential role in maintaining normal immune function and supporting host defense against infections [15]. Deficiency of B vitamins has been associated with impaired humoral and cell-mediated immune responses, whereas adequate B-vitamin status contributes to the proper activation of innate and adaptive immunity, modulation of inflammatory responses, and maintenance of normal respiratory function [15, 19]. During the COVID-19 pandemic, B-complex vitamins were investigated as potential adjunctive therapies because of their immunomodulatory and anti-inflammatory properties. Although several clinical studies have evaluated B-vitamin supplementation in patients with COVID-19, current evidence remains insufficient to support its routine use for the prevention or treatment of COVID-19 beyond correction of nutritional deficiency [15, 19].

Regarding potential interactions with warfarin, no clinically significant interaction between B-complex vitamin supplementation and warfarin has been established. However, observational studies have reported that low levels of certain B vitamins, particularly vitamin B6, are associated with an increased risk of venous thromboembolism, although this association does not indicate a direct interaction with warfarin [40-42]. These findings do not indicate a direct pharmacokinetic or pharmacodynamic interaction with warfarin, and their clinical relevance in patients receiving warfarin remains uncertain. Therefore, routine INR

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monitoring should continue according to standard warfarin management, particularly following the initiation of high-dose vitamin supplementation or substantial changes in nutritional status.

Melatonin

Melatonin is a neuroendocrine hormone primarily produced by the pineal gland, although it is also synthesized in several other tissues outside the pineal gland [43]. In addition to its well-established role in regulating circadian rhythm and sleep, melatonin exhibits potent antioxidant, anti-inflammatory, and immunomodulatory properties that contribute to both innate and adaptive immune responses [43, 44]. Depending on the physiological context, melatonin may enhance immune function under immunosuppressive conditions while attenuating excessive inflammatory responses by modulating oxidative stress and cytokine production [45]. These pleiotropic effects have led to growing interest in melatonin as a potential adjunctive therapy for infectious diseases, including viral infections [46].

During the COVID-19 pandemic, melatonin was investigated as a potential adjunctive treatment because of its antioxidant and immunomodulatory properties. However, although several clinical studies have evaluated melatonin in patients with COVID-19, current evidence remains insufficient to support its routine use for the prevention or treatment of COVID-19 outside established clinical indications [46, 47].

Regarding potential interactions with warfarin, several case reports and small clinical studies have suggested that concomitant administration of melatonin may enhance the anticoagulant effect of warfarin and increase the risk of bleeding; however, the exact mechanism underlying the potential interaction between melatonin and warfarin has not been fully elucidated. Available evidence suggests that any interaction is more likely to be pharmacodynamic than pharmacokinetic, as experimental studies have shown that melatonin inhibits platelet aggregation and thromboxane B_2 production, potentially enhancing the anticoagulant effects of warfarin and increasing bleeding risk [48]. Although the available evidence remains limited and is largely derived from case reports and small observational studies, patients receiving concomitant melatonin and warfarin should undergo close INR monitoring, particularly following the initiation of melatonin therapy or dose escalation, and should be monitored for signs and symptoms of bleeding.

N-Acetylcysteine

N-Acetylcysteine (NAC) is a precursor of glutathione and is widely recognized for its potent antioxidant, anti-inflammatory, and mucolytic properties [49, 50]. Clinically, NAC has long been used as an antidote for acetaminophen poisoning and as a mucolytic agent in chronic respiratory diseases. Beyond these established indications, increasing evidence suggests that NAC modulates oxidative stress, inflammatory signaling, and immune responses, making it a potential adjunctive therapy for several infectious and inflammatory disorders [63–66]. Experimental studies have demonstrated that NAC may inhibit viral replication, reduce oxidative stress, and attenuate the production of pro-inflammatory cytokines, while clinical studies have evaluated its potential role in acute viral respiratory infections and acute respiratory distress syndrome (ARDS) [51-54]. During the COVID-19 pandemic, NAC was investigated as a potential adjunctive therapy because of these biological properties. However, although several clinical studies have examined its use in patients with COVID-19, current evidence remains insufficient to support the routine use of NAC for the prevention or treatment of COVID-19 outside established clinical indications [57].

Regarding its potential interaction with warfarin, no clinically significant pharmacokinetic interaction between NAC and warfarin has been established. Nevertheless, experimental studies suggest that NAC may influence hemostasis by reducing the activity of vitamin K-dependent coagulation factors (II, VII, IX, and X), prolonging prothrombin time, and inhibiting platelet aggregation [58-61]. Although these findings have not consistently translated into clinically significant bleeding events in patients receiving warfarin, they suggest that high-dose NAC may theoretically potentiate the anticoagulant effects of warfarin. Therefore, caution is warranted when high-dose NAC is administered concomitantly with warfarin or other anticoagulant

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and antiplatelet agents. Patients receiving both therapies should undergo routine INR monitoring, particularly following initiation of high-dose NAC or significant changes in treatment, and should be monitored for signs and symptoms of bleeding.

Omega-3 Fatty Acids

Omega-3 fatty acids are essential polyunsaturated fatty acids that play critical roles in maintaining cell membrane integrity, cellular signaling, and physiological homeostasis [62]. The long-chain omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), possess well-established anti-inflammatory and immunomodulatory properties and have been shown to influence both innate and adaptive immune responses [63]. Experimental and clinical studies suggest that the effects of omega-3 fatty acid supplementation on infectious diseases may vary according to the pathogen, dosage, duration of supplementation, and host characteristics [64]. During the COVID-19 pandemic, omega-3 fatty acids were investigated as potential adjunctive therapies because of their ability to modulate inflammatory responses and oxidative stress. However, although several clinical studies have evaluated omega-3 supplementation in patients with COVID-19, current evidence remains inconclusive and does not support its routine use for the prevention or treatment of COVID-19 beyond correction of nutritional deficiency or other established indications [65].

Regarding potential interactions with warfarin, available clinical evidence is mixed. In a randomized, double-blind, placebo-controlled study of 16 patients receiving chronic warfarin therapy, supplementation with either 3 or 6 g/day of fish oil for 4 weeks did not result in a statistically significant change in INR compared with placebo [67]. However, individual case reports have described clinically relevant INR elevations. In one case report, doubling the daily fish oil dose from 1,000 to 2,000 mg was followed by an increase in INR from 2.8 to 4.3 within one month; after the fish oil dose was reduced, the INR decreased to 1.6 one week later [69]. Nevertheless, several case reports have described increases in the international normalized ratio (INR) following the initiation or dose escalation of omega-3 fatty acid supplements in patients with previously stable warfarin therapy, although concomitant medications and clinical factors may have contributed to these events [70-72]. Proposed mechanisms include modulation of platelet function, reduced thrombin generation, and effects on vitamin K-dependent coagulation pathways, although these mechanisms have not been consistently associated with clinically significant bleeding [73]. Therefore, while omega-3 fatty acid supplements appear to be generally safe when used concomitantly with warfarin, caution is warranted, particularly following initiation of high-dose supplementation or substantial dose escalation. Patients receiving both therapies should undergo routine INR monitoring and be advised to report any signs or symptoms of bleeding or excessive bruising promptly.

Coenzyme Q10

Coenzyme Q10 (CoQ10), also known as ubiquinone, is a lipid-soluble, vitamin-like compound that plays a central role in mitochondrial electron transport and cellular energy production [74]. In addition to its role in energy metabolism, CoQ10 functions as an endogenous antioxidant and contributes to the regeneration of other antioxidants, including vitamins C and E [75]. CoQ10 also exerts anti-inflammatory effects by modulating oxidative stress and regulating nuclear factor-κB (NF-κB)-dependent inflammatory pathways [75]. These biological properties have prompted investigations into the potential therapeutic role of CoQ10 in several disorders characterized by oxidative stress and excessive inflammation [76]. During the COVID-19 pandemic, CoQ10 was investigated as a potential adjunctive therapy because of its antioxidant and anti-inflammatory effects. Although several clinical studies have evaluated CoQ10 supplementation in patients with COVID-19, current evidence remains limited and does not support its routine use for the prevention or treatment of COVID-19 beyond established clinical indications [77-79].

Regarding potential interactions with warfarin, the available clinical evidence does not demonstrate a consistent effect of CoQ10 on INR. In a prospective longitudinal study of 171 patients receiving

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warfarin, 36 patients (21%) experienced at least one supratherapeutic INR, defined as an INR at least 0.5 units above the target range; however, the use of complementary and alternative medicines was not independently associated with supratherapeutic INR. CoQ10 use was, nevertheless, independently associated with an increased risk of self-reported bleeding (OR 3.69, 95% CI 1.88–7.24) [80]. In a randomized, double-blind, placebo-controlled crossover trial involving patients receiving stable long-term warfarin therapy, INR remained stable during treatment with CoQ10, and no clinically significant interaction was demonstrated [81]. Experimental studies have suggested that CoQ10 may influence warfarin metabolism or anticoagulant activity, but these findings are primarily based on in vitro and animal studies [82r82, 83]. Therefore, although a consistent effect of CoQ10 on INR has not been established in controlled clinical studies, INR monitoring remains advisable when CoQ10 supplementation is initiated or discontinued in patients receiving warfarin.

Quercetin

Quercetin is one of the most abundant dietary flavonoids and is widely distributed in fruits, vegetables, and medicinal plants. It exhibits a broad spectrum of biological activities, including antiviral, antioxidant, anti-inflammatory, antithrombotic, cardioprotective, and immunomodulatory effects [84]. Experimental studies have demonstrated antiviral activity against a variety of viruses, while both in vitro and in vivo investigations suggest that quercetin may attenuate oxidative stress, inflammatory responses, and lung injury associated with viral respiratory infections [85, 86]. During the COVID-19 pandemic, quercetin was investigated as a potential adjunctive therapy because of these biological properties. However, although several review studies have evaluated quercetin supplementation in patients with COVID-19, current evidence remains limited and does not support its routine use for the prevention or treatment of COVID-19 outside established clinical indications [87, 88].

Regarding potential interactions with warfarin, experimental evidence suggests that quercetin may influence both the pharmacokinetics and pharmacodynamics of warfarin. In vitro studies have shown that quercetin and its metabolites may displace warfarin from plasma albumin binding sites, thereby increasing the unbound plasma concentration of warfarin [89]. In addition, quercetin has been reported to inhibit cytochrome P450 2C9 (CYP2C9), the principal enzyme responsible for the metabolism of S-warfarin, potentially increasing plasma warfarin concentrations [90]. Quercetin has also demonstrated inhibitory effects on thrombin activity and platelet aggregation, suggesting additional anticoagulant and antiplatelet properties that could theoretically increase the risk of bleeding when administered concomitantly with warfarin [91, 92]. A published case report also described a marked increase in the international normalized ratio (INR) following prolonged consumption of quercetin-rich muscadine grapes in a patient receiving stable warfarin therapy [93]. Although current evidence is limited and is derived primarily from experimental studies and isolated case reports, a clinically relevant interaction cannot be excluded. Therefore, patients receiving warfarin should be advised to exercise caution when initiating high-dose quercetin supplementation, and routine INR monitoring is recommended following initiation or substantial dose escalation of quercetin-containing products.

Garlic

Garlic (*Allium sativum* L.) is one of the most widely used medicinal plants and has long been utilized for the prevention and treatment of infectious and cardiovascular diseases [94]. Its biological activities are largely attributed to sulfur-containing compounds, including allicin and its derivatives, such as ajoene, allitridin, and garlicin, which exhibit antiviral, antibacterial, antifungal, antioxidant, anti-inflammatory, and immunomodulatory properties [95, 96]. During the COVID-19 pandemic, garlic was investigated as a potential adjunctive therapy because of these biological properties. However, although several studies have evaluated garlic supplementation in patients with COVID-19, current evidence remains insufficient to support its routine use for the prevention or treatment of COVID-19 outside established clinical indications [97].

Regarding potential interactions with warfarin, available evidence suggests that concomitant use of

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garlic supplements may increase the risk of bleeding, although published clinical data remain limited and are derived primarily from case reports and pharmacologic studies [98]. Proposed mechanisms include inhibition of cytochrome P450 enzymes, particularly CYP2C9, CYP2C19, and CYP3A4, which may alter warfarin metabolism, as well as inhibition of platelet aggregation and modulation of coagulation pathways [99]. The antiplatelet activity of garlic appears to be the principal mechanism underlying its potential to increase bleeding risk [100]. Therefore, patients receiving warfarin should be advised to exercise caution when initiating garlic supplements or substantially increasing garlic intake. Close clinical monitoring for bleeding manifestations is recommended, and INR should be monitored when clinically indicated, particularly following significant changes in garlic supplementation.

Echinacea (*Echinacea purpurea*)

Echinacea purpurea, commonly known as purple coneflower, is one of the most extensively studied medicinal plants used for the prevention and treatment of respiratory tract infections [101]. Its biological activity has been attributed to multiple phytochemical constituents with antiviral, anti-inflammatory, and immunomodulatory properties. During the COVID-19 pandemic, *Echinacea* was investigated as a potential adjunctive therapy because of these biological properties. However, although several clinical studies have evaluated its use in patients with COVID-19, current evidence remains insufficient to support the routine use of *Echinacea* for the prevention or treatment of COVID-19 outside established clinical indications [102].

Regarding potential interactions with warfarin, available evidence indicates that *Echinacea* preparations have minimal effects on the pharmacokinetics and pharmacodynamics of warfarin and are unlikely to produce clinically significant interactions. In a randomized crossover study involving 12 healthy subjects, concomitant administration of Echinacea increased the apparent clearance of S-warfarin; however, this pharmacokinetic change did not result in a clinically significant alteration in anticoagulant response. The mean maximum INR was 1.7 (95% CI 1.5–1.9) with warfarin alone and 1.8 (95% CI 1.6–2.0) during *Echinacea* coadministration, while the geometric mean ratio of INR AUC was 1.09 (90% CI 0.91–1.31) [103]. Therefore, routine avoidance of *Echinacea* in patients treated with warfarin is not currently supported by available evidence. Nevertheless, as with the initiation or discontinuation of any herbal supplement, routine INR monitoring according to standard warfarin management is recommended, particularly following substantial changes in supplement use.

Ginger (*Zingiber officinale* Roscoe)

Zingiber officinale Roscoe (ginger) is a widely used medicinal plant belonging to the family Zingiberaceae. Ginger rhizomes contain numerous bioactive compounds, including gingerols and shogaols, which possess antioxidant, anti-inflammatory, antimicrobial, and antiviral properties [104]. Experimental studies have demonstrated antiviral activity against several respiratory viruses, while both animal and human studies suggest that ginger may attenuate oxidative stress and inflammatory responses associated with viral respiratory infections [105]. During the COVID-19 pandemic, ginger was investigated as a potential adjunctive therapy because of these biological properties. However, although several clinical studies have evaluated ginger supplementation in patients with COVID-19, current evidence remains insufficient to support its routine use for the prevention or treatment of COVID-19 outside established clinical indications [106].

Regarding potential interactions with warfarin, available evidence is inconsistent. A randomized crossover study in healthy volunteers demonstrated that ginger supplementation did not significantly affect the pharmacokinetics or pharmacodynamics of warfarin. The mean ratio of the AUC of INR during ginger coadministration compared with warfarin alone was 1.01 (90% CI 0.93–1.15) [107]. In contrast, several case reports and observational studies have described marked increases in the international normalized ratio (INR) and bleeding events following the concomitant use of ginger products in patients receiving warfarin therapy [108, 109]. Although the underlying mechanism remains

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uncertain, experimental studies suggest that ginger may inhibit platelet aggregation, thereby potentially increasing bleeding risk independent of changes in warfarin metabolism [99]. Given the conflicting evidence, a clinically relevant interaction cannot be excluded. Therefore, patients receiving warfarin should be advised to exercise caution when initiating ginger supplements or substantially increasing ginger intake. Routine INR monitoring is recommended after initiating or increasing ginger-containing products, and patients should be monitored for signs and symptoms of bleeding.

Conclusion

Although evidence on interactions between warfarin and dietary supplements or herbal medicines is limited and, in many cases, conflicting, several products may produce clinically relevant interactions that can enhance or reduce warfarin's anticoagulant effects. Such interactions may increase the risk of bleeding or compromise anticoagulation control, thereby predisposing susceptible patients to thromboembolic complications. The likelihood and clinical significance of these interactions vary considerably by supplement, dose, duration of use, and the quality of available evidence. Therefore, routine avoidance of all dietary supplements and herbal medicines in patients receiving warfarin is not supported by current evidence. Instead, healthcare professionals should obtain a comprehensive history of dietary supplement and herbal medicine use, educate patients regarding the potential risks of self-medication, and encourage them to report the initiation, discontinuation, or substantial changes in the consumption of these products. Appropriate clinical assessment, together with routine INR monitoring when clinically indicated, remains the cornerstone of minimizing clinically significant herb–warfarin interactions and maintaining safe anticoagulation therapy.

Ethical approval and consent to participate

A statement of human and animal rights is not applicable to this paper.

Human and animal rights

Not applicable.

Conflicts of interest

The authors have no conflicts of interest in this study.

Availability of data and material

All data generated or analyzed during this study are included in this published article.

Authors' Contribution in the Manuscript file

All authors contributed to interpreting the data and read and approved the final manuscript.

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