



From Root to Risk: A Systematic Review and Meta-Analysis Evaluating the Hemostatic Effects of Ginger in Healthy Adults

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Abstract

Ginger (*Zingiber officinale*) has traditionally been consumed for its gastrointestinal and anti-inflammatory potentials. Emerging evidence suggests a potential role in modulating haemostasis, raising concerns for individuals on anticoagulants or at risk of bleeding or thromboembolic events. This systematic review and meta-analysis aimed to evaluate the effect of ginger on key haemostatic parameters in healthy volunteers, in order to inform future research and guide recommendations for at-risk populations.

Methods: The study protocol was registered on PROSPERO (CRD42025644443), with a comprehensive search being conducted up to August 2025. Eligible studies assessed the impact of ginger (in various forms) on activated partial thromboplastin time (aPTT), prothrombin time (PT), international normalized ratio (INR), platelet aggregation, thromboxane B₂ (TXB₂), and clotting time in healthy adults.

Results: Fourteen studies were included (6 in vivo, 8 ex. vivo). Ginger in all tested forms, significantly prolonged PT beyond the normal PT range. Ginger reduced platelet aggregation significantly with a pooled percentage change of 55.53% (95% CI 33.13; 77.94) and a mean difference with the 4g dose of 5.26, (95% CI 4.61; 5.92). TXB₂ levels were reduced by ~37%. INR demonstrated a dose-dependent increase, although the effect size was minimal. Clotting time was not significantly prolonged (7.28 ± 0.268 minutes vs 6.7 ± 0.367 minutes in control group), and aPTT findings showed inconsistent results. However, the findings should be interpreted with caution, as the certainty of evidence is considered low for most outcomes.

Conclusion: While dietary ginger is likely safe in healthy individuals, caution is advised in patients with bleeding risk or on anticoagulants, particularly consuming large amounts of ginger. Standardized trials in at-risk populations are needed to guide safe use.

Keywords: Aggregation; aPTT; bleeding; clotting; Ginger; haemostasis; INR; Platelet; PT; *Zingiber officinale*

Introduction

Cardiovascular diseases (CVDs) remain the leading cause of morbidity and mortality worldwide, posing a persistent challenge to global public health. The prevalence of CVDs has surged globally. According to the National Vital Statistics System, CVD-related deaths rose by 9.3% between 2019 and 2022, reaching 454.5 deaths per 100,000 individuals [1]. Thrombosis remains a central mechanism underlying many of these events [2]. Therefore, antithrombotic therapies, such as warfarin,

aspirin, and newer oral anticoagulants (NOACs), are widely employed. However, these agents require careful monitoring due to their significant bleeding risks [3]. Furthermore, individuals with bleeding disorders, such as haemophilia, face further challenges in maintaining haemostatic balance and must avoid substances that could exacerbate coagulation disturbances [4].

Ginger (*Zingiber officinale*) has been widely consumed as a tea or dietary additive, across cultures for managing various types of nausea, ranging from pregnancy-induced nausea to postoperative and chemotherapy-

related nausea. Beyond its antiemetic action, ginger demonstrates potent anti-inflammatory and antioxidant activities, alleviates joint and muscle pain, and lowers blood pressure through calcium channel blockade action. It also contributes to sexual and reproductive health by enhancing sperm quality and relieving dysmenorrhea-related pain [5 - 7]. The antimicrobial activity of ginger contributes to its use in controlling bacterial infections [8]. Furthermore, in traditional Chinese medicine, ginger is utilized to treat colic, dyspepsia, and general atony, as well as to stimulate physiological function [9-12]. In this context, classified as a Yang herb —associated with warmth, energy, and activity—ginger is traditionally believed to counteract Yin qualities such as coldness, lethargy, and fatigue, thereby restoring vitality and promoting physiological stimulation [13,14].

Beyond its traditional and therapeutic uses, ginger has been reported to exert antithrombotic effects, notably through inhibition of thromboxane A₂ (TXA₂) synthesis, an action analogous to that of low-dose aspirin [15]. Bioactive constituents of ginger, particularly [6]-gingerol and [6]-shogaol, demonstrate inhibitory activity against platelet aggregation induced by arachidonic acid, collagen, and other agonists in isolated systems. Derivatives of gingerols, including paradol-type compounds, have likewise been shown to inhibit cyclooxygenase-1 (COX-1) and suppress TXA₂ synthesis, further supporting a mechanistic basis for their antiplatelet effects. In animal models, methanolic ginger extract has been observed to prolong bleeding time, a surrogate marker of antithrombotic activity, although findings for other coagulation parameters such as prothrombin time (PT), activated partial thromboplastin time (aPTT), and thrombin time remain inconsistent. Such effects may confer protection against thrombosis; however, they also raise concern regarding potential bleeding risks, particularly among individuals receiving anticoagulant therapy.

While several investigations have demonstrated anticoagulant and antiplatelet activities, others have yielded inconclusive or contradictory results, underscoring the need for further clarification. At the clinical level, evidence remains equivocal. A systematic review by Marx et al. (2015) [16], encompassing eight clinical trials and two observational studies, reported variable effects of ginger on platelet aggregation, with only half of the studies showing significant inhibition. Similarly, a randomized crossover trial in healthy volunteers found that daily intake of 15 g raw ginger root or 40 g stem ginger for two weeks did not significantly alter thromboxane B₂ (TXB₂) levels compared with placebo. Furthermore, several case reports have highlighted potential interactions with anticoagulant medications—including one involving a warfarin-treated patient who exhibited an elevated international normalized ratio (INR) following ginger supplementation, and another describing hemoptysis in a patient receiving a NOAC, possibly exacerbated by concurrent ginger intake.

Accordingly, this systematic review aimed to evaluate the effect of ginger on key coagulation parameters in healthy individuals, a population selected to isolate ginger's intrinsic haemostatic effects without confounding disease or drug influences. This approach allows a clearer understanding of its baseline pharmacodynamic profile, thereby informing future investigations in vulnerable patients or those receiving antithrombotic therapy.

Methods

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines [17] and was registered in the PROSPERO database (Registration ID: CRD42025644443).

2.1 Eligibility Criteria

We included randomized controlled trials (RCTs), non-randomized clinical trials, and observational studies (including cohort studies, case-control studies, case reports, and case series) that evaluated the effect of ginger on haemostatic parameters, including coagulation indices (aPTT, PT, INR) and platelet function markers (TXB₂, clotting time, and platelet aggregation). Eligible studies assessed any form of ginger, including fresh/raw, capsules, dried, extracts, as well as purified ginger polysaccharides (GP) and sulfated ginger polysaccharides (SGP). To ensure internal validity and comparability, studies were included only when ginger was administered either by oral ingestion to healthy volunteers prior to blood sample collection (in vivo exposure) or by direct addition to blood samples obtained from healthy individuals (ex vivo exposure). In all cases, participants were required to be healthy adults without underlying coagulation disorders.

Studies involving participants with coagulation disorders, thromboembolic diseases, those receiving any antithrombotic therapies, those admitted to intensive care units (ICUs), or those with severe infections were excluded.

2.2 Search Strategy and Information Sources

A comprehensive literature search was performed across PubMed, Scopus, Google Scholar, the Cochrane Central Register of Controlled Trials (CENTRAL), and ClinicalTrials.gov for all relevant studies published up to August 2025. The search was supplemented by manual screening of reference lists from relevant articles and consultation with experts. The search terms in PubMed included:

“Ginger” OR “Zingiber officinale” OR “ginger extract” OR “ginger supplement”) AND (“Coagulation” OR “blood clotting” OR “haemostasis” OR “aPTT” OR “activated partial thromboplastin time” OR “prothrombin time” OR INR OR “platelet aggregation” OR thromboxane OR platelet OR clotting OR bleeding). No restrictions were placed on publication language or year.

2.3. Study Selection

Study selection was conducted in two phases by two independent teams: (i) *Phase 1*: Title and abstract screening using Rayyan.ai software [18], and (ii) *Phase 2*: Full-text review of potentially eligible articles. Disagreements at any stage were resolved through group discussions until consensus was reached.

2.4. Data Extraction

Data extraction was carried out by three independent teams using a standardized form in Google Sheets. Extracted variables included: Study characteristics (design, country, study duration), participant demographics (age, sex, sample size), details of ginger intervention (form, dose, frequency, and duration), comparison groups (when present), and outcomes of interest. Any discrepancies were addressed through consensus discussions.

2.5 Risk of Bias Assessment

The methodological quality of included studies was assessed independently by two reviewers using the Risk of Bias 2 (RoB-2) tool for randomized studies [19] and the Methodological Index for Non-Randomized Studies (MINROS) tool for non-randomized studies [20]

2.6 Outcomes of Interest

Extracted outcomes were categorized according to GRADE, the Grading of Recommendations Assessment, Development, and

Evaluation [21] methodology into: *Primary outcomes*: Changes in aPTT, PT, and INR. *Secondary outcomes*: Changes in platelet aggregation, TXB₂ levels, and clotting time.

2.7 Data Synthesis

Quantitative data were summarized as frequencies, means ± standard deviations (SD), or medians with interquartile ranges (IQR), as appropriate. For outcomes reported in at least two studies, a single-arm meta-analysis was performed using both fixed-effect and random-effect models. Heterogeneity across studies was assessed using Cochran’s Q test and the I² statistic, interpreted as: I² < 40%: Low heterogeneity, 40–60%: Moderate heterogeneity, 60–75%: Substantial heterogeneity, and >75%: Considerable heterogeneity. A sensitivity analysis was performed for outcomes with substantial or considerable heterogeneity (I² ≥ 60%). Meta-analyses were conducted using the “meta”, “metafor”, and “metaprop” packages in R software [22]. Graphical representations were generated using ggplot2 [23]. For categorical outcomes (e.g., platelet count, clotting time, TXB₂), the proportion of participants experiencing the outcome was calculated.

2.8 Certainty of Evidence

The certainty of evidence for each outcome was graded using the GRADE approach [21, 24], classifying evidence into four categories: high, moderate, low, or very low.

Results

3.1 Study Characteristics

As illustrated in **Figure 1**, our screening yielded a total of 14 studies [25-38] . These studies comprised three RCTs, three prospective interventional studies, and eight ex. vivo investigations. Studies were conducted across a diverse range of countries including Sudan [31, 36] , Saudi Arabia [33], Philippines [30,37] , India [26,32] , Netherlands [28], United Kingdom [27] , Nigeria [35] , Turkey [38], Denmark [25], China [34], and Taiwan [29]. The forms of ginger used included water-based suspensions (aqueous extracts and ginger tea), alcohol-based extracts (ethanol and methanol extracts), crude powdered ginger, fresh raw ginger (stem and inner parts), GP, and SGP. Sample sizes ranged from 3 to 80 participants/samples. The ginger exposure period varied from ex vivo applications to intervention durations of up to 14 days (**Table 1**).

Author (Year)	Study Design	Country	Ginger Form Used	Sample Size	Age of participants, years	Ginger exposure period	Main Outcomes
Ahmad et al. (2022)	Ex. Vivo	Sudan	70% ethanol extract (25–75 µL)” cell 4g of ginger powder (prepared as ginger tea/150ml of hot water) once vs. twice daily	60	NA	Ex. Vivo	↑ PT significantly; APTT not significant
Alaskar et al. (2020)	RCT	Saudi Arabia	25%, 50%, 75% ginger extract	19/20	4g: 32.3±8.45 8g: 29.6±5.55	5 days	Significant ↓ of platelet aggregation by ginger 4g, particularly with epinephrine agonist
Aves et al. (2015)	Ex. Vivo	Philippines	10 grams of powder suspended in 100 mL of distilled water (10%)	17	18-35 (females only)	Ex. Vivo	↑ PT and aPTT significantly
Chegu et al. (2018)	Ex. Vivo	India	Raw ginger root (15 g) and stem (40 g)	NA	22±3	14 days	↓ Platelet thromboxane synthesis
Janssen et al. (1996)	Prospective Interventionl	Netherlands	250 mg/mL crude ginger leaf extract by ethanol 70%	18	22-29	Ex. Vivo	↑ PT and APTT significantly vs saline; less potent than heparin
Linconada et al. (2023)	Ex. Vivo	Philippines	2g dried ginger	15	NA	24 hours	no change in platelet aggregation using AA, ADP, Ristocetin or Collagen
Lumb et al. (1994)	RCT	United Kingdom	10g suspended in 100mL of distelled water (10% aqueous extract)	8	NA	Ex. Vivo	↑ PT significantly; APTT not significant
Oduwe et al. (2021)	Ex. Vivo	Nigeria		80			

Özdemir et al. (2024)	Ex vivo	Turkey	water, ethanol, methanol extracts from giniger inner and shell parts	50	NA	Ex. Vivo	↑ PT significantly; APTT not significant
Srivastava (1989)	Prospective Interventionl	Denmark	5 g fresh raw ginger	7			↓ TxB ₂ by ~37%
Taj Eldin et al. (2016)	Ex. Vivo	Sudan	Aqueous extract (5%) in 25–100 μL	30	15-30	Ex. Vivo	↑ PT dose-dependent
Verma et al. (1993)	Prospective Interventionl	India	5g of ginger powder	10	NA	14 days	Significant inhibition in platelet aggregation SGP2 and SGP prolonged APTT and PT (↑ by 1.33x and 1.22x); GP inhibited both intrinsic and extrinsic coagulation pathways. No effect on TT
Wang et al. (2020)	Ex. Vivo	China	Sulfated ginger polysaccharides (GP, GP1, GP2, SGP, SGP1, SGP2)	3	NA	Ex. Vivo	Ginger alone had significant inhibitory effect on platelet aggregation which were maximized when added to nifedipine
Young et al. (2006)	RCT crossover	Taiwan	1 g ginger daily	10	25-60	7 days	

AA: arachnoid acid; ADP: Adenine diphosphate; APTT: activated partial thromboplastin time; SGP: Sulfated ginger polysaccharides; GP: Ginger polysaccharides; PT: prothrombin time; RCT: randomized controlled trial; TxB₂: Thromboxane B₂

Table 1: Study Characteristics of Included Studies.

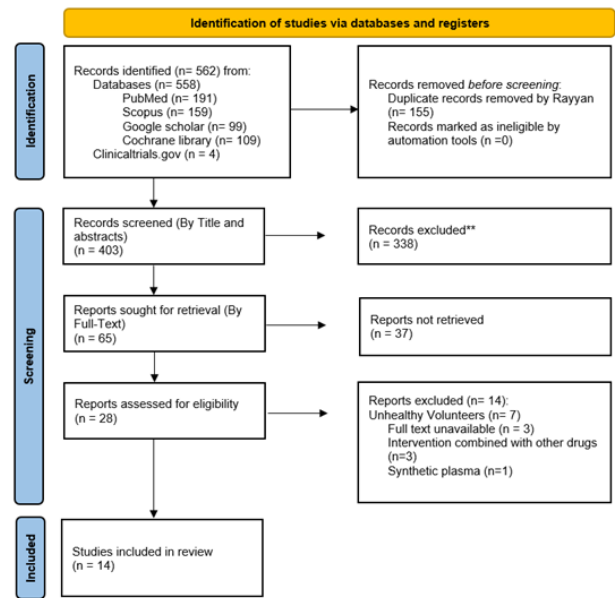


Figure 1: PRISMA 2020 flow diagram for study selection.

3.2 Risk of Bias Assessment

As illustrated in the RoB 2 traffic light plot (Figure 2), the overall risk of bias among the randomized controlled trials varied across studies. Alaskar et al. (2020) [33] and Young et al. (2006) [29] were judged as having *some concerns*, mainly due to unclear randomization and

deviations from intended interventions, while Lumb et al. (1994) [27] was rated at *high risk of bias*, primarily attributed to missing outcome data and incomplete reporting.

For non-randomized studies, methodological quality assessed using the MINORS tool was generally moderate. Most studies clearly stated

their aims, defined appropriate endpoints, and ensured acceptable follow-up periods. However, frequent methodological limitations included non-consecutive participant inclusion, absence of sample size calculation, and limited blinding or incomplete follow-up data. Among these, Janssen et al. (1996) [28] and Özdemir et al. (2024) [38] achieved the highest methodological scores (14/16), reflecting strong design rigor and clarity in reporting, whereas Wang et al. (2020) [34] scored lowest (7/16), mainly due to missing information on patient selection, follow-up, and sample size justification (**Table 2**).

Authors (Year)	Clear Aim & Relevant Question	Consecutive Patients Included	Prospective Data Collection	Appropriate, Clearly Defined Endpoints	Unbiased Endpoint Assessment	Adequate Follow-up Period	Acceptable Loss to Follow-up	Sample Size Calculation	Overall Score
Ahmad et al. (2022)	2/2	1/2	2/2	2/2	1/2	2/2	2/2	0/2	12/16
Aves et al. (2015)	2/2	1/2	2/2	2/2	1/2	2/2	2/2	0/2	12/16
Chegu et al. (2018)	2/2	1/2	2/2	2/2	1/2	2/2	2/2	0/2	12/16
Janssen et al. (1996)	2/2	1/2	2/2	2/2	1/2	2/2	2/2	2/2	14/16
Linconada et al. (2023)	2/2	1/2	2/2	2/2	1/2	2/2	2/2	0/2	12/16
Oduwe et al. (2021)	2/2	1/2	2/2	2/2	1/2	2/2	2/2	0/2	12/16
Özdemir et al. (2024)	2/2	1/2	2/2	1/2	2/2	2/2	2/2	2/2	14/16
Srivastava (1989)	2/2	1/2	2/2	2/2	1/2	2/2	1/2	0/2	11/16
Taj Eldin et al. (2016)	2/2	1/2	2/2	2/2	1/2	2/2	2/2	0/2	12/16
Verma et al. (1993)	2/2	1/2	2/2	2/2	1/2	2/2	1/2	0/2	11/16
Wang et al. (2020)	2/2	0/2	2/2	2/2	1/2	0/2	0/2	0/2	7/16

Table 2: Risk of Bias of non-randomized studies using MINORS tool.

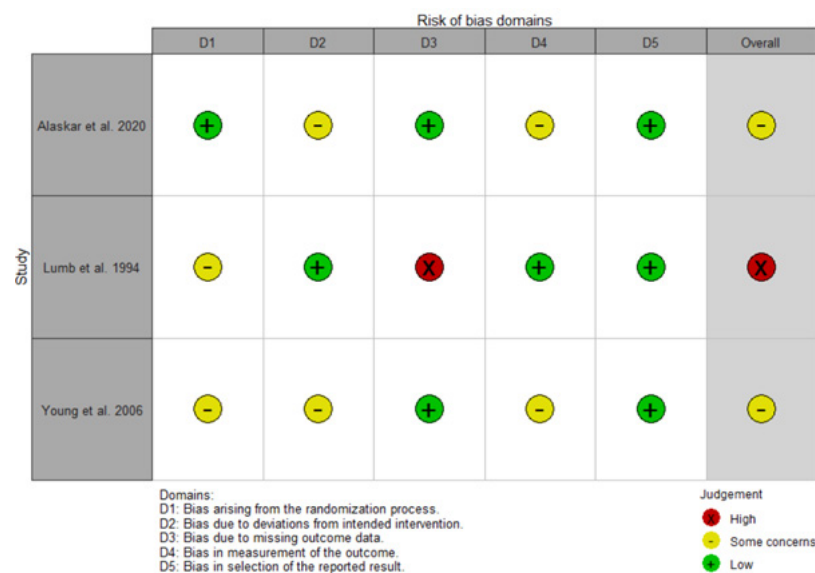


Figure 2: Traffic light plot of risk of bias assessments for randomized controlled trials using RoB 2 tool. Each domain is color-coded to indicate risk level per study.

3.3 Primary Outcomes

3.3.1 Activated Partial Thromboplastin Time (aPTT)

As detailed in **Figure 3** and supported by supplementary **Table 3**. The pooled mean aPTT varied by the form of ginger used as follows: *Water-based* ginger suspensions: 32.7 seconds (95% CI: 23.01–42.38, $I^2=100\%$, $n=380$), *Alcohol-based* ginger extracts: 32.16 seconds (95% CI: 28.06–36.27, $I^2=99.7\%$, $n=795$), *Ginger polysaccharides* (GP): 32.39 seconds (95% CI: 31.39–32.21, $I^2=87\%$, $n=36$), and *Sulfated ginger polysaccharides* (SGP): 34.65 seconds (95% CI: 32.80–36.51, $I^2=95.3\%$, $n=36$).

Sensitivity analyses for *water-based ginger* preparations demonstrated that exclusion of Oduwe et al. (2021) [35] markedly reduced heterogeneity, indicating that this study contributed substantially to overall variability. Similarly, when *alcohol-based* extracts were stratified by solvent type, subgrouping into *ethanol-* and *methanol-based* studies

revealed that heterogeneity was effectively minimized within *methanol-based* trials but persisted among those using ethanol extracts.

In contrast, sensitivity analyses for *GP* and *SGP* forms did not yield significant reductions in heterogeneity (see Supplementary Figures 1S–2S and Supplementary Tables 2S–3S). However, exclusion of the 2.0 mg/mL GP concentration reduced heterogeneity (I^2) to zero, suggesting that this dose accounted for the majority of between-study variance. Furthermore, subgrouping the *SGP* forms based on their chemical structure revealed that *SGP* form 1 exhibited the lowest heterogeneity ($I^2 = 4.6\%$), indicating greater internal consistency among these results.

Consistent with these findings, although not included in the meta-analysis, Aves et al. (2015) [30], in their ex vivo investigation employing *ethanol-based ginger* extracts at concentrations of 25%, 50%, and 75%, reported a notable aPTT (**Table 3**), reinforcing the concentration-dependent anticoagulant potential of *ethanol-extracted* preparations.

Outcome	No. of Studies (Design)	Key Findings	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Certainty of Evidence (GRADE)	Summary Interpretation
Prothrombin Time (PT)	5 (in vitro / ex vivo human & animal) (Özdemir 2024; Ahmad 2022; Taj Eldin 2016; Linconada 2023; Wang et al. 2020)	Significant PT prolongation	Serious → Down graded 1	Moderate → Down graded 1	Not serious → Not Down graded	Serious → Down graded 1	Undetected	Very Low	Ginger significantly prolongs PT in all forms
Activated Partial Thromboplastin Time (aPTT)	5 (in vitro / ex vivo) (Oduwe 2021; Özdemir 2024; Linconada 2023; Wang 2020; Ahmad 2022)	Non-Significant aPTT activity	Serious → Down graded 1	Moderate → Down graded 1	Not serious → Not Down graded	Serious → Down graded 1	Undetected	Very Low	Ginger inhibits the intrinsic coagulation pathway, prolonging aPTT.
INR (Warfarin Interaction)	1 (Özdemir 2024)	Non-significant change in INR, but showed a dose dependent activity	Not serious → Not Down graded	Not serious → Not Down graded	Not serious → Not Down graded	Serious → Down graded 1	Undetected	Moderate	No clinically significant pharmacokinetic or pharmacodynamic interaction between ginger and warfarin.
Platelet Aggregation	2 (in vivo / ex vivo clinical & experimental) (Young et al. 2006; AlAskar et al. 2020)	4g: 5.85 and 95% CI [2.72; 8.98], 8g: -0.13 and 95% CI [-1.74; 1.49]	Moderate → Down graded 1	Serious → Down graded 1	Not serious → Not Down graded	Serious → Down graded 1	Undetected	Very Low	Ginger shows mild anti-platelet activity in vivo, stronger in vitro through COX-1/TxA ₂ inhibition.

Table 3: Certainty of Evidence (GRADE) for the Effect of *Zingiber officinale* (Ginger) on Hemostatic Outcomes.

According to the American Association for Clinical Chemistry (AACC), the normal reference range for aPTT is approximately 25 to 35 seconds [39]. In comparison with the normal aPTT range, as shown in **Figure 3**, alcohol-based ginger extracts and GP forms demonstrated pooled aPTT values were entirely within the normal range. SGP forms

showed a borderline elevation, with the upper limit of the confidence interval slightly exceeding the normal threshold. In contrast, water-based ginger suspensions displayed the widest confidence interval, spanning both below and above the normal range, indicating substantial variability and potential heterogeneity across the included studies.

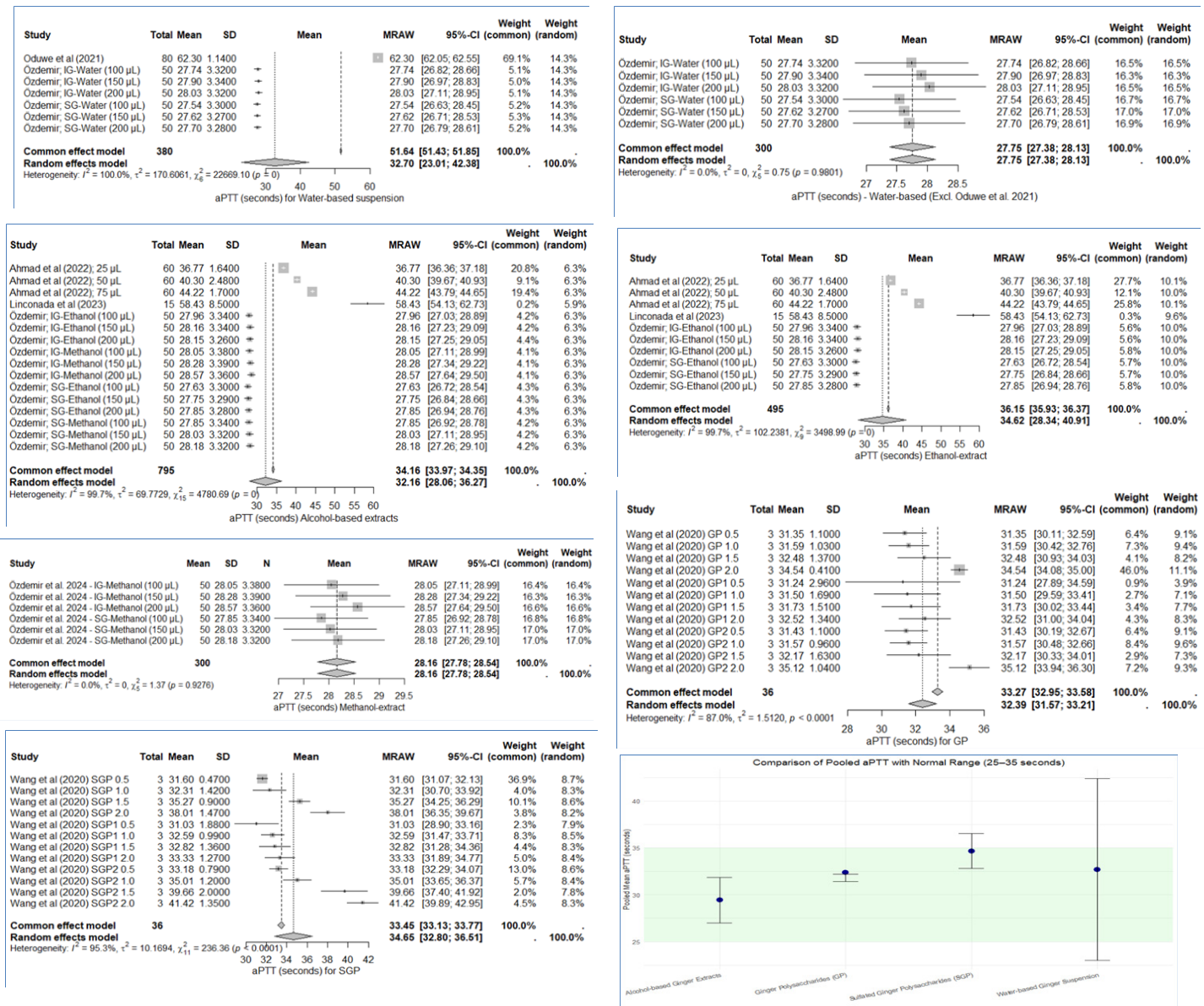


Figure 3: Random-effects model showing standardized mean differences (SMD) and 95% confidence intervals across included studies. From above to below (1st) Forest plot of the effect of water-based ginger suspension (2nd) Sensitivity analysis for the water-based ginger suspension was carried on by excluding Oudwe et al. (2021). The heterogeneity index dropped to zero. (3rd) Forest plot of the effect of alcohol-based ginger extracts. (4th and 5th) Sub-group analysis for the alcohol-based ginger extracts was carried on by evaluating ethanol-based and ethanol-based extracts separately. The heterogeneity index dropped to zero in the methanol-group (5th and 6th) Forest plot of the effect of ginger polysaccharides and sulfated ginger polysaccharides extracts. (7th) Comparison of pooled activated partial thromboplastin time (aPTT) and normal range (shaded in light blue 25-25 second)

GP: Activated Partial Thromboplastin Time (aPTT); Ginger polysaccharide; IG: Inner ginger; SG: stem part of ginger; SGP: Sulfated ginger polysaccharide

3.3.2 Prothrombin Time (PT)

As detailed in **Figure 4**, *Water-based* ginger suspensions yielded a pooled PT of 16.71 seconds (95% CI: 15.00–18.42, $I^2=100\%$, $n=500$), *Alcohol-based* extracts showed a pooled PT of 16.13 seconds (95% CI: 14.34–17.92, $I^2=99.5\%$, $n=795$), *GP* had a pooled PT of 14.41 seconds

(95% CI: 13.62–15.13, $I^2=94.4\%$, $n=36$), and *SGP* had a pooled mean of 14.41 seconds (95% CI: 14.05–14.78, $I^2=83.2\%$, $n=36$). All results showed a high degree of heterogeneity, which failed to be resolved by sensitivity or subgroup analyses, except for subgroup analysis for *GP* and *SGP* forms (Supplementary Figures 3S–4S).

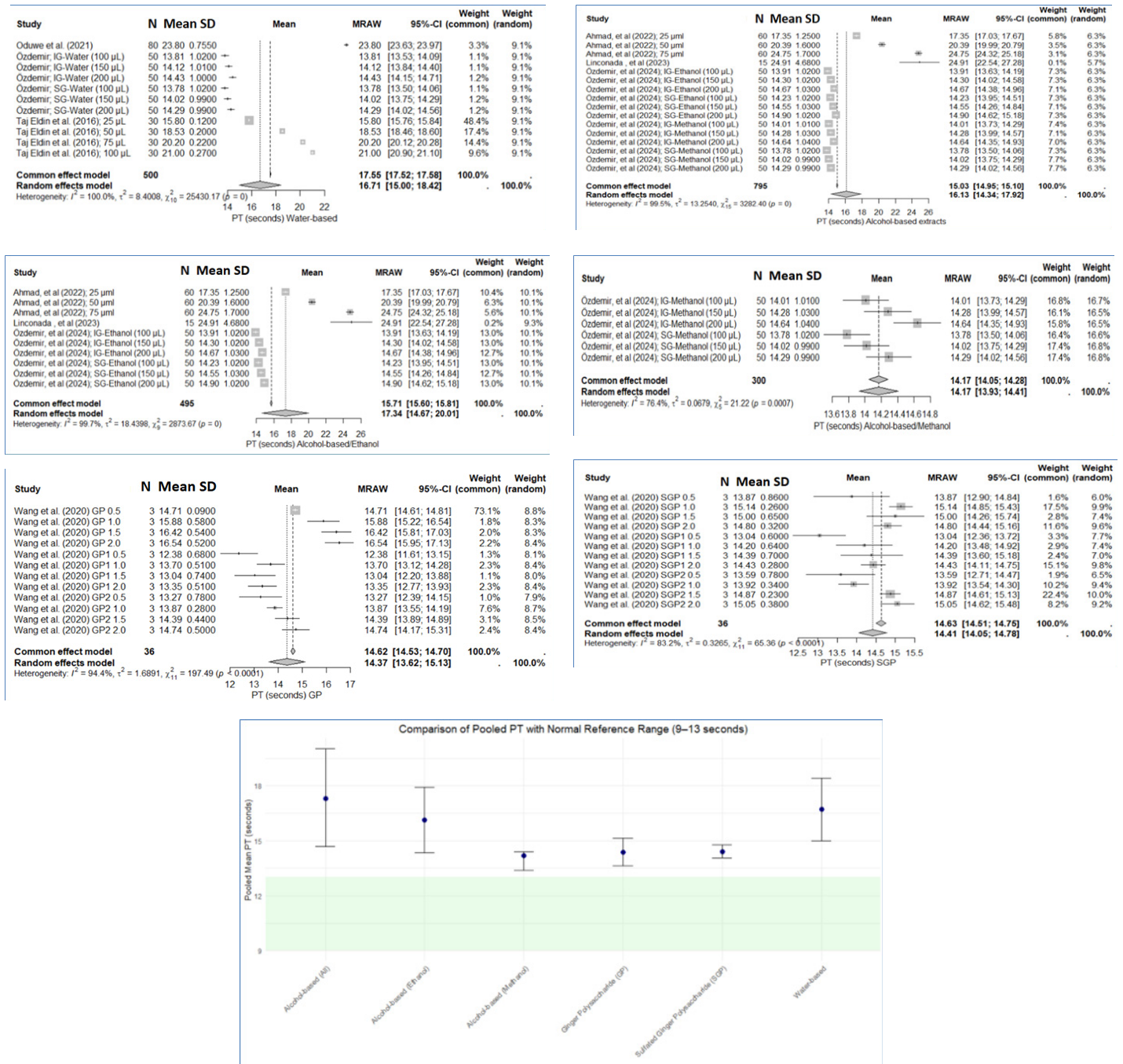


Figure 4: Forest plots of the effect of different ginger forms on Prothrombin Time (PT). Random-effects model showing standardized mean differences (SMD) and 95% confidence intervals across included studies, and Comparison of pooled Prothrombin time (PT) with the normal ranges (shaded in light blue). GP: Ginger polysaccharide; IG: Inner ginger; SG: stem part of ginger; SGP: Sulfated ginger polysaccharide.

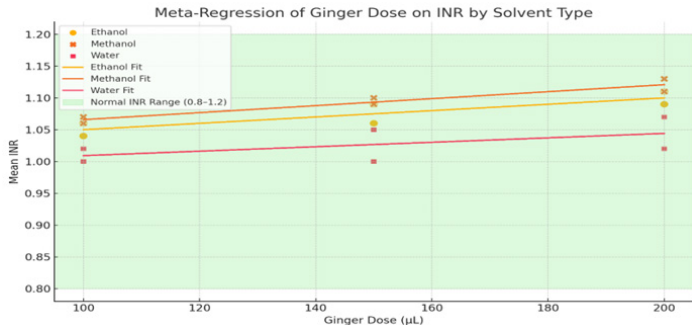
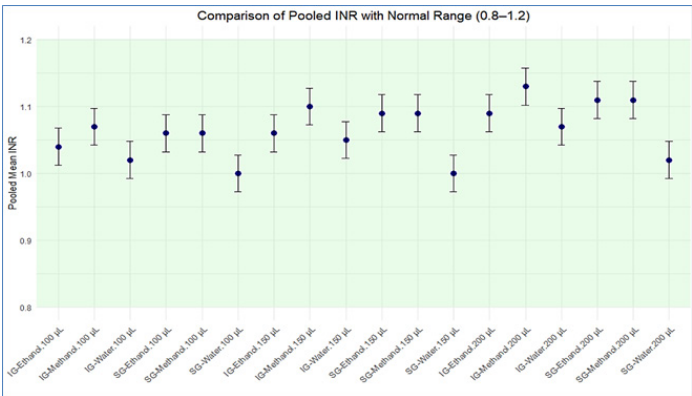
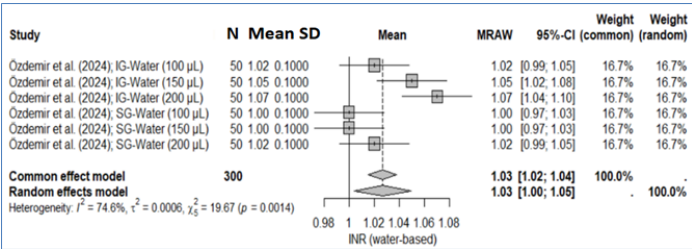
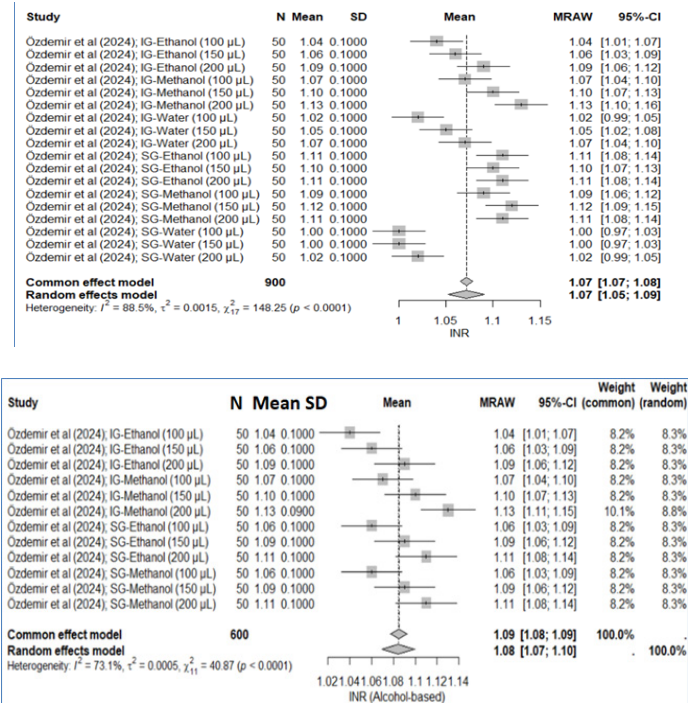
3.3.3 International Normalized Ratio (INR)

Only water- and alcohol-based ginger extracts were evaluated regarding their impacts on INR (Figure 5). The meta-analysis demonstrated that the evaluated ginger preparations did not significantly alter INR levels compared to the normal reference range (0.8–1.2) [39], with a pooled INR of 1.07 (95% CI: 1.05–1.08, n=900), and with considerable heterogeneity ($I^2=88.5\%$), turned into substantial heterogeneity by subgroup analyses.

A meta-regression analysis revealed a statistically significant but a very weak positive relationship between ginger concentration and INR

values (regression coefficient = 0.0005, 95% CI: 5.26e-05–0.001, $p = 0.030$, $R^2 = 0.263$). Each 1 μL increase in ginger concentration was associated with an estimated 0.0005-unit increase in INR, suggesting a mild dose-dependent anticoagulant effect.

When ginger extracts were grouped by solvent type, methanol-based extracts exhibited the most statistically significant association (slope = 0.0005; $p = 0.0033$; $R^2 = 0.91$). Ethanol-based extracts showed a similar slope (slope = 0.0005), but with a lower degree of correlation ($p = 0.0265$; $R^2 = 0.75$). In contrast, water-based extracts demonstrated a non-significant relationship (slope = 0.0004; $p = 0.2498$; $R^2 = 0.31$).



regression analysis showing a positive relationship between g

Figure 5: Forest plots of the effect of different ginger forms on INR (1-3). Random-effects model showing standardized mean differences (SMD) and 95% confidence intervals across included studies. (4th) Comparison of pooled INR with the normal ranges (shaded in light blue). (5-7) Meta-regression showing the positive relationship between ginger concentration and INR whether grouped by solvent type or ginger concentration.

GP: Ginger polysaccharide; IG: Inner ginger; SG: stem part of ginger; SGP: Sulfated ginger polysaccharide.

3.4 Secondary Outcomes

3.4.1 Platelet aggregation

As illustrated in Figure 6, ginger significantly reduced platelet

aggregation in both percentage change and mean change terms as reported by Young et al. (2006) [29] and Alaskar et al. (2019) [33], respectively. Young et al. (2006) [29] demonstrated a significantly mean percentage change of 55.53, (95% CI 33.13; 77.94, $I^2 = 100\%$, $n = 60$).

The marked heterogeneity reflects marked differences between ginger alone and ginger plus nifedipine (G+N) on platelet aggregation, with G+N groups clustering near 70–80% and ginger-only groups clustering near 35–38%.

In Alaskar et al. (2020) [33] all the five studies evaluating 4g ginger with different agonists showed a significant overall increase in mean platelet aggregation inhibition with a pooled mean change of 5.26, (95% CI 4.61; 5.92, $I^2 = 88.7\%$, $n = 95$), random-effects model with the highest inhibition observed with the epinephrine agonist. The observed considerable heterogeneity suggests variability among different agonists (adenosine diphosphate (ADP), arachidonic acid (AA), epinephrine, collagen, and ristocetin) in their responsiveness to ginger. Despite this, the pooled estimate remains consistently positive, indicating efficacy of the 4g dose across conditions.

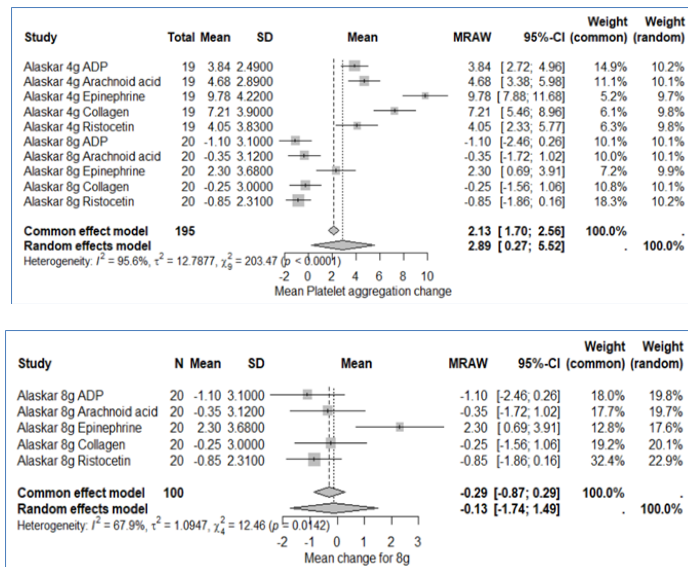


Figure 6: Forest plot of impact of ginger on platelet aggregation displayed as mean change for both the 4g and 8 g studies (Upper panel), and then sub-grouped into 4g and 8g. The lower panel displays the impact of ginger on the percentage change in platelet aggregation).

GP: Ginger polysaccharide; IG: Inner ginger; SG: st

3.4.2 Thromboxane B₂ (TXB₂)

Though excluded from quantitative meta-analysis, Janssen et al. (1996) [28] reported a non-significant reduction in TXB₂ synthesis by approximately 0.7%, while Srivastava (1989) [25] demonstrated a significant reduction in TXB₂ levels by approximately 37%.

3.4.3 Clotting Time

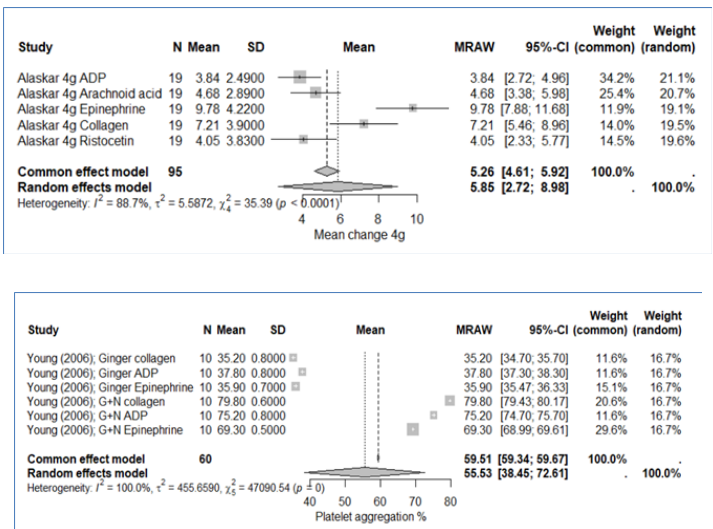
Oduwe et al. (2021) [35] reported a non-significant prolongation of clotting time with ginger aqueous extracts, with a mean value of 7.28 ± 0.27 minutes compared to 6.7 ± 0.37 minutes in the control group; both values remained within the normal clotting time range of 3 to 8 minutes.

3.5 Certainty of Evidence

Based on the GRADE assessment detailed in Table 3, the certainty of evidence for aPTT, PT, and platelet aggregation outcomes is rated as *very low*. This reflects the predominance of non-randomized in vitro or ex vivo designs, the presence of methodological limitations, high heterogeneity in extract types and concentrations, and overall imprecision in effect estimates. Nevertheless, the consistent and statistically significant

In contrast, the 8g ginger group (4g twice daily), showed a non-significant pooled mean change of -0.13 , (95% CI -1.74 ; 1.49 , $I^2 = 67.9\%$, $n = 100$) with none of the individual studies showed statistically significant effects. This suggests that increasing the ginger dose to 8g does not enhance platelet inhibition, potentially indicating a biphasic or saturable dose-response effect.

For studies not included in meta-analysis, Lumb et al. (1994) [27] conducted a randomized trial using 2g of dried ginger and found no significant changes in platelet aggregation in response to ADP, AA, ristocetin, or collagen. In contrast, Verma et al. (1993) [26] reported significant inhibition of platelet aggregation ($p < 0.001$) with 5g of ginger powder over 14 days, particularly in response to ADP and epinephrine.



prolongation of PT observed across several studies suggests a potential pharmacological activity of ginger on the extrinsic coagulation pathway that warrants further controlled clinical investigation.

For INR, evidence derived from a single controlled study demonstrated no clinically significant pharmacodynamic interaction between ginger and INR, although a dose-dependent trend was noted. The certainty of evidence was rated as *moderate*, limited primarily by imprecision but supported by adequate methodological quality, consistency, and directness of the findings.

Discussion

This study was primarily designed to evaluate the safe use of ginger in high-risk patients, beginning with an assessment of its pharmacodynamic activity in healthy individuals. Although the available literature is limited and insufficient to draw firm conclusions, this work serves as a valuable pilot analysis exploring the hemostatic effects of *Zingiber officinale*. The findings of the present meta-analysis indicate that ginger exerts a significant prolongation of PT across different preparation forms, while showing no consistent or significant effect on aPTT, INR,

or platelet aggregation. Moreover, studies by Janssen et al. (1996) [28] and Srivastava (1989) [25], as well as Oduwe et al. (2021) [35], have documented variable degrees of thromboxane B₂ (TXB₂) suppression and prolongation of clotting times, respectively, further supporting the potential modulatory effect of ginger on platelet function and coagulation pathways. Collectively, these findings underscore the need for further well-controlled clinical trials to confirm its safety profile among populations at increased risk of bleeding or thrombosis.

Ginger has been an integral part of traditional medicine for thousands of years. It is widely consumed in various forms, including herbal tea, as a culinary spice, or in dietary supplements, due to its well-recognized gastrointestinal soothing properties and immune-enhancing effects [40]. In a cross-sectional study conducted in Nigeria, 66.14% of respondents reported consuming ginger, with 86.77% using it as a food additive and 41.27% as herbal tea [41]. Similarly, a large-scale Chinese study by Wang et al. (2016) [34] found that 63.3% of participants consumed between 2 and 6 grams of ginger daily. The popularity of ginger supplements has also increased substantially, reflecting a broader trend toward natural remedies. Notably, the global ginger market was valued at USD 4.88 billion in 2024 and is projected to reach USD 5.2 billion in 2025, reflecting the increasing recognition of ginger's therapeutic and health-promoting properties across both traditional and modern medicine sectors. [42].

The antithrombotic properties of ginger have been investigated since the 1980s, when Srivastava et al. (1984) [25] first documented its inhibitory effects on platelet aggregation. Since then, multiple studies have explored ginger's effect on haemostasis, yet results remain inconsistent across assays and formulations.

In a subsequent work by Nurtjahja-Tjendraputra et al. (2003) [43], researchers identified bioactive compounds with the potential to act as natural aspirin analogues. Among these, [6]-gingerol, [8]-gingerol, and [6]-shogaol have been most extensively studied, exhibiting cyclooxygenase-1 (COX1) inhibitory activity and subsequent reduction in TXA₂ synthesis, thereby reducing platelet activation and aggregation [44]. A systematic review by Marx et al. (2015) [16] further highlighted the inconsistency of clinical outcomes, with half of the included trials reporting platelet inhibition and the remainder showing no effect. This heterogeneity is mirrored in observational data and case reports: Rubin et al. (2019) [45] described an INR rise from 2.7 to 10 in a patient taking 48 mg/day of chewable ginger alongside warfarin, while other trials—such as those by Jiang et al. (2005) [46] and Lumb et al. (1994) [27]—found no significant alteration in platelet function or coagulation indices with lower doses (0.4–2 g/day). Bordia et al. (1997) [47] also observed a transient effect at 10 g but not at 4 g/day, supporting a potential biphasic or saturable dose–response pattern, as later suggested by AlAskar et al. (2020) [33].

Notably, ginger's antiplatelet effects may be enhanced when combined with calcium channel blockers, as reported by Young et al. [29] and Srivastava & Mustafa (1989) [15], who demonstrated potentiation via reduced platelet calcium influx. Such interactions highlight the relevance of pharmacodynamic synergy in individuals receiving cardiovascular medications.

The heterogeneity across studies likely reflects differences in extract composition. Ethanol-based ginger extracts, commonly found in herbal tinctures, may demonstrate enhanced anticoagulant activity, partly due to ethanol's inherent blood-thinning properties (Salem et al., 2005) [48]. This raises potential safety concerns for susceptible individuals. In contrast, methanol-based extracts, while potent in *in vitro* studies, are

not applicable to clinical use due to methanol's toxicity. Water-based preparations, such as ginger tea, are safer and more widely consumed, but tend to exhibit weaker anticoagulant effects as water is less efficient at extracting lipophilic compounds like shogaols [49]. Moreover, GPs, the natural carbohydrate fractions isolated from ginger, possess antioxidant, immunomodulatory, and mild anticoagulant activities. Their sulfated derivatives, SGPs, designed to mimic the structure and function of heparin, have also demonstrated significantly stronger anticoagulant effects through direct interference with coagulation factors and enhancement of antithrombin activity, thereby suggesting a potential role as natural heparin analogues [50, 51]. These compositional and structural differences likely contribute to the inconsistency and low certainty of current evidence.

Taken together, these findings suggest that while ginger at typical dietary intake levels is unlikely to produce clinically significant coagulation changes in healthy individuals, higher concentrations, especially in extract or supplement form, may modestly prolong clotting parameters. For individuals on anticoagulants or with bleeding disorders, ginger supplementation should be approached cautiously.

This review has several limitations. First, many of the included studies had small sample sizes and short intervention durations, limiting the generalizability and long-term relevance of the findings. Second, there was substantial heterogeneity in the form and dose of ginger administered across studies, as well as the assays used to evaluate haemostasis, which complicates direct comparisons. Moreover, the evidence base is derived from healthy volunteers, limiting applicability to patients with underlying bleeding or thrombotic disorders.

Despite these limitations, this review offers several strengths. It includes a wide range of haemostatic parameters, used in both clinical and research settings, such as PT, aPTT, INR, platelet aggregation, clotting time, and TXB₂, providing a holistic overview of ginger's potential influence on coagulation and platelet function. Furthermore, by evaluating the impact of different extraction methods and identifying dose-dependent effects, this review provides mechanistic insight into how specific constituents or formulations may influence bioactivity.

Future research should prioritize standardization of ginger extracts by quantifying active constituents (gingerols, shogaols), adopt longer follow-up periods, and include stratified analyses based on baseline coagulation status and concurrent drug use. Incorporating clinically meaningful endpoints such as bleeding or thromboembolic events—rather than laboratory surrogates—will better clarify clinical relevance. Moreover, pharmacokinetic investigations of active compounds may help explain interindividual variability in response.

Conclusion

While typical dietary consumption of ginger is unlikely to cause clinically significant alterations in coagulation for healthy individuals, the findings of this review suggest that caution is warranted. Patients taking vitamin K antagonists (e.g., warfarin), direct oral anticoagulants, or antiplatelet agents may be at increased risk of bleeding when consuming high doses of ginger, especially in concentrated extract or ethanol-based supplement forms. Clinicians should inquire about herbal supplement use during medication counselling and consider advising at-risk patients to avoid high-dose ginger supplements misuse. Preoperative assessment protocols may also benefit from screening for herbal intake, particularly in procedures with a high bleeding risk. Well-designed, high-quality studies are needed to confirm our findings and to establish safe guidelines for ginger use in high-risk patient populations.

Abbreviations List

AA	Arachidonic Acid
ADP	Adenosine Diphosphate
APTT / aPTT	Activated Partial Thromboplastin Time
CVD	Cardiovascular Disease
CI	Confidence Interval
COX-1	Cyclooxygenase-1
GP	Ginger Polysaccharides
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
INR	International Normalized Ratio
IQR	Interquartile Range
PT	Prothrombin Time
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT	Randomized Controlled Trial
RoB-2	Risk of Bias 2 Tool
SD	Standard Deviation
SGP	Sulfated Ginger Polysaccharides
SMD	Standardized Mean Difference
TXA ₂	Thromboxane A ₂
TXB ₂	Thromboxane B ₂

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