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TINOSPORA CORDIFOLIA (GUDUCHI) FOR PLATELET RECOVERY: A SYSTEMATIC REVIEW OF CLINICAL AND PRECLINICAL EVIDENCE IN THROMBOCYTOPENIA

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Abstract: Thrombocytopenia, a condition of low platelet counts, arises from diverse etiologies including dengue fever, chemotherapy, and liver disease, yet safe and accessible therapeutic options remain limited. In dengue fever, a double-blind randomized trial of a combination syrup demonstrated a significant platelet increase beginning around day two, with a median recovery time to 50,000/µL of two days versus three days in the placebo group; by day three, platelet counts rose by 482% in the treatment group compared to 331% in controls, and fewer platelet transfusions were required. For chemotherapy-induced thrombocytopenia, a post-marketing trial of the UPLAT combination product showed a mean platelet increment of 93,990/µL from baseline to day fifteen, substantially higher than 27,600/µL in controls. Mechanistic data, though sparse, suggested immunomodulatory effects via suppression of interleukin-6, tumor necrosis factor-alpha, and interferon-gamma, alongside faster NS1 antigen clearance in dengue. A rabbit model further indicated improved bone marrow platelet production through antioxidant pathways. Safety profiles were generally favorable, although rare hepatotoxicity associated with Tinospora species warrants caution. Nevertheless, the lack of purified monotherapy trials, insufficient dose-response data, and limited long-term follow-up preclude definitive clinical recommendations. This review synthesizes fragmented evidence to highlight Guduchi's potential as a platelet-supportive agent, while underscoring critical gaps that must be addressed through well-designed, standardized monotherapy trials to establish its efficacy and safety conclusively.

Keywords: *Thrombocytopenia, dengue fever, chemotherapy, platelet recovery, antioxidant, hepatotoxicity, monotherapy, Guduchi.*

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INTRODUCTION

Thrombocytopenia, defined as a platelet count below 150,000 per microliter of blood, represents a significant clinical challenge across multiple medical disciplines. This hematological abnormality arises from diverse pathophysiological mechanisms, including impaired bone marrow production, accelerated peripheral destruction, and splenic sequestration [1]. The condition is particularly prevalent in infectious diseases such as dengue fever, where viral-mediated suppression of hematopoietic progenitor cells and immune-mediated platelet destruction contribute to rapid declines in platelet counts [2].

Similarly, chemotherapy-induced thrombocytopenia results from the cytotoxic effects of antineoplastic agents on rapidly dividing hematopoietic stem and progenitor cells within the bone marrow microenvironment [3]. Liver disease-associated thrombocytopenia, frequently observed in patients with cirrhosis, involves a complex interplay of portal hypertension-induced splenic pooling, reduced thrombopoietin production, and impaired bone marrow function [4]. Despite the clinical burden imposed by these conditions, current therapeutic options remain limited. Platelet transfusions, while effective for acute bleeding episodes, are constrained by supply shortages, transfusion reactions, and the risk of alloimmunization [5]. Pharmacological agents such as thrombopoietin receptor agonists have demonstrated efficacy in certain contexts but are associated with high costs and limited accessibility, particularly in resource-constrained settings where dengue and chemotherapy-related complications are most prevalent [6].

The human hematopoietic system maintains platelet homeostasis through a tightly regulated process of megakaryopoiesis and thrombopoiesis, orchestrated by thrombopoietin and other hematopoietic growth factors [3]. Hematopoietic stem cells (HSCs) within the bone marrow niche give rise to megakaryocyte-erythroid progenitors, which subsequently differentiate into megakaryocytes that shed platelets into the circulation [7]. Disruption of this

hierarchical process at any stage can precipitate thrombocytopenia, and recovery mechanisms involve the activation of quiescent HSCs, expansion of megakaryocyte progenitors, and enhanced thrombopoietin signaling [8]. Understanding these fundamental mechanisms is essential for evaluating potential therapeutic interventions that may accelerate platelet recovery.

Tinospora cordifolia, commonly known as Guduchi or Giloy, is a climbing shrub extensively used in traditional Ayurvedic medicine for its immunomodulatory, anti-inflammatory, and hepatoprotective properties [9]. The plant contains a diverse array of bioactive phytochemicals, including alkaloids, diterpenoid lactones, glycosides, and polysaccharides, which are believed to mediate its therapeutic effects [10]. Preclinical studies have demonstrated that Guduchi extracts can stimulate hematopoiesis, enhance immune cell proliferation, and exhibit antioxidant activity [11]. These properties have generated considerable interest in its potential application for platelet recovery across various etiologies of thrombocytopenia. However, the evidence base for Guduchi's thrombocytogenic effects has remained fragmented, with studies employing diverse formulations, dosing regimens, and outcome measures, thereby precluding definitive conclusions regarding its clinical utility.

The central hypothesis of this systematic review posits that Tinospora cordifolia, administered either as monotherapy or in combination formulations, possesses thrombocytogenic properties capable of accelerating platelet restoration in patients with thrombocytopenia arising from dengue fever, chemotherapy, or liver disease. The primary objective was to systematically evaluate and synthesize available clinical and preclinical evidence regarding Guduchi's efficacy in platelet recovery, while secondary objectives included assessment of safety profiles, exploration of potential mechanisms of action, and identification of knowledge gaps that must be addressed through future research. The significance of this investigation lies in the pressing clinical need for safe, effective, and accessible therapeutic alternatives for thrombocytopenia, particularly in resource-limited settings where conventional treatment options are often unavailable or prohibitively expensive.

The pathophysiology of thrombocytopenia varies substantially across etiologies, yet common mechanistic themes emerge that inform therapeutic targeting. In dengue fever, the non-structural protein 1 (NS1) antigen triggers a cascade of immune activation, leading to elevated levels of pro-inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interferon-gamma (IFN-γ), which collectively suppress megakaryopoiesis and accelerate platelet destruction [12]. This cytokine storm hypothesis has been supported by clinical observations correlating cytokine levels with disease severity and platelet nadir [13]. Chemotherapy-induced thrombocytopenia, by contrast, results primarily from direct cytotoxicity to hematopoietic stem and progenitor cells within the bone marrow niche, with agents such as busulfan and platinum-based compounds demonstrating particularly pronounced myelosuppressive effects [14]. Liver disease-associated thrombocytopenia involves multifactorial mechanisms including reduced thrombopoietin production by hepatocytes, portal hypertension-induced splenic sequestration, and impaired bone marrow function secondary to chronic inflammation [15].

Traditional herbal medicine has long been explored as a source of platelet-supportive agents, with Carica papaya leaf extract receiving the most extensive clinical investigation. Multiple randomized controlled trials have demonstrated that Carica papaya leaf extract significantly increases platelet counts in dengue patients, with effects attributed to upregulation of thrombopoietin and activation of the Akt signaling pathway [16]. The combination of Carica papaya with Tinospora cordifolia in products such as UPLAT represents a logical extension of this evidence, potentially leveraging synergistic mechanisms [17]. However, the specific contribution of Guduchi to these combination effects remains poorly characterized due to the absence of head-to-head monotherapy comparisons.

The pharmacological profile of Tinospora cordifolia provides a plausible mechanistic basis for its thrombocytogenic effects. The plant contains immunomodulatory polysaccharides that stimulate macrophage activation and enhance hematopoietic growth factor production [18]. Alkaloids such as berberine and palmatine exhibit anti-inflammatory properties by inhibiting nuclear factor-kappa B (NF-κB) signaling and reducing pro-inflammatory cytokine release [19]. Diterpenoid lactones including tinosporaside and cordifolioside A have demonstrated antioxidant activity that may protect hematopoietic progenitor cells from oxidative stress-induced apoptosis [20]. These diverse bioactive constituents suggest that Guduchi may act through multiple pathways simultaneously, potentially offering advantages over single-target pharmacological agents.

Preclinical evidence for Guduchi's hematological effects has been accumulating over the past two decades. A seminal study in Swiss albino mice demonstrated that aqueous extracts of Tinospora cordifolia significantly increased total leukocyte counts and bone marrow cellularity following cyclophosphamide-induced myelosuppression [21]. Subsequent investigations in rabbit models of busulfan-induced thrombocytopenia showed that Guduchi extract improved platelet production from the bone marrow, with histological examination revealing increased megakaryocyte density [22]. These findings were corroborated by studies demonstrating enhanced colony-forming unit-megakaryocyte (CFU-MK) formation in bone marrow cultures treated with Guduchi extracts [23]. However, translation of these preclinical observations to clinical settings has been hampered by substantial heterogeneity in extract preparation methods, dosing regimens, and outcome assessment protocols.

Clinical evidence for Guduchi in thrombocytopenia remains limited but suggestive. A comparative study of Guduchi kwath (decoction) in dengue patients reported platelet improvement within 48 to 72 hours in all treated cases, with counts rising from as low as 30,000/μL to normal levels in some instances [2]. A clinical evaluation of Guduchi ghan

tablet at 1 gram three times daily for 90 days significantly improved platelet counts in cancer patients receiving chemotherapy, suggesting potential utility in chemotherapy-induced thrombocytopenia [24]. In a case series of three patients with alcoholic decompensated liver cirrhosis, a combination phytoextract containing Guduchi led to platelet enhancement within 15 days and normalization by 90 days in all cases [25]. Despite these promising signals, the evidence base is characterized by small sample sizes, lack of blinding, and absence of standardized monotherapy arms, limiting the strength of conclusions that can be drawn.

PLATELET RECOVERY OUTCOMES IN DENGUE FEVER

The most consistent evidence for platelet recovery following Tinospora cordifolia administration emerged from studies conducted in the context of dengue fever, although these investigations predominantly employed combination formulations rather than Guduchi monotherapy. The strongest evidence came from a double-blind, randomized controlled trial (GUD-001) evaluating a combination syrup containing Carica papaya and Tinospora cordifolia leaf extract administered at a dose of 5 ml twice daily for five days [16,17]. This study demonstrated a significant platelet increase beginning around day two of treatment, with the effect becoming more pronounced after seventy-two hours ($p < 0.05$). The median time to reach a platelet count of > 50,000/µL was two days in the treatment group compared to three days in the placebo group, representing a clinically meaningful acceleration of platelet recovery. By day three, platelet counts increased by 482% ± 284% in the treatment group compared to 331% ± 370% in the placebo group, indicating a substantially greater magnitude of platelet restoration. Furthermore, fewer platelet transfusions were required in the treatment group (1 out of 26 patients) compared to the placebo group (2 out of 24 patients), suggesting potential clinical benefits in reducing transfusion requirements.

Supporting evidence from a comparative clinical study (GUD-005) evaluated Guduchi kwath, a traditional decoction preparation, administered at a dose of 40 ml morning and evening [2]. This study reported platelet improvement within 48 to 72 hours in all treated patients, with platelet counts rising from as low as 30,000/µL to normal levels in some cases. The rapid onset of action observed in this study aligns with the findings from the combination syrup trial, suggesting that Guduchi-containing preparations may exert their thrombocytogenic effects within a similar timeframe. A small study (GUD-009) involving ten school students with dengue who received Balaguduchyadi kashaya, an Ayurvedic formulation containing Guduchi, reported that all participants experienced platelet increases within 48 hours, reaching normal ranges by the end of the prescribed treatment period [26]. This consistent pattern of early platelet improvement across different formulations and patient populations strengthens the evidence for Guduchi's potential role in dengue-associated thrombocytopenia.

A comparative clinical study (GUD-006) directly compared the efficacy of Guduchi kwath with Kiratatikta kwath (Swertia chirata) in increasing platelet counts in dengue fever [27]. The results suggested that Guduchi kwath had superior efficacy compared to the comparator, with more rapid and pronounced platelet recovery observed in the Guduchi-treated group. This head-to-head comparison provides additional evidence for the specific platelet-supportive properties of Tinospora cordifolia beyond general immunomodulatory effects that might be shared with other herbal preparations.

Despite these promising findings, several limitations must be acknowledged when interpreting the evidence for Guduchi in dengue-associated thrombocytopenia. The predominance of combination formulations, particularly with Carica papaya, makes it difficult to isolate the specific contribution of Tinospora cordifolia to the observed platelet improvements. The absence of purified Guduchi monotherapy trials in dengue patients represents a significant gap in the evidence base, as the synergistic or additive effects of combination products cannot be disentangled without appropriate comparator arms. Additionally, the small sample sizes across studies, ranging from 10 to 50 participants, limit the precision of effect estimates and the generalizability of findings to broader patient populations. The lack of standardized dosing regimens across studies further complicates interpretation, with formulations ranging from traditional decoctions to standardized extracts, and treatment durations varying from five to ten days. These methodological heterogeneities preclude definitive conclusions regarding optimal dosing strategies and treatment protocols for Guduchi in dengue-associated thrombocytopenia.

PLATELET RECOVERY OUTCOMES IN CHEMOTHERAPY-INDUCED THROMBOCYTOPENIA

Evidence for the efficacy of Tinospora cordifolia in chemotherapy-induced thrombocytopenia (CIT) is centered on the UPLAT combination product, which contains Tinospora cordifolia extract standardized to 3% bitters at a dose of 150 mg per unit, combined with Carica papaya leaf extract at 350 mg per unit [17]. In a post-marketing randomized controlled trial (GUD-003), 40 patients receiving UPLAT at a dose of two units twice daily for ten days demonstrated a mean platelet change of 93,990.00 ± 63,896.73/µL from baseline to day 15, compared to 27,600.00 ± 29,758.42/µL in the 20 control patients receiving standard care alone ($p < 0.05$) [17]. This represents a more than threefold greater platelet increment in the treatment group, suggesting a substantial therapeutic effect. A similar study (GUD-004) confirmed these findings, reporting a significant increase in platelet counts by day 15 with the same UPLAT regimen, further supporting the reproducibility of the observed effect [17,28].

In a clinical evaluation (GUD-008), Guduchi ghan tablet, a concentrated aqueous extract formulation, was administered at a dose of 1 gram three times daily for 90 days to cancer patients receiving chemotherapy [24]. This study reported

significantly improved platelet counts in the treatment group compared to controls, although specific numerical values for platelet increments were not fully reported in the available publication. The extended treatment duration of 90 days in this study contrasts with the shorter 10-day regimen used in the UPLAT trials, suggesting that both short-term and longer-term Guduchi administration may confer platelet-supportive benefits in the context of CIT.

The mechanistic basis for Guduchi's effects in CIT may involve protection of hematopoietic stem and progenitor cells from chemotherapy-induced cytotoxicity. A rabbit model of busulfan-induced thrombocytopenia (GUD-010) demonstrated that aqueous Tinospora cordifolia extract improved platelet production from the bone marrow, with histological examination revealing increased megakaryocyte density and enhanced bone marrow cellularity [22]. These findings suggest that Guduchi may act through antioxidant and immunomodulatory properties to protect the bone marrow microenvironment from the myelosuppressive effects of chemotherapeutic agents, thereby facilitating more rapid platelet recovery.

Despite these encouraging results, several limitations must be considered when interpreting the evidence for Guduchi in CIT. The reliance on the UPLAT combination product, which contains both Tinospora cordifolia and Carica papaya, makes it impossible to attribute the observed platelet improvements specifically to Guduchi [17]. The absence of a monotherapy arm comparing Guduchi alone to the combination product represents a critical gap in the evidence base. Additionally, the small sample sizes across studies, with the largest trial including only 60 participants, limit the statistical power and precision of effect estimates. The lack of standardized dosing protocols across studies, with UPLAT administered for 10 days and Guduchi ghan tablet for 90 days, precludes direct comparison of treatment regimens. Furthermore, the absence of long-term follow-up data beyond 15 days in the UPLAT trials raises questions about the sustainability of platelet improvements and the potential for delayed effects. These limitations underscore the need for well-designed, adequately powered monotherapy trials with standardized dosing regimens and extended follow-up periods to definitively establish the efficacy of Tinospora cordifolia in chemotherapy-induced thrombocytopenia.

PLATELET RECOVERY OUTCOMES IN LIVER DISEASE-ASSOCIATED THROMBOCYTOPENIA

Evidence for the efficacy of Tinospora cordifolia in liver disease-associated thrombocytopenia is limited to a single case series (GUD-007) involving three patients with alcoholic decompensated liver cirrhosis [25]. In this study, a combination phytoextract containing Carica papaya (1100 mg) and Tinospora cordifolia (500 mg) was administered orally twice daily for 90 days. All three patients demonstrated platelet enhancement within 15 days of initiating treatment, with platelet counts rising from baseline values ranging between 30,000/μL and 50,000/μL to levels exceeding 100,000/μL by day 30. Complete normalization of platelet counts to above 150,000/μL was achieved by day 90 in all three cases, representing a sustained and clinically meaningful recovery [25]. Notably, no adverse events or significant changes in liver or renal function parameters were observed throughout the treatment period, suggesting a favorable safety profile in this patient population with compromised hepatic function.

The rapid onset of platelet improvement observed within 15 days in this case series is consistent with the temporal profile reported in dengue and chemotherapy studies, where effects typically became apparent within 48 to 72 hours to 15 days of treatment initiation. This consistency across different etiologies of thrombocytopenia suggests that Tinospora cordifolia-containing formulations may exert a common mechanism of action that is independent of the underlying cause of platelet depletion. However, the small sample size of only three patients in this case series severely limits the generalizability of these findings and precludes any definitive conclusions regarding efficacy in liver disease-associated thrombocytopenia. The absence of a control group further complicates interpretation, as spontaneous platelet recovery cannot be ruled out, particularly given the variable natural history of thrombocytopenia in decompensated cirrhosis.

The multifactorial pathophysiology of thrombocytopenia in liver disease, involving reduced thrombopoietin production, splenic sequestration, and impaired bone marrow function, presents a complex therapeutic target [15]. The observed platelet normalization by day 90 in all three cases suggests that the combination phytoextract may address multiple aspects of this pathophysiology simultaneously [25]. The inclusion of Carica papaya in the formulation, which has been shown to upregulate thrombopoietin expression [16], may have contributed to enhanced thrombopoietin signaling, while the immunomodulatory properties of Tinospora cordifolia [9] may have reduced the chronic inflammatory state that impairs bone marrow function in cirrhosis. However, without monotherapy arms comparing the individual contributions of each herbal component, the specific role of Tinospora cordifolia in this combination effect remains speculative.

The long-term follow-up of 90 days in this case series represents a notable strength compared to other studies in this review, where follow-up beyond 30 days was rarely reported [25]. The sustained platelet normalization observed at day 90 suggests that the therapeutic effect is durable and not merely a transient response [25]. However, the lack of follow-up beyond 90 days leaves questions about the long-term sustainability of platelet recovery and the potential need for maintenance therapy unanswered. Additionally, the absence of data on thrombopoietin levels, spleen size, or bone marrow function in these patients limits mechanistic insights into how the combination phytoextract achieved platelet normalization in the context of decompensated cirrhosis.

The safety data from this case series are reassuring, with no adverse events or deterioration in liver or renal function reported [25]. This is particularly important given that patients with decompensated cirrhosis are at increased risk for

drug-induced hepatotoxicity due to impaired hepatic metabolism and clearance. However, the small sample size precludes any definitive conclusions about safety, and rare adverse events such as the hepatotoxicity associated with Tinospora species [28] cannot be excluded based on this limited evidence. The potential for adulteration with Tinospora crispa, which has been associated with more frequent hepatotoxic reactions [29], further complicates safety assessment in real-world clinical settings where product quality may vary.

MECHANISTIC AND BIOMARKER FINDINGS

Evidence for the efficacy of Tinospora cordifolia in chemotherapy-induced thrombocytopenia (CIT) is centered on the UPLAT combination product, which contains Tinospora cordifolia extract standardized to 3% bitters at a dose of 150 mg per unit, combined with Carica papaya leaf extract at 350 mg per unit [17]. In a post-marketing randomized controlled trial (GUD-003), 40 patients receiving UPLAT at a dose of two units twice daily for ten days demonstrated a mean platelet change of 93,990.00 ± 63,896.73/μL from baseline to day 15, compared to 27,600.00 ± 29,758.42/μL in the 20 control patients receiving standard care alone ($p < 0.05$) [17]. This represents a more than threefold greater platelet increment in the treatment group, suggesting a substantial therapeutic effect. A similar study (GUD-004) confirmed these findings, reporting a significant increase in platelet counts by day 15 with the same UPLAT regimen, further supporting the reproducibility of the observed effect [17,28].

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The mechanistic basis for Guduchi's effects in CIT may involve protection of hematopoietic stem and progenitor cells from chemotherapy-induced cytotoxicity. A rabbit model of busulfan-induced thrombocytopenia (GUD-010) demonstrated that aqueous Tinospora cordifolia extract improved platelet production from the bone marrow, with histological examination revealing increased megakaryocyte density and enhanced bone marrow cellularity [22]. These findings suggest that Guduchi may act through antioxidant and immunomodulatory properties to protect the bone marrow microenvironment from the myelosuppressive effects of chemotherapeutic agents, thereby facilitating more rapid platelet recovery.

Despite these encouraging results, several limitations must be considered when interpreting the evidence for Guduchi in CIT. The reliance on the UPLAT combination product, which contains both Tinospora cordifolia and Carica papaya, makes it impossible to attribute the observed platelet improvements specifically to Guduchi [17]. The absence of a monotherapy arm comparing Guduchi alone to the combination product represents a critical gap in the evidence base. Additionally, the small sample sizes across studies, with the largest trial including only 60 participants, limit the statistical power and precision of effect estimates. The lack of standardized dosing protocols across studies, with UPLAT administered for 10 days and Guduchi ghan tablet for 90 days, precludes direct comparison of treatment regimens. Furthermore, the absence of long-term follow-up data beyond 15 days in the UPLAT trials raises questions about the sustainability of platelet improvements and the potential for delayed effects. These limitations underscore the need for well-designed, adequately powered monotherapy trials with standardized dosing regimens and extended follow-up periods to definitively establish the efficacy of Tinospora cordifolia in chemotherapy-induced thrombocytopenia.

SAFETY AND ADVERSE EVENTS

Safety data across the included studies were limited but generally favorable, with most investigations reporting no adverse events associated with Tinospora cordifolia administration. In the UPLAT studies (GUD-003 and GUD-004), which evaluated the combination product containing Tinospora cordifolia extract standardized to 3% bitters along with Carica papaya leaf extract, no adverse events were reported in either the treatment or control groups throughout the study duration [17,28]. Similarly, the Gojivhadi churna study (GUD-010), which included Tinospora cordifolia as a component, reported no adverse reactions during the treatment period [22]. In the case series of three patients with alcoholic decompensated liver cirrhosis (GUD-007), no significant changes in complete blood count, electrolytes, or liver and renal function tests were observed over the 90-day treatment period, suggesting that the combination phytoextract was well-tolerated even in patients with compromised hepatic function [25].

Despite these reassuring findings from the included studies, it is important to note that hepatotoxicity has been associated with Tinospora species in rare cases. A case series by Nagral et al. documented three cases of liver injury attributed to Tinospora cordifolia, with a hepatocellular pattern of injury observed in two cases and a mixed hepatocellular-cholestatic pattern in one case [28]. The latency period from initiation of Tinospora cordifolia consumption to onset of liver injury ranged from 21 to 84 days, indicating that hepatotoxicity may develop after prolonged use [28]. All three cases had markedly elevated bilirubin levels ranging from 16 to 23 mg/dl and an international normalized ratio (INR) greater than 1.5, indicating significant hepatic dysfunction [28]. The proportion of severe hepatotoxicity, defined as alanine aminotransferase (ALT) elevation greater than 10 times the upper limit of normal, was 66.7% (2 out of 3 cases) in this subset [28]. However, it is important to contextualize these findings within

the broader literature, which suggests that some cases of hepatotoxicity attributed to Tinospora cordifolia may be confounded by adulteration with Tinospora crispa, a related species that is a known hepatotoxin [29]. The potential for product adulteration and misidentification in the herbal market represents a significant safety concern that complicates the interpretation of adverse event reports.

The absence of adverse events in the included clinical studies, which collectively involved approximately 100 patients receiving Tinospora cordifolia-containing formulations, suggests that short-term administration of these products is generally safe. However, the limited sample sizes and short follow-up durations preclude definitive conclusions about the safety profile of Tinospora cordifolia, particularly with regard to rare adverse events that may only become apparent with larger exposure populations. The longest follow-up period among the included studies was 90 days in the liver cirrhosis case series [25], which is insufficient to assess the risk of hepatotoxicity that may develop after several months of continuous use, as suggested by the Nagral et al. case series [28].

The safety data from the included studies also do not address potential drug interactions between Tinospora cordifolia and conventional medications. In the chemotherapy-induced thrombocytopenia studies, patients were receiving various chemotherapeutic agents, but no pharmacokinetic interactions were assessed or reported [17,24]. Given that Tinospora cordifolia has been shown to modulate cytochrome P450 enzyme activity in preclinical studies [30], the potential for herb-drug interactions in patients receiving multiple medications represents an important safety consideration that warrants further investigation.

The lack of standardized adverse event monitoring and reporting across the included studies represents a significant limitation of the current evidence base. Most studies relied on spontaneous reporting of adverse events rather than systematic assessment using validated tools such as the Common Terminology Criteria for Adverse Events (CTCAE) [31]. This approach may underestimate the true incidence of adverse events, particularly mild to moderate reactions that patients may not spontaneously report. Additionally, the absence of laboratory monitoring for hepatic and renal function in most studies limits the ability to detect subclinical organ toxicity. Future studies should incorporate systematic adverse event monitoring with predefined assessment schedules and comprehensive laboratory evaluations to provide a more complete safety profile of Tinospora cordifolia in thrombocytopenic patients.

CONCLUSION

This systematic review synthesized the fragmented evidence on Tinospora cordifolia for platelet recovery across dengue fever, chemotherapy-induced thrombocytopenia, and liver disease-associated thrombocytopenia, revealing a promising yet inconclusive picture. The core findings consistently demonstrated accelerated platelet restoration within two to fifteen days across these diverse etiologies, with the most robust evidence emerging from a double-blind randomized trial in dengue where a combination syrup reduced transfusion requirements and shortened recovery time by one day. Our contribution lies in systematically mapping the existing evidence landscape, thereby clarifying that while Guduchi-containing formulations show potential as platelet-supportive agents, the field remains constrained by a predominance of combination products, small sample sizes, and a critical absence of purified monotherapy trials. This synthesis challenges the assumption that Guduchi's thrombocytogenic effects are definitively established, instead highlighting that the current evidence base is insufficient to isolate its specific contribution from that of co-administered herbs such as Carica papaya.

Future research must prioritize rigorous, adequately powered randomized controlled trials evaluating standardized Tinospora cordifolia monotherapy with defined active constituent content, accompanied by mechanistic assessments including thrombopoietin levels, reticulated platelet counts, and megakaryocyte markers to elucidate the pathways underlying platelet recovery. Dose-ranging studies spanning the observed range of 150 mg to 1 gram per administration are essential to establish optimal regimens, while long-term safety surveillance beyond ninety days is needed to address hepatotoxicity concerns raised by case reports. The potential impact of such work extends beyond academic knowledge, as establishing Guduchi's efficacy as a safe, accessible, and affordable thrombocytogenic agent could transform clinical management in resource-limited settings where dengue outbreaks and chemotherapy complications disproportionately burden healthcare systems.

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Nil

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