Received: 13 December 2024 | Revised: 14 March 2025 | Accepted: 29 March 2025

DOI: 10.1111/trf.18255

REVIEW ARTICLE

TRANSFUSION

Coagulation factors in spray-dried plasma: A systematic review and meta-analysis

Biswadev Mitra[1,2,3] | **Patrick J. C. Biggins**[3] | **Denese C. Marks**[4,5] | **Michael C. Reade**[6,7]

[1]School of Public Health & Preventive Medicine, Monash University, Melbourne, Victoria, Australia

[2]Emergency & Trauma Centre, The Alfred Hospital, Melbourne, Victoria, Australia

[3]1 Expeditionary Health Squadron, Royal Australian Air Force, Amberley, Queensland, Australia

[4]Research and Development, Australian Red Cross Lifeblood, Alexandria, New South Wales, Australia

[5]Faculty of Medicine and Health, The University of Sydney, Camperdown, New South Wales, Australia

[6]Australian Defence Force Joint Health Command, Canberra, Australian Capital Territory, Australia

[7]Medical School, University of Queensland, Brisbane, Queensland, Australia

Correspondence
Biswadev Mitra, Emergency Research Unit, School of Public Health & Preventive Medicine, Monash University, Level 3, 553 St. Kilda Road, Melbourne, VIC 3004, Australia.
Email: biswadev.mitra@monash.edu

KEYWORDS: emergency medicine, hemorrhage, plasma, spray-dried plasma, wounds and injuries

1 | INTRODUCTION

Hemorrhage is directly responsible for most preventable prehospital trauma deaths and about a third of in-hospital trauma deaths.[1,2] Hemorrhage also contributes to late mortality and morbidity due to multiorgan failure. Hemorrhage control is achieved prehospital through direct pressure and occasionally by tourniquet and in hospital through surgery or interventional radiology. In parallel, shed blood is replaced in hospital using major hemorrhage protocols (MHP), also referred to as massive transfusion protocols. A ratio-based MHP recommends the administration of high volumes of plasma (at least 1 unit for every 2 units of red blood cells), with the aim to prevent and treat trauma-induced coagulopathy.[3] However, in current prehospital practice and some rural and regional centers around the world, plasma is commonly unavailable due to logistical difficulties in supply.

Fresh frozen plasma (FFP) is prepared through separation from donated whole blood or obtained by plasma apheresis, with the freezing process commencing within 18 hours of collection for whole blood plasma and within 8 h of collection for apheresis plasma. It is then stored at −18°C or colder with a shelf life of up to 3 years. The thawing process requires a 30–37°C agitated water bath or a warming device, taking 15–30 min, and is challenging outside the hospital setting. Thawed FFP should be used immediately but can be stored between 1 and 6°C for up to 5 days as "extended life plasma (ELP)" with similar (not identical) clotting factors—but may result in wastage if not subsequently used.[4]

Abbreviations: °C, degrees celsius; 95%CI, 95% confidence intervals; aPTT, activated partial thromboplastin time; ELP, extended life plasma; FDP, freeze-dried plasma; FFP, fresh frozen plasma; FLYP, French Lyophilized Plasma; HCl, hydrochloric acid; MD, mean difference; MeSH, medical subject headings; MHP, major hemorrhage protocol; NOS, Newcastle-Ottawa Scale; ODP, on-demand plasma; PT, prothrombin time; SDP, Spray-dried plasma; vWF, von Willebrand factor.

Freeze-dried plasma (FDP) is made from human plasma after lyophilization to produce a freeze-dried product, allowing it to be reconstituted and administered. FDP is made from plasma from either single (e.g., LyoPlas-Nw; German Red Cross) or multiple donors (e.g., French lyophilized plasma (FLYP)). Freeze drying, or lyophilization, is a dehydration process used to preserve the structural integrity and the qualities of plasma. FDP has been used in clinical trials and is feasible for transport, storage, and delivery.[5–8] However, widespread use outside the countries of manufacture is constrained by the complexities of the manufacturing processes and supply limitations.

Spray-dried plasma (SDP) is manufactured by feeding liquid plasma into a stream of pressurized drying gas and was developed by Entegrion, with ability to dry a unit of plasma in about 10 min.[9] This can be achieved in substantially shorter times than freeze-drying and uses equipment with a smaller laboratory footprint than lyophilization. This may enable decentralized manufacturing of dried plasma in-house in regional blood services. Another name for SDP is on-demand plasma (ODP™).

The aim of this study was to collate the reported concentrations of coagulation factors in SDP, compared with other plasma preparations. This will serve as a benchmark for future assessment of newer SDP products and inform any changes that may be required in clinical practice when using SDP compared with other plasma products. The secondary aim was to compare the tests of coagulation function between SDP and other plasma products.

2 | MATERIALS AND METHODS

This systematic review was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines. The protocol was published in Prospero prior to initiating the search.[10]

2.1 | Studies

This review sought to include reports on SDP obtained from human plasma, compared with FFP or another plasma product. The review also sought to include data in which human-derived SDP was assessed in laboratory (in vitro) or humans. To be included, the studies had to report the measures of at least one coagulation factor or test of coagulation function.

2.2 | Exposure and controls

The exposure variable was the assessment of SDP for the composition of coagulation factors or coagulation function. The control arm could contain the assessment of FFP, FDP, or another plasma product.

2.3 | Outcome measures

We extracted data on coagulation factor concentrations and other coagulation proteins as outcome measures. In addition, the tests of coagulation function were extracted as assessed by standard laboratory tests or viscoelastic hemostatic assays.

2.4 | Search methods

We searched Medline (from January 1, 2000 to October 31, 2024), Embase (January 1, 2000 to October 31, 2024), Cochrane Controlled Trials Register (from January 1, 2000 to October 31, 2024), and Google Scholar (first 200 hits). The search was not restricted by language or publication status. Search terms were defined a priori and by reviewing the Medical Subject Headings terms of articles identified in preliminary literature searches. A sensitive search strategy combining Medical Subject Headings (MeSH) headings and the keywords "plasma," "spray-dried plasma," and "frozen plasma" was used. The final search was performed in November 2024.

2.5 | Data abstraction

Title searching was performed by a single investigator (BM). Next, two review authors (BM and PB), not blinded to the journal, institutions, or authors, independently examined abstracts and full texts to identify manuscripts for data extraction. References within each included full text were searched for additional citations. Disagreements were resolved by consensus or with another investigator (DM or MR). Only published data were included. Investigators were not contacted to obtain additional data.

2.6 | Risk of bias assessment

Risk of bias was assessed using the modified Newcastle-Ottawa Scale (NOS). The NOS assesses the following domains: selection of exposed and nonexposed cohorts, comparability of cohorts, assessment of outcomes, and adequacy of follow-up and was limited to seven domains that were relevant for the research question. Using the modified NOS, a score of ≤ 2 was considered high risk of bias; 3–5, moderate risk of bias; and >5, low risk of bias.

2.7 | Analyses

For each study, we reported the source of the plasma, manufacturer of SDP, methods of reconstitution, and the outcome measures. Clinical and methodological heterogeneity across the studies was assessed by examining the details of the subjects, the baseline data, the interventions, and the outcomes to determine whether the studies were sufficiently similar. Statistical heterogeneity was determined using the I^2 statistic. Studies were combined in meta-analyses using a random effects model, as it was assumed that the true effect size (θ) could vary across studies. Differences in concentrations of coagulation factors, proteins, and tests for coagulation factors were reported using mean differences (MD) and 95% confidence intervals (95% CI). The percentage difference was calculated using the pooled mean difference as the numerator and the pooled mean of observed values for FFP as the denominator. A p-value of <0.05 was defined to be statistically significant. All analyses were undertaken using Stata v 18.0 (College Station, TX, USA).

3 | RESULTS

There were 95 manuscripts identified after initial searches, with 84 manuscripts excluded after title and abstract screening (Figure 1). There were 11 manuscripts assessed with full-text review. Of these, Bercovitz et al. reported on microfluidic analysis of thrombus formation; Potter et al. reported on pulmonary vascular permeability and inflammation; Wataha et al. reported on permeability and inflammation in vitro in vascular endothelial cells, all without assays of coagulation factors or coagulation function, and were excluded.[11–13] A further three manuscripts without original data were excluded.[14–16] Finally, a screened manuscript by Shuja et al. did not report on characteristics of SDP and was also excluded.[17] A further manuscript by Pusateri et al. reported comparative data between SDP and FFP from an undetermined source but was included for analysis as the relevant data were available.[18]

There were seven preparations of SDP tested in the four manuscripts (Table 1). All preparations were performed using instruments manufactured by Velico Medical, Inc. (Beverly, MA, USA). In the analysis by Booth et al., SDP was reconstituted with either 1.5% glycine (a) or de-ionized water (b).[19] In the analysis by Meledeo et al., two groups of SDP aliquots were pretreated with excipients prior to drying and rehydrated with water: the first group pretreated with 20 mM glycine-HCl, whereas the second was pretreated with 20 mM glycine-HCl/50 mM glycine. A third group of aliquots was not pretreated but was reconstituted with water containing 20 mM glycine-HCl/50 mM glycine.[20] All studies used human FFP from sources different from the SDP and were performed in vitro, and none used FDP in the comparator group.

The concentration of coagulation factors in SDP, compared with FFP, is displayed in Figure 2. Compared with the equivalent preparation of FFP, there were significantly lower concentrations of fibrinogen by 16.9% (pooled MD −47.74; mg/dL; 95%CI: −62.65 to −32.83), Factor VII by 7.5% (pooled MD −6.99 mg/dL; 95%CI: −11.99 to −1.99), Factor VIII by 29.7% (pooled MD −34.83 mg/dL; 95%CI: −60.04 to −9.63), Factor IX by 9.7% (pooled MD −11.16 mg/dL; 95%CI: −16.46 to −5.86), and Factor X by 12% (MD −12.10 mg/dL; 95%CI: −17.90 to −6.30) in SDP.

A comparison of other relevant components of the clotting cascade is displayed in Figure 3. Compared with equivalent preparation of FFP, there were significantly lower concentrations of Protein C by 6.5% (pooled MD −6.4 IU/dL; 95% CI: −11.77 to −1.04) and Protein S by 12.6% (pooled MD −13.69 IU/dL; 95% CI: −22.23 to −5.15) in SDP. Von Willebrand activity (pooled MD

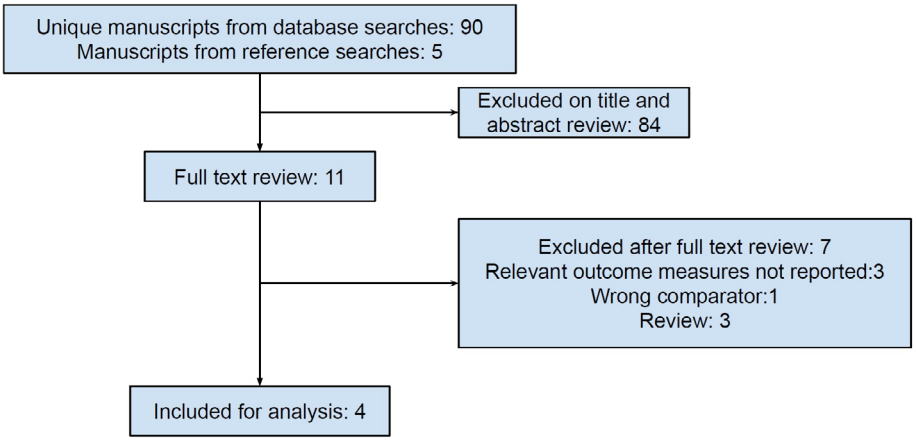

FIGURE 1 Selection of manuscripts. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 1 Study characteristics.

Author (year)	Source of SDP	Substrate for SDP	Manufacturer of SDP	Reconstitution of SDP	Source of FFP	Study setting
Booth (2011)a	Human donors; O+	Whole blood plasma separated within 1 h of collection	Velico Medical, Inc	30 mL of 1.5% glycine	Human donors; O+	Laboratory; in vitro
Booth (2011)b	Human donors; O+	Whole blood plasma separated within 1 h of collection	Velico Medical, Inc	30 mL of deionized water	Human donors; O+	Laboratory; in vitro
Pusateri (2016)	Human donors	Obtained from Velico	Velico Medical, Inc	Not reported	Human donors	Laboratory; in vitro
Lui (2019)	Not reported	Never frozen plasma	Velico Medical, Inc	Water	Not reported	Laboratory; in vitro
Meledeo (2019)a	Human donors; Group A and O	Obtained from Velico	Velico Medical, Inc	Water (DSP pretreated with 20 mM of glycine-HCl)	Human donors; Group A and O	Laboratory; in vitro
Meledeo (2019)b	Human donors; Group A and O	Obtained from Velico	Velico Medical, Inc	Water (SDP pretreated with 20 mM glycine-HCl and 50 mM glycine)	Human donors; Group A and O	Laboratory; in vitro
Meledeo (2019)c	Human donors; Group A and O	Obtained from Velico	Velico Medical, Inc	Water containing 20 mM of glycine-HCl and 50 mM of glycine	Human donors; Group A and O	Laboratory; in vitro

−41.81 IU/dL; 95% CI: −56.19 to−27.23) was lowered by 32.9%, and von Willebrand Ristocetin Cofactor levels (pooled MD −62.10; 95% CI: −79.14 to −45.05) were also significantly lower by 53.3% in SDP. There were no differences observed in levels of Protein S antigen, von Willebrand factor (vWF) antigen, antithrombin III, and ADAMTS-13 concentrations.

In studies that reported tests of coagulation function, prothrombin time (PT) was significantly longer with SDP by 7.5% (pooled MD 0.85 secs; 95% CI: 0.16–1.53), but similar activated partial thromboplastin times (aPTT) between assays of FFP and SDP were reported (Figure 4). When assessed using viscoelastic hemostatic assays, the clot profile after treatment with SDP was reported to have significantly longer clotting times by 11.7% (pooled MD 0.75 s; 95% CI: 0.16–1.35), lower angles by 4.9% (pooled MD −3.53 degrees; 95% CI: −5.42 to −1.65), and lower maximum amplitudes by 12.5% (pooled MD −5.71 mm; 95% CI: −9.31 to −2.12). The detailed results of the meta-analysis are provided in Tables S1–S3, including measures of statistical heterogeneity.

All studies were assessed to have moderate risk of bias (Table 2). As studies were all conducted in vitro, representativeness of the exposed human cohort in critical bleeding scenarios remains unknown, and all studies were marked down. Assessment of outcomes was not reported to be in duplicate, and all studies were marked down on that domain. Finally, the report by Pusateri et al., did not have sufficient detail on the methodology to assess comparability of the cohorts.[18]

4 | DISCUSSION

SDP is an attractive preparation that is similar to fresh frozen plasma in containing relevant coagulation factors and proteases. A small number of in vitro analyses, using SDP from a single manufacturer, have reported significant differences between SDP and FFP in the concentration of coagulation factors and antithrombotic proteins. It is likely that the different composition of SDP results in weaker blood clots that take longer to form in vitro, when compared with FFP. There are some theoretical and as yet unproven concerns that these differences may impact clinical outcomes after resuscitation and necessitate alterations to major hemorrhage protocols that may recommend SDP instead of FFP.

SDP offers substantial benefits over both FFP and FDP with regard to the rate of manufacture, portability, reconstitution, throughput, and equipment needs.[19] Importantly, these efficiencies do not negatively affect endothelial permeability or inflammation, with FFP and SDP reported to equivalently modulate both at the molecular and cellular levels.[12] Similarly, FFP and SDP have been shown to both preserve the integrity of endothelial cell monolayers and result in similar gene expression

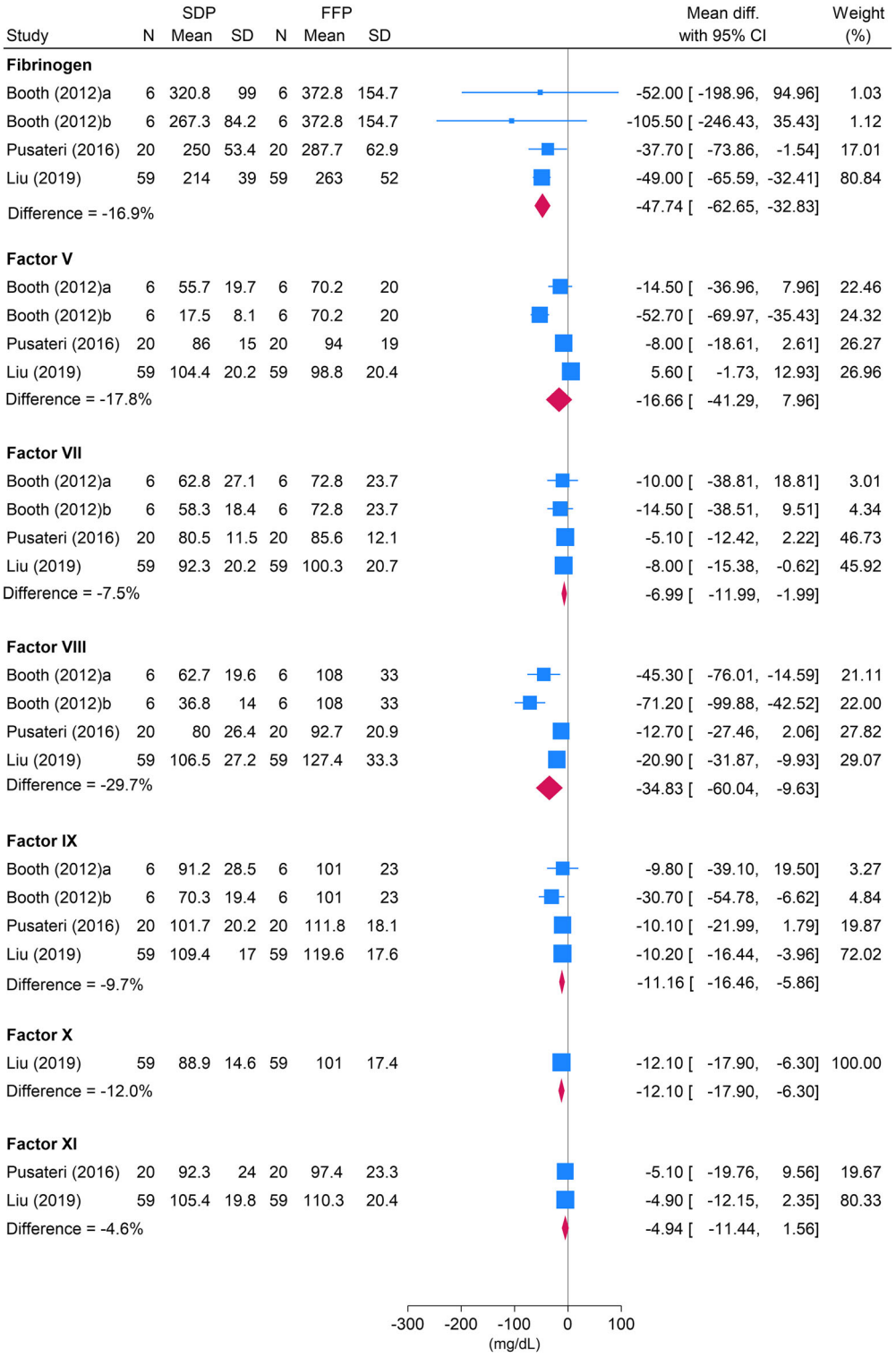

FIGURE 2 Concentrations of coagulation factors in spray-dried plasma compared with fresh frozen plasma. (a) Reconstituted using 1.5% glycine; (b) Reconstituted using de-ionized water. [Color figure can be viewed at wileyonlinelibrary.com]

patterns and cytokine/growth factor production. Furthermore, FFP and SDP reduced shock-induced pulmonary vascular permeability in animal models to a similar extent.[13] Therefore, while there are significant differences among these plasma products, SDP contains clinically meaningful levels of coagulation activity and, even though the clotting profile appears weaker than FFP, there is a consistent ability to generate thrombus.[14]

However, in addition to the differences in coagulation factors and profiles, other differences have been reported, necessitating caution before equivalent replacement of other plasma preparations.[15] Spinella et al. reported initial total thrombin formation was higher in SDP compared with FFP. The reduced time to peak and higher peak thrombin generation in the SDP suggest that more rapid and stronger thrombin generation is followed by a

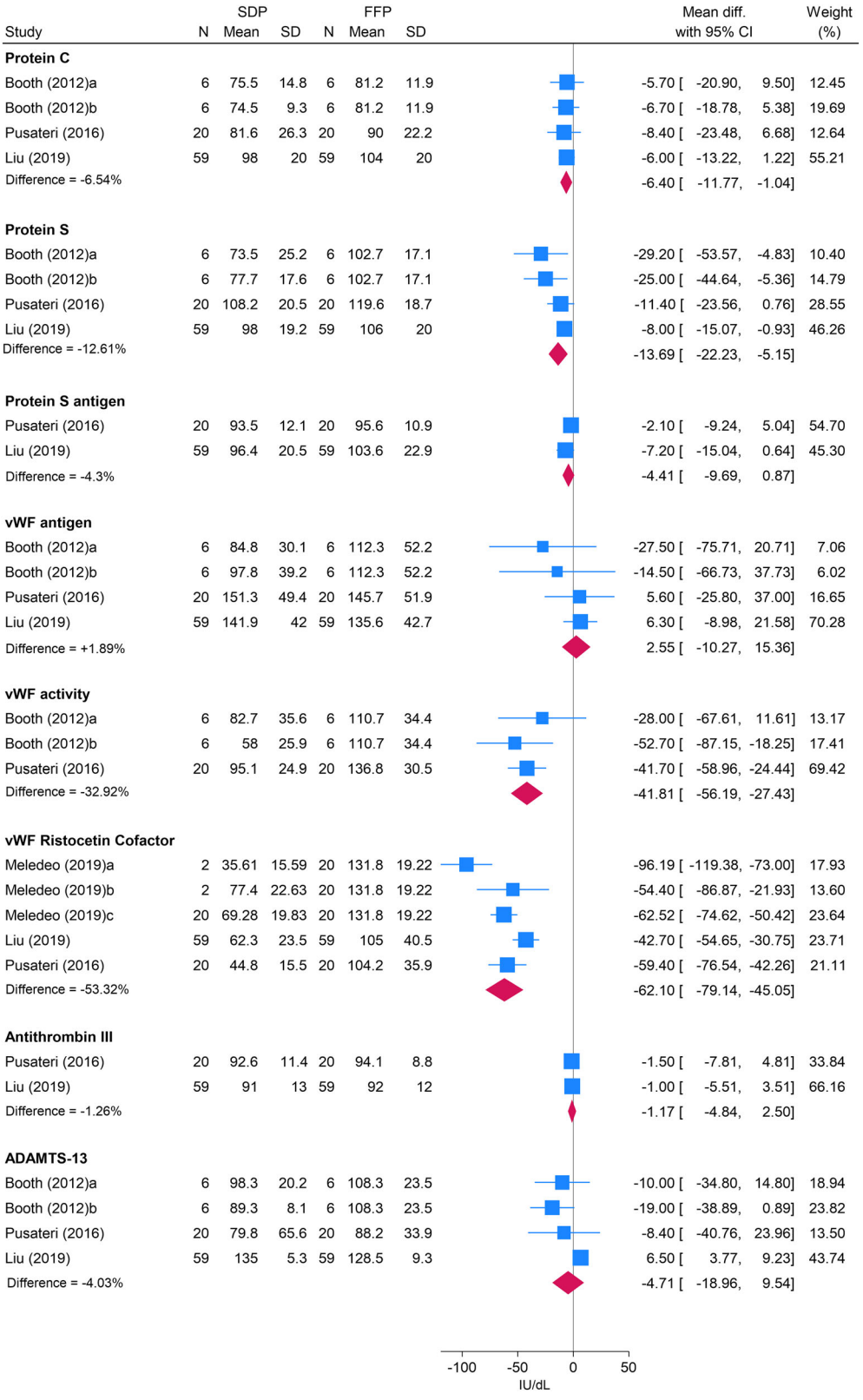

FIGURE 3 Coagulation factors in spray-dried plasma compared with fresh frozen plasma. (a) Reconstituted using 1.5% glycine; (b) Reconstituted using de-ionized water. [Color figure can be viewed at wileyonlinelibrary.com]

precipitous decline compared with single-donor plasma products. They raised the concern that this early, elevated thrombin generation peak could promote thromboembolic events.[15]

The beneficial properties of SDP, with similarities in constituency and activity to FFP, plus ease of manufacture, reconstitution, and delivery when compared with both FFP and FDP, suggest that it could be effective as a first-line product in MHPs. There are many scenarios where patients with critical bleeding are currently managed with crystalloids or red cells only, sometimes for prolonged periods. These include prehospital

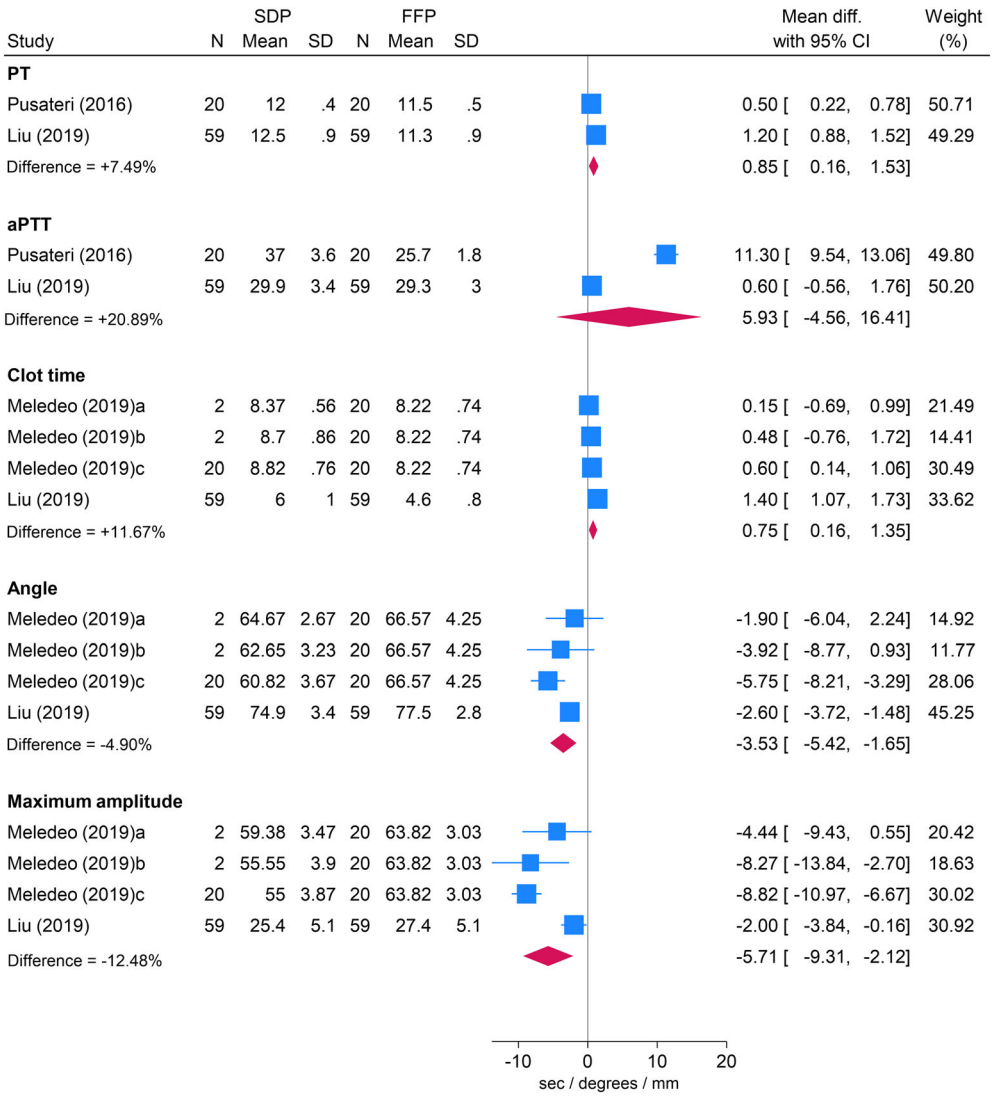

FIGURE 4 Comparisons of clotting function of FFP versus SDP. (a) Pretreated with 20 mM of glycine-HCl; (b) Pretreated with 20 mM glycine-HCl; (c) Reconstituted with water containing 20 mM of glycine-HCl and 50 mM of glycine. [Color figure can be viewed at wileyonlinelibrary.com]

	D1	D2	D3	D4	D5	D6	D7	Overall
Booth (2011)		★	★	★		★	★	★★★★★
Pusateri (2016)		★	★			★	★	★★★★
Lui (2019)		★	★	★		★	★	★★★★★
Meledeo (2019)		★	★	★		★	★	★★★★★

TABLE 2 Modified Newcastle-Ottawa assessment of included manuscripts.

Note: D1: Representativeness of the exposed cohort; D2: Selection of the non-exposed cohort; D3: Outcome blinded; D4: Comparability of cohorts; D5: Assessment of outcome; D6: Length of follow-up; D7: Adequacy of follow-up.

care where mission times are long, some rural and regional centers where there is limited or no availability of blood components, and in the military setting in forward treatment centers. The evidence for pre-emptive, high-volume transfusion of plasma in such scenarios, however, is uncertain; there were conflicting outcomes from randomized controlled trials of prehospital plasma, though post-hoc analyses suggested a benefit when prehospital times were in excess of 20 minutes.[21] Such scenarios, with recruitment of a patient population at risk of trauma-induced coagulopathy, would be the ideal setting for a randomized trial of SDP compared with standard practice.

This systematic literature review was limited in seeking data on the composition of SDP, rather than clinical effectiveness. Previous studies have demonstrated the benefits of SDP in animal models or in other outcomes such as modulation of endothelial

function and inflammation.[12,22] However, at the time of the search, there were no known results from human trials available, with a study to assess the safety of infusing increasing doses of SDP in healthy volunteers registered in November 2024.[23] Even within the small number of studies, there were differences in the manufacturing and reconstitution processes of SDP that have evolved over time. If considering human trials to assess the effectiveness of SDP, these processes should be considered to estimate the effect and dosing of SDP. All analyses were conducted in vitro, with some variability in the constituents of the FFP product. However, the reported levels of coagulation factors and other proteins in FFP controls were similar to the expected minimum values following the manufacture of a human plasma.[24] All studies reported used whole-blood-derived plasma as the substrate for the manufacture of SDP. However, many centers worldwide collect clinical plasma by apheresis, which may introduce further variability in the constituents and function of SDP. The varied processes for the reconstitution of SDP exaggerated the differences between different plasma products. When embarking on human trials, it is expected that one agreed process would limit the variability in the preservation of coagulation factors and activity.

At the time of this research, there were fourFDP products available: French FDP (FLyP), German FDP (LyoPlas), OctaplasLG- Lyo, and Bioplasma FDP, the last of which is produced by the National Bioproducts Institute of South Africa. This analysis did not seek to compare SDP with FDP, but observational studies have demonstrated the efficacy of FDP in prehospital settings.[25] It has been suggested that the key shortcoming of FDP lies in dependence on a centralized source of plasma and manufacturing, in addition to limited suppliers. A decentralized approach to the manufacturing of SDP can mitigate these issues of plasma supply through sourcing of plasma from local donors and production facilities close to the end user.[14]

Presently, the small number of analyses limits confidence in the point estimates for the differences. In particular, the observed differences in clotting times are unlikely to be clinically significant. But the slower speed of clot formation and lower strength of clots with SDP may have clinical implications. Finally, all SDP products were provided using devices by one manufacturer, so potential differences in the final product may arise should devices from other manufacturers become available, or with differences in the composition of liquid plasma (e.g., pooled vs. single donor; solvent/detergent treated vs. untreated) used as the starting material in the spray-drying process.

5 | CONCLUSIONS

SDP, when compared with freeze-dried or fresh frozen plasma, is an attractive plasma product that offers substantial benefits with regards to manufacture, storage, transport, reconstitution, and delivery. However, there are significant differences in the concentrations of coagulation factors and clotting activity in SDP compared with FFP. In the setting of critical bleeding, the substitution of FFP with SDP may not translate to the same effectiveness and safety profiles. Human trials, which would enroll patients most likely to benefit from early administration of plasma, are indicated to determine the effectiveness, safety, and optimal dosing of SDP.

AUTHOR CONTRIBUTIONS

Biswadev Mitra: Conceptualization; methodology; data curation; writing—original draft preparation; writing—reviewing and editing. **Patrick Biggins:** Data curation; validation; writing—reviewing and editing. **Denese Marks:** Validation; writing—reviewing and editing. **Michael Reade:** Conceptualization; writing—reviewing and editing.

ACKNOWLEDGMENT

Open access publishing facilitated by Monash University, as part of the Wiley - Monash University agreement via the Council of Australian University Librarians.

CONFLICT OF INTEREST STATEMENT

The authors have disclosed no conflicts of interest.

ORCID

Biswadev Mitra https://orcid.org/0000-0002-0508-2450
Patrick J. C. Biggins https://orcid.org/0000-0002-9388-1411
Denese C. Marks https://orcid.org/0000-0002-3674-6934
Michael C. Reade https://orcid.org/0000-0003-1570-0707

REFERENCES

1. Latif RK, Clifford SP, Baker JA, Lenhardt R, Haq MZ, Huang J, et al. Traumatic hemorrhage and chain of survival. Scand J Trauma Resusc Emerg Med. 2023;31(1):25.
2. Tien H, Chu PTY, Brenneman F. Causes of death following multiple trauma. Curr Orthop. 2004;18(4):304–10.
3. Mitra B, Jorgensen M, Reade MC, Keegan A, Holley A, Farmer S, et al. Patient blood management guideline for adults with critical bleeding. Med J Aust. 2024;220(4):211–6.
4. Menzies Wojtowicz M, Motum P, Dhir V. Extended life plasma: blood wastage and opportunities. Transfus Med. 2020;30(2):161–3.
5. Jost D, Lemoine S, Lemoine F, Derkenne C, Beaume S, Lanoë V, et al. Prehospital lyophilized plasma transfusion for

trauma-induced coagulopathy in patients at risk for hemorrhagic shock: a randomized clinical trial. JAMA Netw Open. 2022;5(7):e2223619.
6. Sheffield WP, Singh K, Beckett A, Devine DV. Prehospital freeze-dried plasma in trauma: a critical review. Transfus Med Rev. 2024;38(1):150807.
7. Crombie N, Doughty HA, Bishop JRB, Desai A, Dixon EF, Hancox JM, et al. Resuscitation with blood products in patients with trauma-related haemorrhagic shock receiving prehospital care (RePHILL): a multicentre, open-label, randomised, controlled, phase 3 trial. Lancet Haematol. 2022;9(4):e250–61. https://doi.org/10.1016/S2352-3026(22)00040-0
8. Mitra B, Meadley B, Bernard S, Maegele M, Gruen RL, Bradley O, et al. Pre-hospital freeze-dried plasma for critical bleeding after trauma: a pilot randomized controlled trial. Acad Emerg Med. 2023;30(10):1013–9.
9. Pusateri AE, Given MB, Macdonald VW, Homer MJ. Comprehensive US government program for dried plasma development. Transfusion. 2016;56(Suppl 1):S16–23.
10. Mitra B, Reade M, Marks D, Biggins P. Coagulation factors in spray-dried plasma: a systematic review and meta-analysis. PROPSERO. 2024. CRD42024608389. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42024608389
11. Bercovitz RS, Drew CS, Bushee CL, Popovsky MA, Friedman KD, Anani WQ. A microfluidic analysis of thrombus formation in reconstituted whole blood samples comparing spray-dried plasma versus fresh frozen plasma. Vox Sang. 2021;116(5):540–6.
12. Wataha K, Menge T, Deng X, Shah A, Bode A, Holcomb JB, et al. Spray-dried plasma and fresh frozen plasma modulate permeability and inflammation in vitro in vascular endothelial cells. Transfusion. 2013;53(Suppl 1):80s–90s.
13. Potter DR, Baimukanova G, Keating SM, Deng X, Chu JA, Gibb SL, et al. Fresh frozen plasma and spray-dried plasma mitigate pulmonary vascular permeability and inflammation in hemorrhagic shock. J Trauma Acute Care Surg. 2015;78(6 Suppl 1):S7–s17.
14. Popovsky MA, White N. Spray-dried plasma: a post-traumatic blood "bridge" for life-saving resuscitation. Transfusion. 2021;61(Suppl 1):S294–300.
15. Spinella PC, Frazier E, Pidcoke HF, Dietzen DJ, Pati S, Gorkun O, et al. All plasma products are not created equal: characterizing differences between plasma products. J Trauma Acute Care Surg. 2015;78(6 Suppl 1):S18–25.
16. Pusateri AE, Malloy WW, Sauer D, Benov A, Corley JB, Rambharose S, et al. Use of dried plasma in prehospital and austere environments. Anesthesiology. 2022;136(2):327–35.
17. Shuja F, Finkelstein RA, Fukudome E, Duggan M, Kheirbek T, Hamwi K, et al. Development and testing of low-volume hyperoncotic, hyperosmotic spray-dried plasma for the treatment of trauma-associated coagulopathy. J Trauma. 2011;70(3):664–71.
18. Pusateri AE, Given MB, Schreiber MA, Spinella PC, Pati S, Kozar RA, et al. Dried plasma: state of the science and recent developments. Transfusion. 2016;56(Suppl 2):S128–39.
19. Booth GS, Lozier JN, Nghiem K, Clibourn D, Klein HG, Flegel WA. Spray: single-donor plasma product for room temperature storage. Transfusion. 2012;52(4):828–33.
20. Meledeo MA, Liu QP, Peltier GC, Carney RC, McIntosh C, Taylor AS, et al. Spray-dried plasma deficient in high-molecular-weight multimers of von Willebrand factor retains hemostatic properties. Transfusion. 2019;59(2):714–22.
21. Pusateri AE, Moore EE, Moore HB, le TD, Guyette FX, Chapman MP, et al. Association of Prehospital Plasma Transfusion with Survival in trauma patients with hemorrhagic shock when transport times are longer than 20 minutes: a post hoc analysis of the PAMPer and COMBAT clinical trials. JAMA Surg. 2020;155(2):e195085.
22. McDaniel S, Golla S, Moore AN, DaCorta J, Bode A, Pati S, et al. Resuscitation of hypotensive traumatic brain injured animals with spray-dried plasma does not adversely Alter physiology and improves blood–brain barrier function. Mil Med. 2017;182(7):e1706–11. https://doi.org/10.7205/MILMED-D-16-00185
23. Popovsky MA. Evaluation for the safety of FrontlineODP™ in a multidose randomized cohort study compared with PF24. ClinicalTrialsgov 2024. NCT05629338.
24. Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee. Validation of Dried Plasma. 2022. Available from: https://www.transfusionguidelines.org
25. Mok G, Hoang R, Khan MW, Pannell D, Peng H, Tien H, et al. Freeze-dried plasma for major trauma – systematic review and meta-analysis. J Trauma Acute Care Surg. 2021;90(3):589–602.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Mitra B, Biggins PJC, Marks DC, Reade MC. Coagulation factors in spray-dried plasma: A systematic review and meta-analysis. Transfusion. 2025;65(5):1012–20. https://doi.org/10.1111/trf.18255