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ORIGINAL RESEARCH

TRANSFUSION

Spray-dried plasma is comparable to conventional plasma products used in the resuscitation of major hemorrhage: In vitro characterization

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Abstract

Background: Prehospital transfusion of blood products to patients at risk for hemorrhagic shock reduces mortality. Prehospital availability of blood products is limited by logistical constraints. This study evaluated the characteristics and stability of a product manufactured using a novel system for spray-drying and packaging plasma into plastic transfusion bags suitable for prehospital use.

Study Design and Methods: Plasma units dried using the spray-drying system (FrontlineODP-OnDemand Plasma), were rehydrated and compared to paired, frozen controls across a range of characterization assays. Testing was completed for initial characterization, stability post-rehydration to 26 h at refrigeration (1°C–6°C) and room temperature (20°C–24°C), and long-term stability at refrigeration for 24 months and at room temperature for 6 and 12 months.

Results: The spray-drying process converted liquid plasma into a fine, dry powder stored in a plastic transfusion-ready bag. The mean time to rehydrate was 2 min and 37 s. The characterization study demonstrated that dried plasma units were comparable to paired controls with similar coagulation factor activities, clotting times, balance of pro- and anticoagulation factor activities, markers of activation, pH, and chemistries. Spray-dried plasma was stable after rehydration for 26 h at refrigeration and room temperature. Spray-dried plasma maintained functional characteristics for 24 months at refrigeration and demonstrated comparability to 5-day thawed plasma after room temperature storage for 12 months.

Discussion: Spray-dried plasma rehydrates rapidly and has in vitro characteristics comparable to standard-of-care products after storage at room temperature for 1 or 2 years refrigerated. Clinical study of spray-dried plasma is warranted.

1 | INTRODUCTION

There are approximately 25,000 potentially preventable deaths due to traumatic hemorrhage in the Unites States annually and approximately 30,000 in Europe.[1–3] If non-traumatic causes of hemorrhage are added, the preventable death toll due to hemorrhage is significantly greater. Patients succumb to the "diamond of death" of acidosis, hypothermia, coagulopathy, and derangements of calcium metabolism.[4] The concept of damage control resuscitation (DCR) addresses these pathophysiologic processes by restoring hemostatic potential as well as oxygen carrying capacity through the transfusion of whole blood or blood components in a ratio of red blood cells:plasma:platelets of 1:1:1.[5–7] Experience obtained from the battlefield and the civilian sector has shown that early administration of blood components results in improved clinical outcomes.[8,9] Pre-hospital infusion of thawed plasma to patients with traumatic hemorrhage at risk for hemorrhagic shock, compared to crystalloid infusion, has demonstrated a 30% reduction in relative risk of 30-day mortality, particularly when transportation time to hospital from scene exceeds 20 min.[10,11] Despite these encouraging results, very few patients receive thawed or liquid plasma pre-hospital. The long thawing process for fresh frozen plasma (FFP), the challenges of maintaining cold storage, and the waste associated with shelf-life reduction of liquid plasma products are barriers to widespread availability.[12]

Dried plasma products, produced by lyophilization or spray-drying and consisting of powdered or caked plasma proteins and other constituents that can be reconstituted with sterile water for injection on demand are an alternative to thawed or liquid plasma. Dried plasma has been shown to be comparable in hemostatic function and biophysical properties to fresh plasma[13] Lyophilization is a capital- and energy-intensive industrial process that entails the sublimation of ice from large batches of frozen plasma units in a thermo-cycling vacuum chamber over the course of several days, resulting in a cake of proteins and other plasma constituents. Spray-drying involves atomization of plasma proteins into fine droplets which are exposed to a warm drying gas. Rapid evaporation results in the production of a powder ready for reconstitution. A compact spray-drying system has been developed by Velico Medical for distributed manufacturing in blood centers to dry single units of plasma in approximately 37 min per cycle.

Lyophilized plasma was used successfully in mid-20th century conflicts, but production was discontinued due to viral disease transmission (e.g. hepatitis B) in products made from large pools of plasma units. While newer versions of lyophilized plasma have mitigated this infectious disease risk through screening and pathogen inactivation technologies, global manufacturing capacity is limited, and current products are not widely licensed.[14]

Spray-dried plasma produced in blood centers from single units of licensed plasma represents a new product and a new, modular, scalable, distributed manufacturing concept, requiring only modest capital expenditure, that can significantly increase dried plasma availability for the timely treatment of hemorrhage[15] Replacing thawed plasma or liquid (never frozen) plasma with room-temperature stable spray-dried plasma offers a logistical advantage with comparable function, enabling broader and more reliable access to hemostatic resuscitation support across prehospital and rural or other remote settings. A successful clinical safety trial of spray-dried plasma has been recently reported[16] This manuscript describes the characterization and stability of spray-dried plasma manufactured using the FrontlineODP (On Demand Plasma) System by Velico Medical.

2 | STUDY DESIGN AND METHODS

2.1 | FrontlineODP manufacturing

The FrontlineODP System is a Class III medical device for manufacturing spray-dried, rehydratable plasma for transfusion. The spray-drying system is designed for decentralized manufacturing in blood center laboratories and does not require a cleanroom, as opposed to centralized manufacturing of lyophilized plasma in cleanroom industrial facilities. This unique system is comprised of a Frontline Dryer, Frontline Sealer, and associated sterile consumables, including the Plasma Pretreatment Container (PPC), plasma drying chamber (PDC), and FrontlineODP sterile water for injection (SWFI). Sterile connections are made using standard sterile connecting devices. Prior to spray-drying, 275 (265–285) mL of plasma is introduced into a PPC containing approximately 50 mL of a glycine and hydrochloric acid solution that stabilizes plasma proteins during the drying process and offsets the manufacturing impact on pH to yield a final rehydrated product of physiologic pH. The pretreated plasma is connected using a standard sterile connecting device to a single use, sterile PDC and loaded into the Frontline Dryer. The spray-drying process during which the liquid plasma is atomized with an aerosolization air stream and rapidly dried with a heated air stream takes approximately 37 min. At completion of the drying, the PDC is removed from the Dryer and loaded onto the Sealer where it undergoes a seal and separate process that concentrates the dried powder into its final packaged unit. The final primary packaging is then placed into a

pouch with a desiccant, sealed and then placed in storage. The FrontlineODP Unit is rehydrated using 200 mL of SWFI connected to the unit using a commercially available fluid transfer set. Once the SWFI is transferred into the FrontlineODP Unit pouch, the unit is manually mixed until there are no visible clumps or dry powder present. Once rehydrated, the unit is ready for transfusion utilizing a commercially available blood administration set following standard administration procedures.

2.2 | Characterization study sample preparation

Spray-dried plasma (ODP) was manufactured on the FrontlineODP System with whole blood-derived citrate-phosphate-dextrose anticoagulant plasma frozen within 24 h (PF24; $n = 60$–90). PF24 was prepared from donated whole blood by standard blood center centrifugation and separation protocols. Testing was completed with the execution of two studies, an initial verification of the phase I clinical trial system ($n = 60$) and a follow up study of the commercial version of the system ($n = 30$). In some instances, assays were not repeated for the second study; details for each assay sample size are detailed in Table 1 caption. Data from these two studies were determined to be comparable and combined for a robust characterization. Velico utilized a 95% confidence and 90% reliability model for verification testing in accordance with ISO 16269-6, table E.1 (i.e., that there is 95% confidence that 90% of the samples are within the specified tolerance).

For each spray dried unit, the paired control was refrozen at the time the FrontlineODP Unit was manufactured and then thawed prior to testing for a direct comparison. Sample blood types were approximately 45% A, 45% O, and 10% B to represent the US blood type distribution. Time to rehydrate ODP was measured for a subset ($n = 30$). Rehydrated ODP and thawed paired controls were tested in parallel for 45 assays detailed in Tables 1–3 and Data S1, Supporting Information. Reference ranges and sources are detailed in Data S2.

2.3 | Shelf-life study sample preparation

ODP units were manufactured from pools of 8–9 plasma units of thawed PF24. ODP units from each pool were stored at either refrigeration (1°C–6°C) for 24 months or room temperature (20°C–24°C) for 6 months. For each storage condition, units from three pools were evaluated. Rehydrated ODP and thawed paired controls were tested in parallel for 21 assays detailed in Table 4 and Data S1. A separate, fourth pool was evaluated at $t = 0$ and $t = 12$ months at room temperature storage and compared to 5-day thawed plasma; assays are detailed in Table 5 and Data S1. Reference ranges and sources are detailed in Data S2.

2.4 | Rehydrated ODP shelf-life sample preparation

ODP samples made from pooled plasma as described above ($n = 3$) were rehydrated and each divided into six 5 mL aliquots to account for each timepoint tested. One aliquot from each unit was frozen immediately ($t = 0$) as a comparator. Then, five aliquots were stored at refrigeration (1°C–6°C), and five aliquots were stored at room temperature (22°C–24°C) for the remaining timepoints. An aliquot from each storage condition was placed in the freezer (<−18°C) for preservation of the given timepoint at $t = 5$, 8, 20, 23, and 26 h post-rehydration. To allow for testing at once and the same number of freeze/thaw cycles per sample, all samples of a given pool were then thawed the same day. Samples at later timepoints were compared to the initial timepoint ($t = 0$) to determine coagulation preservation across 24 assays for both refrigeration (Table 6) and room temperature (Table 7) storage conditions. Assays are detailed in Tables 6 and 7 and Data S1. Reference ranges and sources are detailed in Data S2.

2.5 | Laboratory analysis

ODP and paired control plasmas were evaluated for factor activities and antigens, clotting times, complement, markers of activation and chemistries. ODP rehydration and paired control plasma thawing (1:1, direct comparison) were completed at the same time and tested in parallel. Activated partial thromboplastin time (aPTT), prothrombin time (PT), thrombin time (TT), fibrinogen, factor (F) II, FV, FVII, FVIII, FIX, FX, FXI, FXII, FXIII antigen, antithrombin III (ATIII), Protein (P) S, PC, Free PS, von Willebrand Factor (vWF) activity, vWF antigen (Ag), Plasminogen, α2-antiplasmin and C1 esterase inhibitor were tested on the Instrumentation Laboratory ACL TOP700 according to assay manufacturer instructions. vWF:RCo, D-Dimer, and FXIII were tested on the Siemens BCS XP. Total protein, albumin, calcium, total cholesterol, low-density lipoprotein, high-density lipoprotein, triglycerides, immunoglobulin (Ig) A, IgG, IgM and α-1 Proteinase Inhibitor were tested on the Selectra ProM. ELISAs were performed according to manufacturer instructions for Zymutest FV:Ag, Affinity Biologicals VisuLize FVII:Ag and FVIII:Ag, Quidel Microvue C3a

TABLE 1 FrontlineODP coagulation factor characterization study results.

Assays	Clinical reference ranges	Control plasma		FrontlineODP				% Change compared to control plasma		95% confidence interval (% change)	$n =$
		Mean	SD	Mean	SD	Range (min–max)		Mean	SD		
aPTT (s)	(22–35)	29.3	3.2	30.4	4.0	19.5	41.9	4	8	2, 5	90
PT (s)	(10–14)	11.5	0.8	12.3	0.9	10.3	15.1	7	3	6, 7	90
TT (s)	(14.5–20.5)	13.5	1.4	17.7	1.5	14.7	23.1	31	10	29, 33	90
FII (%)	50–150)	95.6	10.9	85.6	10.6	56.9	111.4	−10%	5	−11, −9	90
FV (%)	(50–200)	91.4	17.7	88.0	17.4	25.4	136.0	−4	6	−5, −2	90
FV:Ag (IU/mL)	(50–175)	71.5	14.0	65.6	14.0	34.3	98.6	−8	9	−11, −6	60
FVII (%)	(50–200)	91.2	17.7	81.8	16.3	46.2	127.2	−10	5	−11, −9	90
FVII:Ag (IU/mL)	(0.7–1.46)	1.01	0.14	0.96	0.15	0.63	1.32	−4	6	−6, −3	60
FVIII (%)	(50–200)	106.1	40.5	84.1	32.0	36.1	221.2	−20	10	−22, −18	90
FVIII:Ag (IU/mL)	(0.7–1.46)	1.24	0.30	1.18	0.28	0.58	1.98	−5	5	−7, −4	60
FIX (%)	(50–200)	104.5	14.0	90.2	12.1	60.0	121.2	−13	7	−15, −12	90
FX (%)	(50–200)	93.9	13.7	82.4	12.9	53.4	120.3	-12	4	−13, −11	90
FXI (%)	(50–200)	106.1	17.7	96.6	17.0	58.9	139.1	−9	8	−10, −7	90
FXII (%)	(50–200)	118.1	24.7	99.9	21.5	43.6	148.7	−15	5	−16, −14	90
FXIII (%)	(57–192)	121.9	22.1	102.3	19.9	58.8	170.0	−16	7	−18, −15	90
FXIII:Ag (%)	(75.2–154.8)	106.3	21.8	94.0	17.1	63.3	152.1	−11	6	−13, −10	60
Fibrinogen (mg/dL)	(150–400)	268	52	240	45	151	370	−10	7	−11, −8	90
Free protein S (%)	(55–124)	99.0	15.0	92.0	15.2	59.3	134.7	−7	4	−8, −6	90
Plasminogen (%)	(70–150)	93	11	89	11	52	115	−4	4	−5, −3	90
Plasmin Inhibitor (%)	(85–156)	102	10	98	11	67	138	−4	4	−5, −3	90
C1 Esterase Inhibitor (%)	(70–130)	102	13	97	13	68	134	−4	5	−5, −3	90
Protein C (%)	(70–140)	107	17	99	17	71	146	−8	4	−9, −7	90
Protein S (%)	(60–150)	102.0	14.2	88.0	13.4	52.9	120.0	−14	5	−15, −13	90
ATIII (%)	(80–120)	100	10	92	11	61	120	−8	5	−9, −7	90
vWF activity (%)	(50–200)	112.1	34.6	73.7	21.9	40.6	129.6	−34	10	−36, −31	87
vWF antigen (%)	(50–200)	131.0	39.2	127.1	33.8	70.6	228.4	−2	7	−3, 0	87
vWF:RCo (%)	(50–200)	92.4	33.8	40.0	13.0	21.0	80.6	−55	8	−57, −54	90
C3a (ng/mL)	(55–486)	223	121	292	138	105	1076	37	31	31, 44	90
C5a (ng/mL)	(4.70–74.00)	7.3	5.4	38.5	10.5	17.8	61.2	701	859	524, 878	90
D-Dimer (mg/L)	(0.00–0.50)	0.62	0.89	0.65	0.75	0.18	4.43	18	26	12, 24	75
Alpha 1-proteinase inhibitor (mg/dL)	(90–200)	109.2	11.2	104.8	11.2	68.4	129.0	−4	4	−5, −3	60
PF 1 + 2 (pmol/L)	(91–137)	153	124	159	144	58	1095	14	53	1, 28	60
TAT (μg/L)	(0–4)	5.1	11.9	5.1	12.2	0.4	85.2	10	53	−4, 23	59

Note: Sample size for each assay includes both control and ODP pairs. Factor V:Ag (IU/mL), Factor VII:Ag (IU/mL), Factor VIII:Ag (IU/mL), Factor XIII:Ag (%), Alpha 1-Proteinase Inhibitor (mg/dL), PF 1 + 2 (pmol/L), and TAT (μg/L) were only completed in the initial verification of the clinical phase I system ($n = 60$). von Willebrand Factor Activity (%) and vWF Antigen (%) had a sample size of $n = 87$ due to three failed samples due to analytical instrument "Coagulation Error" flag. D-Dimer (mg/L) had a sample size of $n = 75$ due to 14 measurements were below the assay's measuring range for the control plasma or both control plasma and FrontlineODP and 1 unit was determined to be an outlier. TAT had a sample size of $n = 59$ due to 1 measurement was below the assay's measuring range.

TABLE 2 FrontlineODP chemistry characterization study results.

Assays	Clinical reference ranges	Control plasma		FrontlineODP				% change compared to control plasma		95% confidence interval (% change)	$n =$
		Mean	SD	Mean	SD	Range (min–max)		Mean	SD		
pH	(6.5–7.6)	7.42	0.08	7.13	0.20	6.74	7.71	−4	3	−4, −3	90
Osmolality (mOsm/kg)	(>240)	309	6.1	377	15.3	327	429	22	5	21, 23	90
Total protein (g/dL)	(>4.50)	5.60	0.37	5.40	0.35	4.53	6.52	−4	3	−4, −3	90
Cholesterol (mg/dL)	(0–200)	143	36	136	33	76	288	−5	3	−6, −4	90
LDL (mg/dL)	(0–100)	89	32	78	26	32	203	−11	5	−12, −10	90
HDL (mg/dL)	(35–100)	43	14	36	10	18	68	−15	6	−16, −13	90
Triglycerides (mg/dL)	(0–150)	112	61	109	60	23	343	−2	4	−3, −1	90
Albumin(g/dL)	(3.30–5.00)	3.77	0.23	3.58	0.24	3.05	4.25	−5	3	−5, −4	90
Calcium(mg/dL)	(8.60–10.30)	6.48	0.28	6.19	0.33	5.31	6.86	−4	3	−5, −4	90
IgA (mg/dL)	(69–309)	180	80	171	76	21	423	−5	4	−6, −4	90
IgG (mg/dL)	(614–1295)	833	215	798	202	509	1695	−4	4	−5, −3	90
IgM (mg/dL)	(53–334)	74	44	70	42	11	192	−6	4	−7, −5	90

Note: Sample size for each assay includes both control and ODP pairs. All chemistries were within 20% except for osmolality. There was a 21% change with osmolality for FrontlineODP Unit compared to its paired control. The European Pharmacopeia specifies the minimum osmolality of 240 mOsm/kg for Human Plasma (pooled and treated for virus inactivation).

Plus and C5a, and Siemens Prothrombin Fragment 1 + 2 (PF1 + 2) and Thrombin Antithrombin (TAT). pH was measured with accumet AB15/AB150 and osmolality was measured with Advanced Instruments osmometer 3320/3300. Moisture content was measured with Mettler Toledo C30S coulometric Karl Fischer titrator. Analyzer and Assay information is detailed in Data S1.

Results are reported as means, standard deviations, 95% confidence intervals, and mean percent changes. Comparability was determined by mean percent change and comparison to clinical reference range as suggested by regulatory agencies. For characterization, a difference of less than or equal to 20% in recovery of an individual coagulation activity compared to control, or within the clinical reference range, was considered comparable because of laboratory assay variability. For shelf-life studies, a difference of 25% in recovery of an individual coagulation activity compared to control, or within the clinical reference range, was considered comparable because of laboratory assay variability. Reference ranges and sources are detailed in Data S2.

3 | RESULTS

The FrontlineODP spray-drying process converted liquid plasma into a fine, dry powder stored in a plastic transfusion-ready bag. The moisture content of ODP at the time of manufacturing was 1.46 ± 0.14% ($n = 20$, mean ± SD). Moisture content stayed below 1.6% throughout shelf life, measuring 1.36 ± 0.18% ($n = 3$) at 24 months refrigerated and 1.21 ± 0.07% ($n = 3$) after 6 months at room temperature. Mean time to rehydrate spray-dried plasma was 2 min and 37 s ($n = 30$).

The results of the characterization study are summarized in Table 1 (coagulation factors) and Table 2 (chemistries). FrontlineODP units were comparable to paired, control PF24 plasma and have similar levels of coagulation factor activities, clotting times, balance of pro- and anticoagulation factor activities, markers of activation, pH, osmolality and chemistries. Recoveries were within ±20% paired controls or within clinical reference ranges for all assays except for vWF:RCo activity and C5a, although the C5a values were within the reference range reported for apheresed plasma of 4.9–74 ng/mL. vWF:RCo and vWF:Ag of FrontlineODP Units by blood types A, B, and O are summarized in Table 3. vWF:RCo in blood type A was 43.9 ± 14.3 and higher than in blood type O 36.0 ± 10.6 ($n = 37$, mean ± SD) due to the lower vWF:Ag observed in blood type O group.[17]

The results of the shelf-life study, with storage at 1°C–6°C for up to 24 months and at 20°C–24°C for up to 6 months are summarized in Table 4. Storage for 24 months refrigerated demonstrates assay values ±25% compared to $t = 0$ or

TABLE 3 vWF levels in spray-dried plasma by blood group.

Assays	Clinical reference range	Type A ODP mean	Type A ODP SD	Type A $n =$	Type B ODP mean	Type B ODP SD	Type B $n =$	Type 0 ODP mean	Type 0 ODP SD	Type 0 $n =$
vWF:Ag (%)	(50–200)	136.9	37.8	35	139.0	33.9	16	112.3	23.3	36
vWF:RCo (%)	(50–200)	43.9	14.3	37	40.0	12.8	16	36.0	10.6	37

Note: Sample size for each assay includes both control and ODP pairs. vWF Antigen (%) had a total sample size of $n = 87$ due to three failed samples due to analytical instrument "Coagulation Error" flag. vWF:RCo (%) had a total sample size of $n = 90$.

TABLE 4 FrontlineODP shelf-life study results with storage at 1°C–6°C for 24 months and at 20°C–24°C for 6 months.

Assays	Clinical reference range	Refrigeration (1°C–6°C) 24 months ($n = 3$ pools of 9 units) $ODP_{t=0}$ (mean ± SD)	Refrigeration (1°C–6°C) 24 months ($n = 3$ pools of 9 units) $ODP_{t=24}$ (mean ± SD)	Refrigeration (1°C–6°C) 24 months ($n = 3$ pools of 9 units) % $\Delta ODP_{t=0}$	Room temperature (20°C–24°C) 6 months ($n = 3$ pools of 9 units) $ODP_{t=0}$ (mean ± SD)	Room temperature (20°C–24°C) 6 months ($n = 3$ pools of 9 units) $ODP_{t=6}$ (mean ± SD)	Room temperature (20°C–24°C) 6 months ($n = 3$ pools of 9 units) % $\Delta ODP_{t=0}$
aPTT (s)	(22–35)	28.0 ± 2.6	31.4 ± 2.5	12	29.7 ± 1.0	37.7 ± 2.7	27%
PT (s)	(10–14)	12.5 ± 0.4	12.5 ± 0.3	0	13.0 ± 0.4	14.1 ± 0.5	9%
INR	(0.9–1.1)	1.00 ± 0.03	0.99 ± 0.02	−1	1.04 ± 0.04	1.14 ± 0.04	9%
TT (s)	(14.5–20.5)	17.8 ± 0.5	18.4 ± 0.4	4	16.9 ± 1.0	20.3 ± 0.5	21%
Fib (mg/dL)	(150–400)	256 ± 3	217 ± 17	−15	269 ± 26	181 ± 15	−32%
FV Act (%)	(50–200)	108 ± 4	91 ± 10	−17	90 ± 3	69 ± 1	−24%
FVII Act (%)	(50–200)	86 ± 5	93 ± 8	7	79 ± 3	72 ± 2	−8%
FVIII Act (%)	(50–200)	92 ± 14	87 ± 5	−4	81 ± 10	59 ± 8	−28%
FIX Act (%)	(50–200)	92 ± 8	88 ± 6	−3	94 ± 9	81 ± 9	−13%
FX Act (%)	(50–200)	82 ± 5	90 ± 7	11	79 ± 2	70 ± 1	−12%
FXI Act (%)	(50–200)	92 ± 9	96 ± 1	5	108 ± 16	87 ± 4	−18%
FXIII Act (%)	(57–192)	110 ± 8	104 ± 13	−6	110 ± 9	90 ± 15	−18%
FXIII Ant (%)	(75.2–154.8)	108 ± 5	95 ± 7	−12	107 ± 8	110 ± 18	2%
PC Act (%)	(70–140)	100 ± 9	99 ± 7	−1	101 ± 2	96 ± 6	−5%
PS Act (%)	(60–150)	88 ± 7	87 ± 5	−2	91 ± 5	86 ± 6	−6%
AT III Act (%)	(80–120)	91 ± 4	83 ± 7	−9	86 ± 5	85 ± 11	−1%
Plasminogen (%)	(70–150)	81 ± 6	80 ± 7	−1	86 ± 5	82 ± 3	−4%
Plasmin Inhibitor(%)	(85–156)	95 ± 3	77 ± 6	−19	98 ± 2	93 ± 4	−5%
vWF:RCo (%)	(50–200)	55 ± 5	47 ± 1	−14	41 ± 9	39 ± 5	−3%
vWF Ant (%)	(50–200)	138 ± 12	150 ± 8	9	135 ± 21	131 ± 19	−3%
TAT (μg/L)	(0–4)	3.3 ± 1.8	4.9 ± 2.7	44	2.3 ± 0.6	2.9 ± 0.5	30%
C5a (ng/mL)	(4.7–74.0)	33.4 ± 5.3	37.9 ± 2.1	16	35.8 ± 11.2	39.9 ± 4.5	17%

within the normal reference range for all test parameters except TAT. Storage for 6 months at room temperature demonstrates assay values ±25% compared to $t = 0$ or within the normal reference range for all test parameters except aPTT, paralleling reductions in FVIII.

The results of the shelf-life study of storage for 1 year at room temperature are summarized in Table 5 and demonstrate assay values ±25% compared to $t = 0$ or within the normal reference range for all test parameters except aPTT, FVIII, and TAT. These assay values are

TABLE 5 FrontlineODP shelf-life study results with storage at 20°C–24°C for up to 12 months with comparison to 5-day thawed plasma.

Timepoint		$t = 0$		Room temperature (20°C–24°C) 12 months ($n = 3$ pools of 9 units)			Refrigeration (1°C–6°C) 5-day thawed plasma	
Assay	Clinical reference range	Control (mean ± SD)	ODP (mean ± SD)	Control (mean ± SD)	ODP (mean ± SD)	% $\Delta ODP_{t=0}$	$t = 0$ (mean ± SD)	$t = 5$ days (mean ± SD)
aPTT (s)	(22–35)	29.1 ± 1.4	30.8 ± 1.0	28.2 ± 1.8	43.9 ± 0.4	43	38.5 ± 3.26	43.7 ± 4.78
PT (s)	(10–14)	11.2 ± 0.3	11.9 ± 0.2	11.5 ± 0.4	14.7 ± 0.2	23	11.3 ± 0.83	13.3 ± 1.01
INR	(0.9–1.1)	0.89 ± 0.02	0.95 ± 0.02	0.9 ± 0.03	1.2 ± 0.02	23	-	-
TT (s)	(14.5–20.5)	13.4 ± 0.8	17.5 ± 0.7	14.2 ± 0.7	24.6 ± 1.4	40	-	-
Fibrinogen (mg/dL)	(150–400)	282 ± 26	254 ± 24	290 ± 40	150 ± 24	−41	238.4 ± 55.02	219.3 ± 53.03
FV act (%)	(50–200)	106 ± 7	104 ± 5	93 ± 6	70 ± 2	−33	85.7 ± 20.80	66.3 ± 15.72
FVII act (%)	(50–200)	100 ± 5	91 ± 8	77 ± 6	61.4 ± 2	−33	104.8 ± 23.22	70.6 ± 15.7
FVIII act (%)	(50–200)	97 ± 12	74 ± 12	86.2 ± 12	38.7 ± 6	−48	71.6 ± 22.40	36.9 ± 17.75
FIX act (%)	(50–200)	103 ± 9	92 ± 4	101 ± 11	64 ± 6	−31	96.2 ± 13.22	91.5 ± 12.48
FX act (%)	(50–200)	97 ± 6	89 ± 6	91 ± 5	66 ± 3	−25	101.0 ± 18.02	67.0 ± 35.52
FXI act (%)	(50–200)	111 ± 6	94 ± 7	99 ± 12	71 ± 5	−25	-	-
FXIII act (%)	(57–192)	118 ± 7	97 ± 5	126 ± 4	73 ± 10	−25	-	-
FXIII ant (%)	(75.2–154.8)	111 ± 8	102 ± 6	113 ± 7	105 ± 8	3	-	-
PC act (%)	(70–140)	110 ± 3	105 ± 4	109 ± 3	90 ± 2	−14	-	-
PS act (%)	(60–150)	98 ± 7	90 ± 9	100 ± 3	85 ± 2	−6	-	-
AT III act (%)	(80–120)	92 ± 4	90 ± 4	92 ± 4	74 ± 3	−18	-	-
Plasminogen (%)	(70–150)	92 ± 4	92 ± 2	92 ± 4	87 ± 3	−5	-	-
Plasmin inhibitor (%)	(85–156)	104 ± 2	102 ± 3	100 ± 3	90 ± 5	−12	-	-
vWF:RCo (%)	(50–200)	97 ± 20	43 ± 4	96 ± 22	34 ± 3	−22	-	-
vWF ant (%)	(50–200)	123 ± 20	128 ± 22	121 ± 19	118 ± 19	−8	110.8 ± 39.01	67.0 ± 35.52
TAT (μg/L)	(0–4)	3.3 ± 1.0	3.3 ± 1.1	3.9 ± 1.9	4.8 ± 1.2	44	-	-
C5a (ng/mL)	(4.7–74.0)	6.8 ± 0.6	34.8 ± 1.9	6.4 ± 0.7	39 ± 4.0	12	-	-

TABLE 6 Twenty-six hour refrigerated rehydrated stability ($n = 3$), % change compared to ODP at $t = 0$.

Assays	T = 0 h after rehydration Mean ± SD	T = 5 h after rehydration Mean ± SD	% change from $t = 0$ to $t = 5$ h	T = 8 h after rehydration Mean ± SD	% change from $t = 0$ to $t = 8$ h	T = 20 h after rehydration Mean ± SD	% change from $t = 0$ to $t = 20$ h	T = 26 h after rehydration Mean ± SD	% change from $t = 0$ to $t = 26$ h
aPTT (s)	28.3 ± 1.1	28.9 ± 0.7	2	29.1 ± 0.9	3	30.6 ± 0.8	8	30.4 ± 0.6	7
PT (s)	12.1 ± 0.7	12.1 ± 0.7	0	12.3 ± 0.8	2	12.4 ± 0.7	3	12.2 ± 0.6	1
INR	0.96 ± 0.06	0.96 ± 0.06	0	0.97 ± 0.06	1	0.98 ± 0.05	2	0.97 ± 0.05	0
TT (s)	18.9 ± 2.1	19.1 ± 2.1	1	19.1 ± 2.1	1	18.8 ± 2.8	−1	19.1 ± 2.6	1
FV act (%)	82.2 ± 13	82.4 ± 14.5	0	78 ± 12.4	−5	75.2 ± 12.9	−9	73 ± 7.9	−11
FVII act (%)	88.5 ± 20.1	90.3 ± 18.5	2	91.6 ± 20	4	89.1 ± 19.6	1	96.7 ± 18.7	10
FVIII act (%)	94.8 ± 15.6	85.3 ± 12	−9	82.8 ± 11.3	−12	68.5 ± 8.1	−27	63.5 ± 10.8	−33
FIX act (%)	99.4 ± 15	97.7 ± 14.3	−2	94.3 ± 8.9	−5	97.2 ± 12.7	−2	103.1 ± 20.9	3
FX act (%)	100.3 ± 15.1	99.2 ± 15.6	−1	99.2 ± 13.2	−1	97.5 ± 13.9	−3	103.2 ± 18	3
FXI act (%)	97.6 ± 11.6	92.8 ± 9.8	−5	96 ± 10	−1	88.9 ± 9.2	−9	97.8 ± 13.3	0
FXIII act (%)	89.4 ± 7.9	89.5 ± 6.6	0	90 ± 6.1	1	89.2 ± 6.2	0	87.7 ± 6.6	−2
FXIII ant (%)	73.8 ± 3.9	75.5 ± 1.7	3	76.3 ± 5.5	4	73.3 ± 1.9	0	76.3 ± 3.1	4
Fibrinogen (mg/dL)	230 ± 42	231 ± 38	1	234 ± 36	2	227 ± 31	−1	243 ± 49	6
Plasminogen (%)	105 ± 22	106 ± 20	1	107 ± 21	2	106 ± 20	0	104 ± 19	−1
Plasmin inhibitor (%)	89 ± 11	88 ± 11	−1	89 ± 10	0	89 ± 14	0	89 ± 9	0
PC act (%)	91 ± 17	93 ± 18	2	94 ± 19	3	91 ± 19	0	91 ± 18	0
PS act (%)	109.2 ± 0.3	99.4 ± 1.3	−9	98.4 ± 0.3	−10	95.2 ± 0.8	−13	99.3 ± 5.8	−9
AT III act (%)	81 ± 5	83 ± 6	2	84 ± 8	3	82 ± 8	1	81 ± 10	0
vWF activity (%)	54 ± 19	54 ± 18	1	56 ± 19	5	55 ± 18	3	53 ± 17	0
vWF ant (%)	110.3 ± 27.1	108.7 ± 24.7	−1	110.3 ± 27	0	110.5 ± 25	1	112.8 ± 26.9	2
vWF:RCo (%)	33.5 ± 10.2	35 ± 10.8	4	36.6 ± 11	9	38.4 ± 10.5	16	38.1 ± 13.9	13
C5a (ng/mL)	33.2 ± 1	33.9 ± 2.4	2	33.5 ± 1.4	1	34 ± 0.8	2	33.7 ± 2.4	1
PF 1 + 2 (pmol/L)	100.9 ± 46.5	83.2 ± 12.2	−7	98.5 ± 45.1	−2	105.6 ± 38.9	7	79.6 ± 1.4	−11
TAT (μg/L)	1.77 ± 0.71	1.86 ± 0.85	8	2.12 ± 0.6	27	1.86 ± 0.96	2	2.11 ± 0.66	26

Note: $t = 23$ h is not shown.

TABLE 7 Twenty-six hour room temperature rehydrated stability ($n = 3$), % change compared to ODP at $t = 0$.

Assays	T = 0 h after rehydration Mean ± SD	T = 5 h after rehydration Mean ± SD	% change from $t = 0$ to $t = 5$ h	T = 8 h after rehydration Mean ± SD	% change from $t = 0$ to $t = 8$ h	T = 20 h after rehydration Mean ± SD	% change from $t = 0$ to $t = 20$ h	T = 26 h after rehydration Mean ± SD	% change from $t = 0$ to $t = 26$ h
aPTT (s)	28.3 ± 1.1	28.1 ± 0.7	−1	28 ± 1.1	−1	28.0 ± 1.1	−2	28.3 ± 1.2	0
PT (s)	12.1 ± 0.7	11.9 ± 0.7	−2	11.9 ± 0.8	−2	11.9 ± 0.8	−3	11.9 ± 0.7	−2
INR	0.96 ± 0.06	0.94 ± 0.06	−2	0.95 ± 0.06	−2	1.0 ± 0.1	−3	0.9 ± 0.1	−2
TT (s)	18.9 ± 2.1	19.4 ± 2.3	2	19.2 ± 2.3	1	19.2 ± 2.5	1	19.1 ± 2.4	1
FV act (%)	82.2 ± 13	83.3 ± 11.7	2	83.9 ± 11.4	2	83.9 ± 11.4	−2	79.6 ± 11.1	−3
FVII act (%)	88.5 ± 20.1	97.9 ± 21.6	11	98.5 ± 24.2	11	98.5 ± 24.2	14	109.9 ± 26.3	24
FVIII act (%)	94.8 ± 15.6	90.2 ± 16.3	−5	87.5 ± 12.2	−7	87.5 ± 12.2	−12	73.9 ± 14.2	−22
FIX act (%)	99.4 ± 15	97.3 ± 14.4	−2	100.2 ± 11.3	1	100.2 ± 11.3	−1	105.2 ± 16.3	6
FX act (%)	100.3 ± 15.1	103.3 ± 16.7	3	101.4 ± 15.1	1	101.4 ± 15.1	2	104.0 ± 16.3	3
FXI act (%)	97.6 ± 11.6	94.4 ± 11.7	−3	93.3 ± 9.1	−4	93.3 ± 9.1	−9	94.4 ± 13.9	−3
FXIII act (%)	89.4 ± 7.9	90.2 ± 7.7	1	91 ± 7.9	2	91.0 ± 7.9	0	87.7 ± 10.2	−2
FXIII ant (%)	73.8 ± 3.9	74.5 ± 4.2	1	76.5 ± 3.5	4	76.5 ± 3.5	0	75.2 ± 3.9	2
Fibrinogen (mg/dL)	230 ± 42	224 ± 28	−2	225 ± 31	−2	225 ± 31	−2	225 ± 40	−2
Plasminogen (%)	105 ± 22	107 ± 20	2	104 ± 22	−1	104 ± 22	0	104 ± 19	−1
Plasmin inhibitor (%)	89 ± 11	89 ± 11	0	90 ± 14	1	90 ± 14	−1	87 ± 9	−2
PC act (%)	91 ± 17	93 ± 18	1	94 ± 20	2	94 ± 20	−2	91 ± 19	0
PS act (%)	109.2 ± 0.3	95.8 ± 1.2	−12	89.5 ± 10.3	−18	89.5 ± 10.3	−33	62.0 ± 15.6	−43
AT III act (%)	81 ± 5	81 ± 7	−1	81 ± 9	−1	81 ± 9	−4	78 ± 10	−4
vWF activity (%)	54 ± 19	55 ± 20	3	56 ± 18	5	55.9 ± 18.0	3	53.3 ± 18.8	0
vWF Ant (%)	110.3 ± 27.1	111.7 ± 27.3	1	109.6 ± 25.7	0	109.6 ± 25.7	2	111.5 ± 26.6	1
vWF:RCo (%)	33.5 ± 10.2	36.7 ± 11.1	10	38.1 ± 11.1	14	38.1 ± 11.1	20	37.3 ± 12.0	11
C5a (ng/mL)	33.2 ± 1	32.9 ± 1.5	−1	33.1 ± 1.9	0	33.10 ± 1.90	−6	31.20 ± 2.70	−6
PF 1 + 2 (pmol/L)	100.9 ± 46.5	89.4 ± 14.5	−4	78.8 ± 8	−14	78.8 ± 8.0	−21	77.8 ± 22.5	−18
TAT (μg/L)	1.77 ± 0.71	1.85 ± 0.94	0	1.78 ± 1.11	−2	1.78 ± 1.11	14	2.60 ± 0.89	51

Note: $t = 23$ h is not shown.

comparable to those of FFP thawed and stored for 5 days refrigerated.

The results of the post-rehydration stability study, with storage at refrigeration (1°C–6°C) and at room temperature (20°C–24°C) for 26 h are summarized in Tables 6 and 7 respectively. At refrigeration, differences in FVIII and TAT exceeded 25% from T = 0, but were within the clinical reference range (FVIII mean 63.5 ± 10.8% within range of 50%–200% and TAT mean 2.11 ± 0.66 μg/L within range of 0–4 μg/L). At room temperature, TAT also exceeded 25% change from T = 0, but was also within the clinical reference range (TAT mean 2.60 ± 0.89 μg/L within range of 0–4 μg/L). A decrease in Protein S is observed at room temperature storage at 26 h (mean 62.0 ± 15.6 % and a mean % change of −43% ± 14%) but the mean value is within the clinical reference range (57%–155%). At approximately 8 h post-rehydration, the refrigerated and room temperature Protein S activity levels are similar (98.4 ± 0.3 and 89.5 ± 10.3, respectively). The percent change for Protein S exceeded 25% between the $t = 8$ and $t = 20$ h timepoints.

4 | DISCUSSION

Early infusion of up to 2 units of plasma following traumatic injury has been shown to increase survival, but the logistics and cold chain requirements of thawed or liquid plasma limit the feasibility of providing plasma for prehospital resuscitation[10,12] Spray-dried plasma provides an alternative to thawed and liquid plasma that is comparable with respect to coagulation factor activity and chemistries and has proven to be safe in human subjects[16] The present study demonstrates acceptable spray-dried plasma stability during storage for up to 12 months at 20°C–24°C and for up to 24 months at 1°C–6°C. The moderate changes in coagulation factors and markers of activation observed after drying and storage result in a product similar to standard-of-care products used around the world. Overall, previous studies have documented changes in plasma characteristics in a variety of products and storage durations that are broadly similar to those documented in this study[18–21]

In the ODP manufacturing process, stability of coagulation factor proteins is improved by addition of the commonly used excipient, glycine. The total glycine concentration of 70 mM used for pretreating plasma prior to spray drying is similar to those found in other approved plasma and plasma-derived products[22] The removal of water and dissolved carbon dioxide in spray drying (and also in lyophilization) results in a basic pH (typically in the range of 8.0) upon reconstitution with sterile water for injection. To achieve a more physiologic pH after reconstitution, the plasma is pretreated with HCl. This also contributes to stabilizing certain proteins including vWF. The reduction in vWF:RCo during spray drying has been previously investigated. The vWF:RCo assay is known to be sensitive to high molecular weight vWF multimers, though it poorly predicts bleeding risk across the range of type 1 von Willebrand disease to low-normal levels[23,24] Spray drying causes cleavage of ultra-high molecular weight multimers, shifting the vWF multimer pattern toward medium and lower molecular weight multimers with reduction of vWF:RCo to the low-normal range. Total vWF antigen is preserved, as well as hemostatic function as measured in thromboelastographic and microfluidic assays that can assess vWF function under venous and arterial shear regimes[25,26] Taken together, the results of the current study as well as the thromboelastographic and microfluidic assay results suggest that the atomization and heat treatment that are integral to spray drying, while altering vWF multimer size distribution, nevertheless yield a product that can support primary hemostasis to the extent this can be assessed by in vitro methods. In addition, these changes in vWF size distribution are not likely to be of clinical significance in the setting of traumatic hemorrhage due to the release of large quantities of ultra-high molecular weight vWF multimers from the endothelium[27] These large vWF multimers may contribute to trauma pathophysiology, particularly in traumatic brain injury, and a resuscitation product with relatively reduced large vWF multimers may avoid exacerbating vWF-mediated pathology[28,29] Further study of the role of vWF in trauma and resuscitation is warranted.

Interpretation of this study is subject to several limitations. In vitro assays of hemostatic function may not fully characterize the in vivo function of spray-dried plasma. Furthermore, the limited selection of assays performed was guided by regulatory authorities and generally accepted clinical considerations. Other technical approaches used in protein chemistry could provide a deeper understanding of molecular changes that may occur in spray drying. Stability of spray-dried plasma was assessed under a limited number of environmental conditions and may not reflect stability under a wider range of temperatures encountered in prehospital use.

Spray-dried plasma offers distinct advantages over other plasma products. It reduces cold chain dependence for transport and storage. It eliminates the problem of wastage inherent in the use of short shelf-life thawed plasma. It can be more effectively deployed in rural or austere settings. Spray-dried plasma is stored in transfusion-ready plastic bags, bypassing the challenge presented by fragile glass containers used with other dried plasma products. Indeed, a recent study comparing

dried plasma products documented user preference for a plastic bag system over glass bottles.[30] Dried plasma products are not a replacement for full resuscitation with components or whole blood but can serve as a bridge in DCR when other products are unavailable. Governments have recognized the need for dried plasma products and funded their development. Spray drying represents a scalable, distributed manufacturing approach to meeting this public health need. The results presented herein suggest that spray-dried plasma production results in a product with in vitro characteristics comparable to currently accepted standard-of-care products. Further development and study of spray-dried plasma is warranted.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author.

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REFERENCES

1. Spinella PC, Cap AP. Prehospital hemostatic resuscitation to achieve zero preventable deaths after traumatic injury. Curr Opin Hematol. 2017;24(6):529–35.
2. Halvachizadeh S, Mariani D, Pfeifer R. Impact of trauma on society. Eur J Trauma Emerg Surg. 2025;51(1):155.
3. Juarez-Vela R, Andres-Esteban EM, Santolalla-Arnedo I, Ruiz de Vinaspre-Hernandez R, Benito-Puncel C, Serrano-Lazaro A, et al. Epidemiology and associated factors in transfusion management in intensive care unit. J Clin Med. 2022;11(12):3532.
4. Chapman MP, Moore EE, Moore HB, Gonzalez E, Morton AP, Chandler J, et al. The "death diamond": rapid thrombelastography identifies lethal hyperfibrinolysis. J Trauma Acute Care Surg. 2015;79(6):925–9.
5. Holcomb JB, Jenkins D, Rhee P, Johannigman J, Mahoney P, Mehta S, et al. Damage control resuscitation: directly addressing the early coagulopathy of trauma. J Trauma. 2007;62(2):307–10.
6. Holcomb JB, Tilley BC, Baraniuk S, Fox EE, Wade CE, Podbielski JM, et al. Transfusion of plasma, platelets, and red blood cells in a 1:1:1 vs a 1:1:2 ratio and mortality in patients with severe trauma: the PROPPR randomized clinical trial. JAMA. 2015;313(5):471–82.
7. Cap AP, Pidcoke HF, Spinella P, Strandenes G, Borgman MA, Schreiber M, et al. Damage control resuscitation. Mil Med. 2018;183(suppl_2):36–43.
8. Shackelford SA, Del Junco DJ, Powell-Dunford N, Mazuchowski EL, Howard JT, Kotwal RS, et al. Association of prehospital blood product transfusion during medical evacuation of combat casualties in Afghanistan with acute and 30-day survival. JAMA. 2017;318(16):1581–91.
9. Deeb AP, Guyette FX, Daley BJ, Miller RS, Harbrecht BG, Claridge JA, et al. Time to early resuscitative intervention association with mortality in trauma patients at risk for hemorrhage. J Trauma Acute Care Surg. 2023;94(4):504–12.
10. Sperry JL, Guyette FX, Brown JB, Yazer MH, Triulzi DJ, Early-Young BJ, et al. Prehospital plasma during air medical transport in trauma patients at risk for hemorrhagic shock. N Engl J Med. 2018;379(4):315–26.
11. 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.
12. Adams PW, Warren KA, Guyette FX, Yazer MH, Brown JB, Daily BJ, et al. Implementation of a prehospital air medical thawed plasma program: is it even feasible? J Trauma Acute Care Surg. 2019;87(5):1077–81.
13. 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.
14. 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.
15. Pusateri AE, Given MB, Macdonald VW, Homer MJ. Comprehensive US government program for dried plasma development. Transfusion. 2016;56(Suppl 1):S16–23.
16. Popovsky MBL, Leitman S, Nestheide S, Munoz D, Treml A, Post S, et al. 2025 abstract information: spray-dried plasma: a multi-center, prospective, randomized, dose-escalation cohort safety clinical trial. Transfusion. 2025;65(S2):13A.
17. Gill JC, Endres-Brooks J, Bauer PJ, Marks WJ Jr, Montgomery RR. The effect of ABO blood group on the diagnosis of von Willebrand disease. Blood. 1987;69(6):1691–5.
18. 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.
19. Meledeo MA, Peltier GC, McIntosh CS, Bynum JA, Corley JB, Cap AP. Coagulation function of never frozen liquid plasma stored for 40 days. Transfusion. 2021;61(Suppl 1):S111–8.
20. Meledeo MA, Peltier GC, McIntosh CS, Bynum JA, Cap AP. Optimizing whole blood storage: hemostatic function of 35-day stored product in CPD, CP2D, and CPDA-1 anticoagulants. Transfusion. 2019;59(S2):1549–59.
21. Matijevic N, Wang YW, Cotton BA, Hartwell E, Barbeau JM, Wade CE, et al. Better hemostatic profiles of never-frozen liquid plasma compared with thawed fresh frozen plasma. J Trauma Acute Care Surg. 2013;74(1):84–90. discussion-1.
22. Hubbard A, Bevan S, Matejtschuk P. Impact of residual moisture and formulation on factor VIII and factor V recovery in lyophilized plasma reference materials. Anal Bioanal Chem. 2007;387(7):2503–7.
23. Woods AI, Blanco AN, Chuit R, Meschengieser SS, Kempfer AC, Farias CE, et al. Major haemorrhage related to surgery in patients with type 1 and possible type 1 von Willebrand disease. Thromb Haemost. 2008;100(5):797–802.

24. Favaloro EJ, Bonar R, Chapman K, Meiring M, Funk Adcock D. Differential sensitivity of von Willebrand factor (VWF) 'activity' assays to large and small VWF molecular weight forms: a cross-laboratory study comparing ristocetin cofactor, collagen-binding and mAb-based assays. J Thromb Haemost. 2012;10(6):1043–54.
25. Meledeo MA, Liu QP, Peltier GC, Carney RC, CS MI, 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.
26. 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.
27. Dyer MR, Plautz WE, Ragni MV, Alexander W, Haldeman S, Sperry JL, et al. Traumatic injury results in prolonged circulation of ultralarge von Willebrand factor and a reduction in ADAMTS13 activity. Transfusion. 2020;60(6):1308–18.
28. Xu X, Wang C, Wu Y, Houck K, Hilton T, Zhou A, et al. Conformation-dependent blockage of activated VWF improves outcomes of traumatic brain injury in mice. Blood. 2021;137(4): 544–55.
29. Zeineddin A, Dong JF, Wu F, Terse P, Kozar RA. Role of Von Willebrand factor after injury: it may do more than we think. Shock. 2021;55(6):717–22.
30. Ehn K, Skallsjo G, Romlin B, Sandstrom G, Sandgren P, Wikman A. An experimental comparison and user evaluation of three different dried plasma products. Vox Sang. 2025; 120(11):1058–65.

SUPPORTING INFORMATION

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

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