AWARD NUMBER: W81XWH-20-1-0406

TITLE: Novel Dried Cryoprecipitate-Based Intervention to Improve Outcomes from Trauma and Hemorrhagic Shock: Applicability for Multidomain Operations

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CONTRACTING ORGANIZATION: University of Maryland, Baltimore, MD

REPORT DATE: October 2023

TYPE OF REPORT: Final

PREPARED FOR: U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
October 2023	Final	15Jun2020 – 14Jun2023

4. TITLE AND SUBTITLE

Novel Dried Cryoprecipitate-Based Intervention to Improve Outcomes from Trauma and Hemorrhagic Shock: Applicability for Multidomain Operations

5a. CONTRACT NUMBER
W81XWH-20-1-0406

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

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8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Purpose of this study was to define the role of 5PRC and LPRC using 2 different small animal models of HS to examine the effect of these novel products on both hemostasis and endothelial protection. The long-term goal is FDA approval of these products for clinical and field use after HS. We HYPOTHESIZE that pathogen reduced cryoprecipitate-based interventions will decrease both early hemorrhagic deaths and later multiple organ failure (MOF) through their dual effects on hemostasis and endothelial stability. To test this hypothesis, two specific aims were carried out: SA1. Determine the effect of early cryoprecipitate on hemostasis, organ function, and mortality in a short- term mouse model of trauma and uncontrolled hemorrhage (UCH). SA2. Determine the effect of early cryoprecipitate on endothelial protection, MOF and mortality in a mouse model of sustained hypotensive resuscitation (SHR). Results from the current study have for the first time demonstrated in military relevant mouse models of hemorrhagic shock that cryoprecipitate has resuscitative and endothelial protective effects similar to that of plasma. Importantly, we have shown that immediate use cryoprecipitate is feasible and effective with newly developed pathogen-reduced long post thaw (five day) shelf-life cryoprecipitate (now FDA approved) and pathogen-reduced lyophilized cryoprecipitate, paving the way for their use in severely injured warfighters.

15. SUBJECT TERMS Hemorrhagic shock, prolonged hypotensive resuscitation, cryoprecipitate, endotheliopathy of trauma, pathogen reduced 5-day shelf life cryoprecipitate, pathogen reduced lyophilized cryoprecipitate

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRDC
Unclassified	Unclassified	Unclassified	Unclassified	21	19b. TELEPHONE NUMBER *(include area code)*

TABLE OF CONTENTS

1. INTRODUCTION:

Hemorrhagic shock (HS) remains the leading cause of early death among the severely injured in both civilian and military settings. Through the institution of early and balanced resuscitation strategies, hemorrhagic deaths have decreased. This decrease in mortality from plasma-based resuscitative strategies appears to extend beyond its ability to correct trauma-induced coagulopathy and provide hemorrhage control and is hypothesized to involve additional protective effects to the post-shock dysfunctional endothelium. Survivors of HS demonstrate an endotheliopathy of trauma (EoT). Advances in hemostatic resuscitation have not only improved outcomes in injured patients with HS but have been accompanied by a more in-depth knowledge of how hemostatic blood products mitigate the EoT and repair the dysfunctional endothelium. We have shown that fibrinogen is a key molecule in plasma that binds to endothelial syndecan-1, the backbone of the endothelial glycocalyx, to mitigate the EoT. In the US, cryoprecipitate is used to replace fibrinogen as part of massive transfusion protocols (MTPs) to control bleeding after trauma. In the US, at best, MTPs include cryoprecipitate only late in the protocol and/or in response to low plasma fibrinogen levels. Additionally, logistic challenges exist in the use of conventional cryoprecipitate (CC) in the battlefield and even in many civilian centers. CC is stored frozen, similar to plasma, and thus requires time and specialized equipment to thaw. Once thawed, shelf life of CC is limited to four to six hours. *Recognizing this gap* and the risk of disease transmission with all blood products, a pathogen-reduced long post thaw (five day) shelf-life cryoprecipitate (5PRC) and a pathogen-reduced lyophilized cryoprecipitate (LPRC) are being developed that could provide early cryoprecipitate -based resuscitation en-route and in the forward environment. The major ***objective*** of this effort is to define the role of 5PRC and LPRC using 2 different small animal models of HS to examine the effect of these novel products on both hemostasis and endothelial protection. The ***long-term goal*** is FDA approval of these products for clinical and field use after HS. We ***HYPOTHESIZE*** that pathogen reduced cryoprecipitate-based interventions will decrease both early hemorrhagic deaths and later multiple organ failure (MOF) through their dual effects on hemostasis and endothelial stability. To test this hypothesis, two ***specific aims*** were carried out: ***SA1***. ***Determine the effect of early cryoprecipitate on hemostasis, organ function, and mortality in a short- term mouse model of trauma and uncontrolled hemorrhage (UCH). SA2. Determine the effect of early cryoprecipitate on endothelial protection, MOF and mortality in a mouse model of sustained hypotensive resuscitation (SHR).*** The proposed research and downstream investigations will improve treatment of HS by providing critical information about cryoprecipitate-based resuscitation that would be of benefit to both military and civilian populations. Short-term, we will obtain a better understanding of the effects of cryoprecipitate-based resuscitation on both hemostasis and organ function. Long-term, our findings lay the groundwork for identifying best practices for next generation cryoprecipitate-based product resuscitation, specifically 5PRC and LPRC, and their ability to mitigate the consequences of hemorrhage in the prolonged care construct.

2. KEYWORDS:

hemorrhagic shock, cryoprecipitated fibrinogen complex, prolonged hypotensive resuscitation, lyophilized cryoprecipitate; von Willebrand Factor; ADAMTS13; endotheliopathy of trauma; mouse model of polytrauma and uncontrolled hemorrhage

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Specific Aim 1. Determine the effect of early cryoprecipitate on hemostasis, endothelial protection, organ(lung) function, and mortality in a short term mouse model of trauma and uncontrolled hemorrhage (UCH)	**Timeline**	**Site 1**
Major Task 1	Months	
Subtask 1. Obtain local IACUC approval (estimated total number 159)	0-2	Completed
Subtask 2. Obtain ARUCO approval	0-4	Completed
Milestone Achieved: HRPO/ACURO Approvals	4	*Completed*
Major Task 2		
Subtask 1 Develop/optimize mouse model UCH (n=10)	4	Completed
Subtask 2. Complete mouse surgeries UCH (n=72)	4-10	completed
Subtask 3. Coagulation, hemostasis, shed syndecan	10-12	completed
Subtask 4 Lung histology, MPO, syndecan immunostaining and BAL protein	10-12	completed
Subtask 5: Lung VE-cadherin and vWF	10-12	completed
Subtask 6: Data Analysis	13-14	completed
Milestone(s) Achieved: Completion of SA1	14	
Specific Aim 2. SA2. Determine the effect of early cryoprecipitate on endothelial protection, organ failure and mortality in a mouse model of sustained hypotensive resuscitation (SHR).		
Major Task 3		
Subtask 1 Develop/optimize mouse model SHR (n=5)	12	Completed
Subtask 2. Complete mouse studies SHR (n=72)	13-20	completed
Subtask 3. Lung assays	20-23	completed
Subtask 4. Lung VE-cadherin and vWF	20-23	completed
Subtask 5. Small bowel histology	20-23	completed
Subtask 7 Serum biomarkers of renal and liver injury	20-23	completed
Subtask 7: Data analysis	23-24	completed
Milestone(s) Achieved: Completion of SA2	24	
Major Task 4		
Subtask 1. Write abstracts/posters/manuscripts	23-24	completed
Milestone(s) Achieved: Results dissemination: manuscript and abstracts publications and presentations	24	

What was accomplished under these goals?

Specific Aim 1. Determine the effect of early cryoprecipitate on hemostasis, organ function, and mortality in a short- term mouse model of trauma and uncontrolled hemorrhage (UCH).
Recent studies in severely injured patients suggest an important role of von-Willebrand Factor (VWF) and ADAMTS13 in the endotheliopathy of trauma (EoT). We *hypothesized* that the early use of cryoprecipitate would be effective as an endothelial protector by supplementing physiologic VWF and ADAMTS13 to reverse the EoT. We tested a pathogen-reduced lyophilized cryoprecipitate (LPRC) that could expedite the early administration of cryoprecipitate in the battlefield. Using **a** mouse polytrauma model with uncontrolled hemorrhage (UCH) from liver injury was utilized followed by hypotensive resuscitation (MAP 55-60) x 3 hours with Lactated Ringers (LR), fresh frozen plasma (FFP), conventional pathogen-reduced cryoprecipitate (CPRC) and LPRC. Blood was collected for measurement of syndecan-1, von Willebrand Factor (VWF), and ADAMTS13 by ELISA. Lungs were stained for histopathologic injury and syndecan-1 and bronchial alveolar lavage (BAL) fluid harvested for protein as an indicator of permeability. Statistical analysis was by ANOVA followed by Bonferroni correction. Following polytrauma and UCH, blood loss was similar across groups while volume of resuscitation was higher in the LR group compared to the other resuscitation groups (**Table 1**). Mean arterial pressure was improved by resuscitation with the cryoprecipitate products, comparable to plasma (**Fig. 1**). Lung histopathologic injury (Fig 2), syndecan-1 immunostaining (**Fig 3**) and BAL protein (**Fig 2**) were higher with LR compared to resuscitation with FFP and CPRC, while LPRC further reduced BAL compared to FFP and CPRC. ADAMTS13:VWF ratio (**Fig 4**) was significantly lower in LR but improved with FFP and CPRC, comparable to shams while LPRC further increased this ratio. In summary, the protective effects of CPRC and LPRC were comparable to FFP in ameliorating the endotheliopathy of trauma in our murine polytrauma and UCH model. LPRC may also provide additional benefit by enhancing the ADAMTS13:VWF ratio. These data provide evidence of the safety and efficacy of LPRC and warrants further investigation for its potential application in military settings once approved for human administration.

Table 1. Physiologic parameters across experimental groups

Group	Sample Size	Mortality (%)	Volume of hemoperitoneum (ul)	Blood removed to achieve shock state (ul)	Volume resuscitationin ul (ml/kg)
Sham	17	0	N/A	N/A	N/A
LR	15	5 (33%)	676±211	262±94	1270±340 (43±10)
FFP	14	3 (14%)	634±180	302±96	364±106 (11±3)
CPRC	15	5 (33%)	592±254	358±127	337±108 (11±4)
LPRC	13	4 (31%)	729±222	273±174	481±156 (16±5)
p value		NS	NS	NS	<0.01

LR=Lactated Ringers, FFP= fresh frozen plasma; CPRC=conventional pathogen-reduced cryoprecipitate; LPRC=lyophilized pathogen-reduced cryoprecipitate

Figure 1.

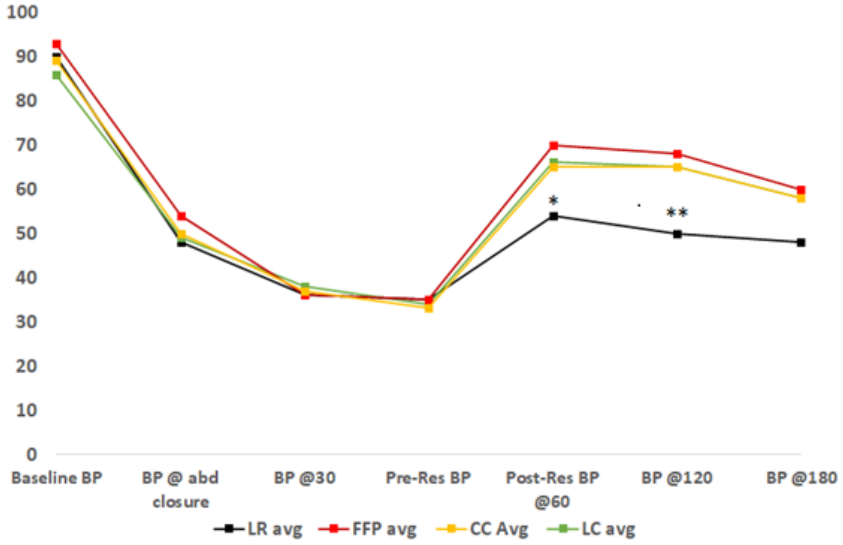

Figure 1. Mean arterial pressure after polytrauma and hypotensive resuscitation is improved by resuscitation with cryoprecipitate products. Mice underwent polytrauma with muscle crush and tibia fracture followed by laparotomy and liver injury with 60 minutes of uncontrolled hemorrhagic shock then resuscitation to a MAP of 55-60 mm Hg for 3 hours with Lactated Ringers (LR), Fresh Frozen Plasma (FFP), Conventional Pathogen-Reduced Cryoprecipitate (CC), and Lyophilized Pathogen-Reduced Cryoprecipitate (LPRC) and compared to shams. Blood pressure is shown at baseline, abdominal closure after liver laceration (BP @ abd closure), 30 minutes after reaching shock state (BP @ 30), 60 minutes after reaching shock state which was also just prior to the start of resuscitation (pre-res BP @60), then at 60, 120, and 180 minutes after resuscitation (post-res BP). Results were analyzed by ANOVA with Tukey post hoc with multiple comparisons corrections; n=9-11/group.

Figure 2.

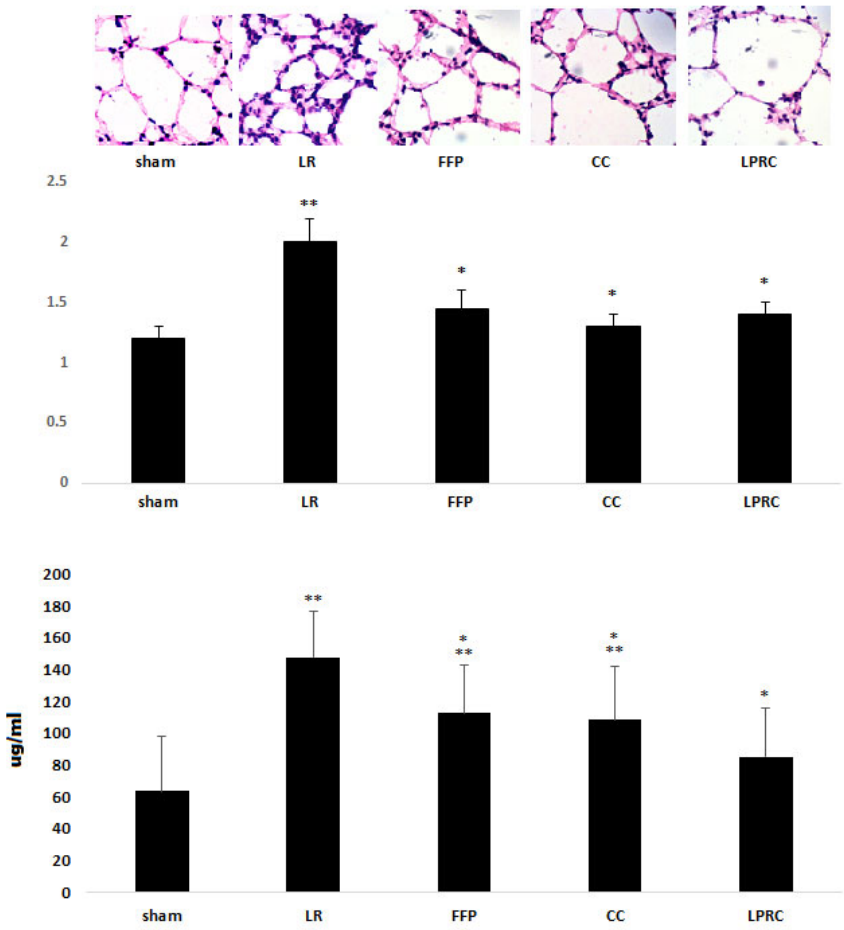

Figure 2. **Lung injury and permeability reduced by cryoprecipitate products**. Mice underwent polytrauma with muscle crush and tibia fracture followed by laparotomy and liver injury with 60 minutes of uncontrolled hemorrhagic shock then resuscitation to a MAP of 55-60 mm Hg for 3 hours with Lactated Ringers (LR), Fresh Frozen Plasma (FFP), Conventional Pathogen-Reduced Cryoprecipitate (CC), and Lyophilized Pathogen-Reduced Cryoprecipitate (LPRC) and compared to shams. Lung tissue and bronchoalveolar lavage (BAL) collected at the time of euthanasia. **Upper panel)** Lung Histopathologic Injury. Shown are representative images and the corresponding lung injury scores and **Lower panel**.) Lung bronchial alveolar lavage (BAL) protein as an indicator of permeability. Data is reported as mean ±SD, n=5-8 /group and analyzed by one-way ANOVA with Bonferroni post hoc; **$p<0.05$ vs sham; * $p<0.05$ vs LR.

Figure 3.

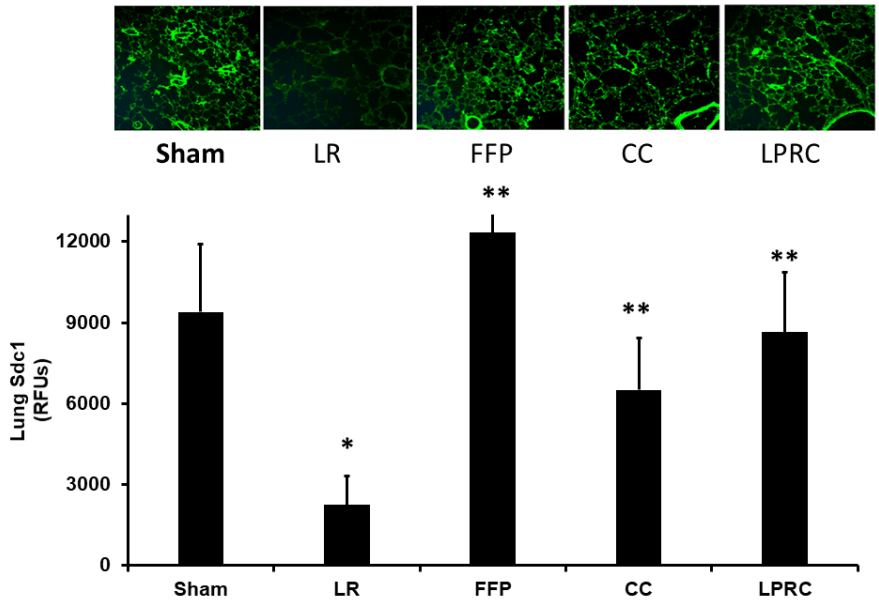

Figure 3. Lung syndecan-1 immunostaining enhanced by cryoprecipitate products. Mice underwent polytrauma with muscle crush and tibia fracture followed by laparotomy and liver injury with 60 minutes of uncontrolled hemorrhagic shock then resuscitation to a MAP of 55-60 mm Hg for 3 hours with Lactated Ringers (LR), Fresh Frozen Plasma (FFP), Conventional Pathogen-Reduced Cryoprecipitate (CC), and Lyophilized Pathogen-Reduced Cryoprecipitate (LPRC) and compared to shams. Lung tissue was stained with anti-mouse syndecan-1 antibody and Alexa Fluor 488 goat anti-mouse IgG and imaged with a fluorescent microscope. Shown are representative images and the corresponding relative fluorescent units (RFUs). Data is reported as mean ±SD, n= 4/group with a minimum of three images per animal and analyzed by one-way ANOVA with Bonferroni post hoc. **p<0.05 vs sham; * p<0.05 vs LR.

Figure 4.

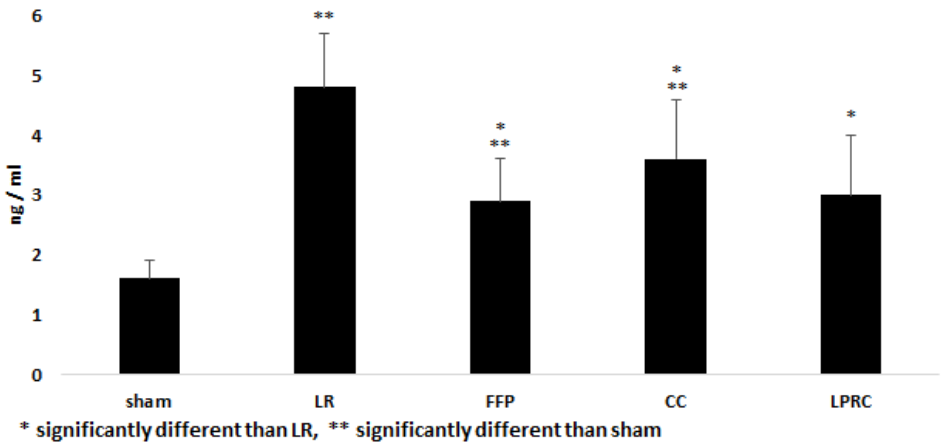

Figure 4. Systemic syndecan shedding was lessened by cryoprecipitate products. Mice underwent polytrauma with muscle crush and tibia fracture followed by laparotomy and liver injury with 60 minutes of uncontrolled hemorrhagic shock then resuscitation to a MAP of 55-60 mm Hg for 3 hours with Lactated Ringers (LR), Fresh Frozen Plasma (FFP), Conventional Pathogen-Reduced Cryoprecipitate (CC), and Lyophilized Pathogen-Reduced Cryoprecipitate (LPRC) and compared to shams. Blood was obtained at the time of euthanasia for measurement of syndecan-1 by ELISA. Data is reported as mean ±SD, n= 5-8/group and analyzed by one-way ANOVA with Bonferroni post hoc. **p<0.05 vs sham; * p<0.05 vs LR.

Figure 5.

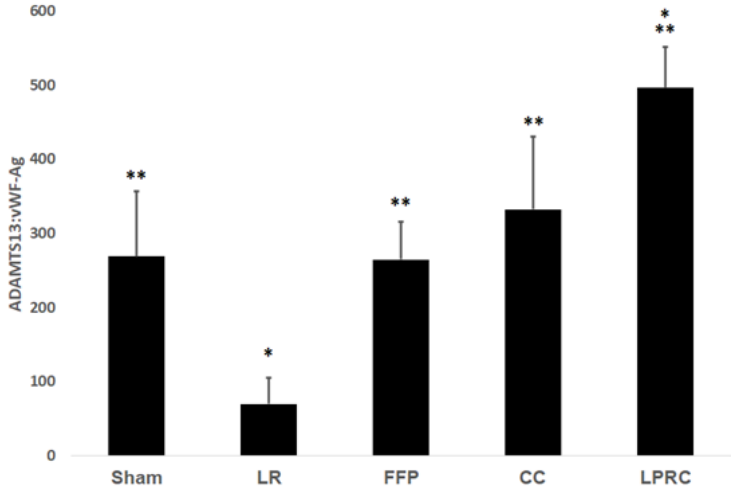

Figure 5. Ratio of ADAMTS13:VWF is improved by cryoprecipitate products. Mice underwent polytrauma with muscle crush and tibia fracture followed by laparotomy and liver injury with 60 minutes of uncontrolled hemorrhagic shock then resuscitation to a MAP of 55-60 mm Hg for 3 hours with Lactated Ringers (LR), Fresh Frozen Plasma (FFP), Conventional Pathogen-Reduced Cryoprecipitate (CC), and Lyophilized Pathogen-Reduced Cryoprecipitate (LPRC) and compared to shams. Blood was obtained at the time of euthanasia for measurement of VWF and ADAMTS13 by ELISA. Shown is the ratio of ADAMTS13: VWF Ag. n=4-8/group. **p<0.05 vs sham; * p<0.05 vs LR.

Specific Aim 2. Determine the effect of early cryoprecipitate on endothelial protection, MOF and mortality in a mouse model of sustained hypotensive resuscitation (SHR).

Cryoprecipitate (CP) can augment hemostasis after hemorrhagic shock (HS). Similar to fresh frozen plasma (FFP), CP may provide short-term endothelial protection. We tested a new 5-day post thaw CP (pathogen-reduced cryoprecipitated fibrinogen complex; 5PRC) and lyophilized pathogen-reduced cryoprecipitate (LPRC) to overcome challenges of early administration and hypothesized that 5PRC and LPRC would provide lasting organ protection in a rodent model of HS. Mice underwent trauma/HS (laparotomy then HS, mean arterial pressure (MAP) 35 x 90 minutes then 6

hours hypotensive resuscitation (MAP 55-60) with lactated Ringers (LR), FFP, CP, 5PRC or LPRC and compared to shams. Animals were followed for 72 hours. Organs and blood were collected. Data presented as mean +/-SD, ANOVA with Bonferroni post-hoc. MAP was comparable between experimental groups at baseline, pre-resuscitation and 6 hours per protocol. However, volume needed to resuscitate to target MAP over 6 hours was less than half for CP, 5PRC, LPRC and FFP compared to LR, suggesting that CP products can serve as effective resuscitative agents. MAP at 72 hours was also significantly higher in the CP, 5PRC and FFP groups compared to LR. Resuscitation with CP, 5PRC, and LPRC provided lasting protection from gut injury (**Fig 6**) and enhanced syndecan immunostaining (**Fig 7**) comparable to FFP, while LR mice demonstrated persistent organ dysfunction. Sustained endothelial protection was demonstrated by lessened lung permeability (**Fig 8**) and while Cystatin C as an indicator of kidney function and liver AST and ALT returned to sham levels in all groups **(Table 2**). In summary, cryoprecipitate products can provide lasting organ protection comparable to FFP in a sustained rodent model of trauma/HS and hypotensive resuscitation. The availability of 5PRC and LPRC will allow for investigation into the immediate use of cryoprecipitate for severely injured patients. As lyophilized products such as cryoprecipitate become available clinically, their use has important implications for pre-hospital, rural and battlefield usage.

Figure 6.

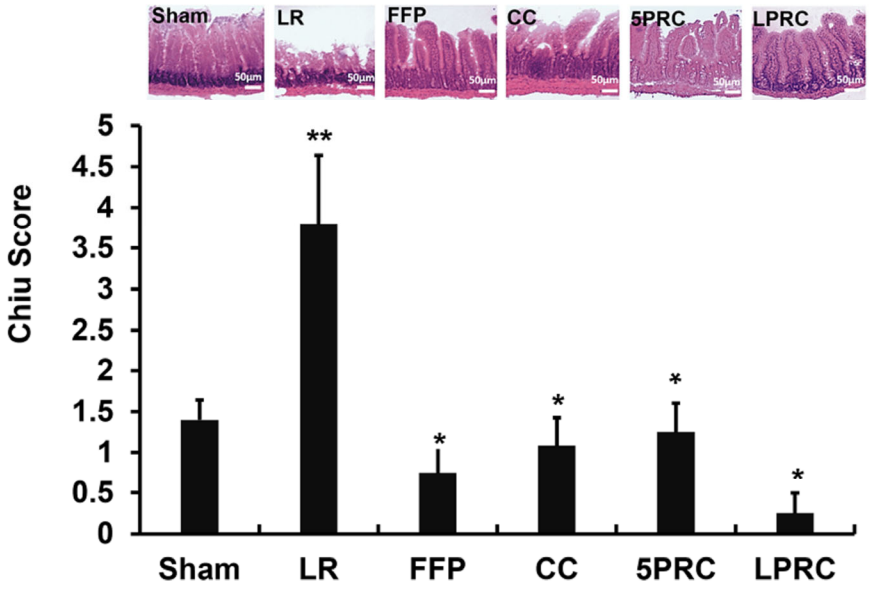

Figure 6. Gut histopathologic injury was reduced by the cryoprecipitate groups and FFP compared to LR. Mice underwent trauma/hemorrhagic shock for 90 minutes followed by prolonged hypotensive resuscitation with either LR, FFP, CC, 5PRC, or LPRC and compared to sham mice. Shown are representative images and the corresponding gut injury scores. Data is reported as mean ±SD, n=5-6 /group and analyzed by one-way ANOVA with Bonferroni post hoc. **p<0.05 vs sham; * p<0.05 vs LR. Abbreviations: LR= lactated Ringers; FFP= fresh frozen plasma; CC=conventional cryoprecipitate; 5PRCP= 5-day post thaw pathogen reduced cryoprecipitate; LPRC=lyophilized pathogen reduced cryoprecipitate.

Figure 7.

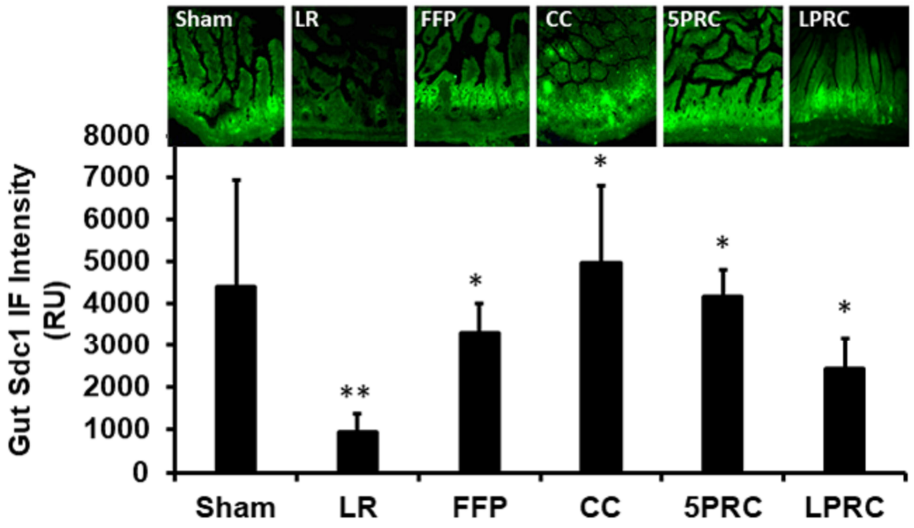

Figure 7. Gut syndecan-1 immunostaining. Mice underwent trauma/hemorrhagic shock for 90 minutes followed by prolonged hypotensive resuscitation with either LR, FFP, CC, 5PRC, or LPRC and compared to sham mice. Shown are representative images and the corresponding RFUs. Data is reported as mean ±SD, n=3-4 /group and analyzed by one-way ANOVA with Bonferroni post hoc. **p<0.05 vs sham; * p<0.05 vs LR. Abbreviations: LR= lactated Ringers; FFP= fresh frozen plasma; CC=conventional cryoprecipitate; 5PRCP= 5-day post thaw pathogen reduced cryoprecipitate; LPRC=lyophilized pathogen reduced cryoprecipitate: RFU= relative fluorescent units.

Figure 8.

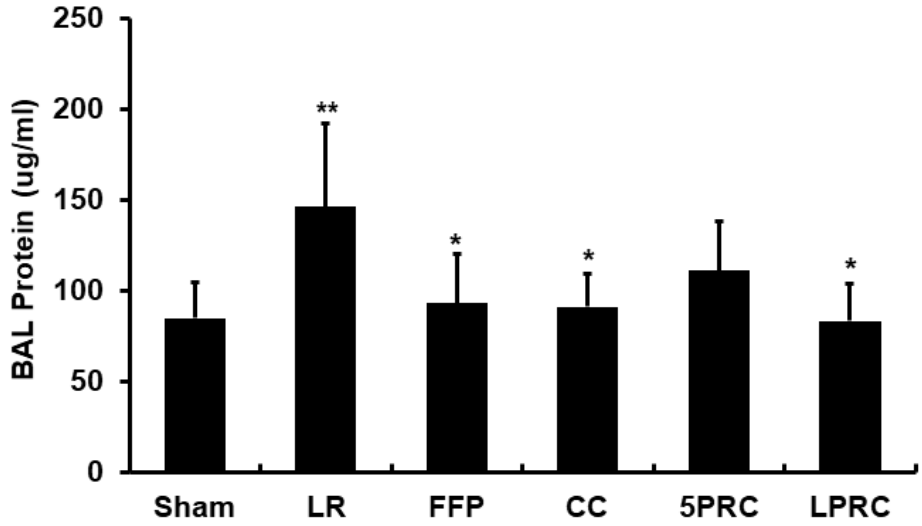

Figure 8. Lung permeability reduced by cryoprecipitate and FFP compared to LR. Mice underwent trauma/hemorrhagic shock for 90 minutes followed by prolonged hypotensive resuscitation with either LR, FFP, CC, 5PRC, or LPRC and compared to sham mice. Bronchoalveolar fluid was obtained at the time of euthanasia and protein measured as an indicator

of lung permeability. Data is reported as mean ±SD, n=5-7/group and was analyzed by one-way ANOVA with Bonferroni post hoc. **p<0.05 vs sham; * p<0.05 vs LR. Abbreviations: LR= lactated Ringers; FFP= fresh frozen plasma; CC=conventional cryoprecipitate; 5PRCP= 5 day post-thaw pathogen reduced cryoprecipitate; LPRC=lyophilized pathogen reduced cryoprecipitate.

Table 2. Indices of organ injury.

Group	Lung Histology Score	Lung syndecan RFUs	Cystatin C ng/ml	AST ng/ml	ALT ng/ml	Plasma Syndecan ng/ml	Plasma VWF ng/ml
Sham	2.2 ± 0.4	7277 ± 713	1288 ± 219	55.6 ± 13.0	19.9 ± 8.5	74 ± 6.4	0.8 ± 0.9
LR	2.5 ± 0.4	7131 ± 412	1279 ± 109	66.1 ± 10.9	36.2 ± 3.1*	74 ± 1.0	0.7 ± 1.3
FFP	2.5 ± 0	6891 ± 311	1261 ± 153	53.6 ± 5.5	26.0 ± 10.1	63 ± 5.5	1.3 ± 1.2
CC	2.5 ± 0	7109 ± 686	1223 ± 189	57.6 ± 9.4	27.2 ± 8.1	83 ± 10	1.4 ± 0.4
5PRC	2.4 ± 0.3	5767 ± 277	1494 ± 159	53.5 ± 10.4	24.8 ± 5.4	56.3 ± 3.3	0.6 ± 0.2
LPRC	2.3 ± 0.3	5596 ± 161	1416 ± 268	63.9 ± 7.1	31.1 ± 9.4	62 ± 7.8	1.4 ± 0.6

*p<0.05 vs sham, #p<0.05 vs LR
LR=lactated Ringers, FFP=fresh frozen plasma, CC=conventional cryoprecipitate, LPRC=lyophilized pathogen reduced cryoprecipitate, 5PRC 5-day pathogen reduced cryoprecipitate; RFUs= relative fluorescent units; VWF=von Willebrand Factor

What opportunities for training and professional development has the project provided?

Nothing additional to report

How were the results disseminated to communities of interest?

Data generated from the current project was presented in part at the following meetings:

52nd Annual Meeting of the Western Trauma Association March 5-10, 2023 in Alberta, Canada

Cellular Therapeutics in Trauma and Critical Care, Phoenix, AZ May 2023.

46th Annual Conference, Shock Society, Portland. OR, June 2023

What do you plan to do during the next reporting period to accomplish the goals?

Nothing additional to report

4. **IMPACT:**

What was the impact on the development of the principal discipline(s) of the project?

Results from the current study have for the first time demonstrated in military relevant mouse models of hemorrhagic shock that cryoprecipitate has resuscitative and endothelial protective effects similar to that of plasma. Importantly, we have shown that immediate use cryoprecipitate is feasible and effective with newly developed pathogen-reduced long post thaw (five day) shelf-life cryoprecipitate (now FDA approved) and pathogen-reduced lyophilized cryoprecipitate, paving the way for their use in severely injured warfighters. Data from this project was used in a recent DOD submission to test the 5-day post shelf-life cryoprecipitate in a prospective randomized clinical trial.

What was the impact on other disciplines?

It is possible that the early use of cryoprecipitate can similarly be used in other patient populations with hemorrhage and risk of coagulopathy such as in post-partem hemorrhage and massive gastrointestinal bleeds.

What was the impact on technology transfer?

Cerus Corporation provided the cryoprecipitate products and were actively involved in the project. Results from this study are being used a preliminary data in the above-mentioned clinical trial that was submitted to the DOD and includes the use the 5 day shelf-life product by Cerus

What was the impact on society beyond science and technology?

Nothing additional to report

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

Nothing additional to report

Actual or anticipated problems or delays and actions or plans to resolve them

Nothing additional to report

Changes that had a significant impact on expenditures

Nothing additional to report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/ or select agents

Significant changes in use or care of human subjects

Nothing to report, no human subjects were involved in the current project

Significant changes in use or care of vertebrate animals

Nothing to report

Significant changes in use of biohazards and/or select agents

Nothing to report

6. PRODUCTS:

- **Publications, conference papers, and presentations**
  Journal publications.

Zeineddin A, Wu F, Cao S, Corash L, Pati S, Kozar RA. Immediate Use Cryoprecipitate Products Provide Lasting Organ Protection in a Rodent Model of Trauma/Hemorrhagic Shock and Prolonged Hypotensive Resuscitation: Cryoprecipitate Provides Prolonged Organ Protection. J Trauma Acute Care Surg. 2023 Jun 14. Epub ahead of print. Acknowledgement of federal funding: yes

Zeineddin A, Wu F, Dong JF, Vesselinov R, Neal MD, Corash L, Pati S, Kozar RA. Early lyophilized cryoprecipitate enhances the ADAMTS13/VWF ratio to reduce systemic endotheliopathy and lessen lung injury in a mouse multiple-trauma hemorrhage model. J Trauma Acute Care Surg. 2023 Aug 1;95(2S Suppl 1):S137-S143. Epub 2023 May 22 Acknowledgement of federal funding: yes

Books or other non-periodical, one-time publications.

Nothing additional to report

Other publications, conference papers and presentations.

Nothing additional to report

Website(s) or other Internet site(s)

Nothing additional to report

Technologies or techniques

Nothing additional to report

Inventions, patent applications, and/or licenses

Nothing additional to report

Other Products

We expanded on our previously developed military-relevant mouse model of hemorrhagic shock and prolonged hypotensive resuscitation to now include a polytrauma model with hemorrhagic shock and prolonged hypotensive resuscitation.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Rosemary Kozar
Project Role: Principal Investigator
Researcher Identifier (e.g. ORCID ID): 0000-0002-9198-7351
Nearest person month worked: 1.8
Contribution to Project: Designed study, oversees all aspects and conduct of the study

Name: Feng Wu
Project Role: Research Associate
Researcher Identifier (e.g. ORCID ID): 0000-0003-3113-2332
Nearest person month worked: 2.4
Contribution to Project: Assisting with assays

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period

Nothing additional to report

What other organizations were involved as partners?

Organization Name: Cerus Corporation
Location of Organization: Concord, CA
Partner's contribution to the project: Provided in-kind support: supplied the tested pathogen-reduced cryoprecipitate products

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:

QUAD CHARTS:

9. APPENDICES: