

Characteristics of Liquid Plasma Treated with the INTERCEPT Blood System for Pathogen Inactivation and Stored at 4°C for 14 Days



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Background

There is increased interest in the use of refrigerated (never-frozen, frozen-thawed or liquid) plasma components in emergency room applications and their use can improve plasma utilization^{1a}. Use in trauma situations for critically bleeding patients may improve speed of treatment, eliminating delays associated with thawing frozen plasma, and thereby improve patient care^{1b}.

In Sweden, liquid plasma refrigerated for up to 14 days is considered to be clinically equivalent to FFP for many indications, even though use within 7 days is recommended². Pathogen inactivation of plasma components may be even more important for a blood product stored refrigerated for 1-2 weeks.

The INTERCEPT Blood System™ (IBS) for Plasma was CE marked in 2006 for pathogen inactivation treatment of plasma collected by apheresis, or prepared from whole blood, and is in routine use in several European countries. Disposable sets to manufacture approximately 250,000 plasma sets have been sold since its introduction. IBS is currently not FDA approved for use in the United States.

The INTERCEPT™ process uses amotosalen and UVA illumination to effect pathogen inactivation (Figure 1) in an integrated disposable and residual compounds are removed by a flow compound adsorption device (Figure 2). The treatment has been shown in past studies^{3,4,11} to inactivate a broad spectrum of viruses, bacteria and parasites, as well as leukocytes that contaminate blood products. Coagulation factors and antithrombotic proteins found in fresh, or previously frozen apheresis and WB-derived plasma have been found to be retained well (Table 1). INTERCEPT treated FFP can be stored frozen at ≤-25°C for up to 2 years prior to use.

Table 1: Maintenance of Clotting Time, Plasma Coagulation Factor and Anti-thrombotic Protein Activity after INTERCEPT Treatment* (From Singh et al.³)

Coagulation parameter	Reference range†	Pre-PCT	Post-PCT	Post/pre (%retention)
PT (n=14) sec	11.1-13.5	11.2±0.3	11.6±0.3	1.0±0.1 ‡
APTT (n=13) sec	23.0-35.0	26.9±1.4	31.6±2.1	4.3±1.8 ‡
Fibrinogen (n=91) mg/dL	167-379	290±48	209±36	72±5
FII (n=59) IU/dL	71-127	96±11	85±11	88±4
FV (n=91) IU/dL	77-153	130±21	119±19	92±7
FVII (n=91) IU/dL	58-166	123±26	95±20	78±6
FVIII (n=91) IU/dL	67-235	157±36	115±28	73±7
FIX (n=91) IU/dL	63-143	108±19	88±16	82±4
FX (n=59) IU/dL	66-134	100±13	86±11	86±3
FXI (n=91) IU/dL	62-142	103±22	87±18	85±4
FXIII (n=16) IU/dL	NA	110±11	102±10	93±3
VWF:RCo (n=12) IU/dL	NA	114±44	111±41	98±8
Antithrombotic Protein				
PC (n=25)		109±15	102±14	95±9
PS (n=25)		109±12	107±12	98±5
Antithrombin III (n=26)		94±5	91±6	96±3
a2-Antiplasmin (n=26)		93±5	75±6	80±4

IU/dL = International Units/deciliter.

PCT= INTERCEPT treatment

†The reference range was calculated from the mean SD of untreated, conventional plasma.

‡For PT and PTT, the effect of PCT was calculated by subtracting the pre-PCT values.

*The numbers were corrected to correspond to data audited post publication.

Aims

This study investigated the impact of IBS on coagulation parameters of liquid plasma stored refrigerated for a period of 14 days and compared it to control liquid plasma.

Figure 1: INTERCEPT Mechanism of Action

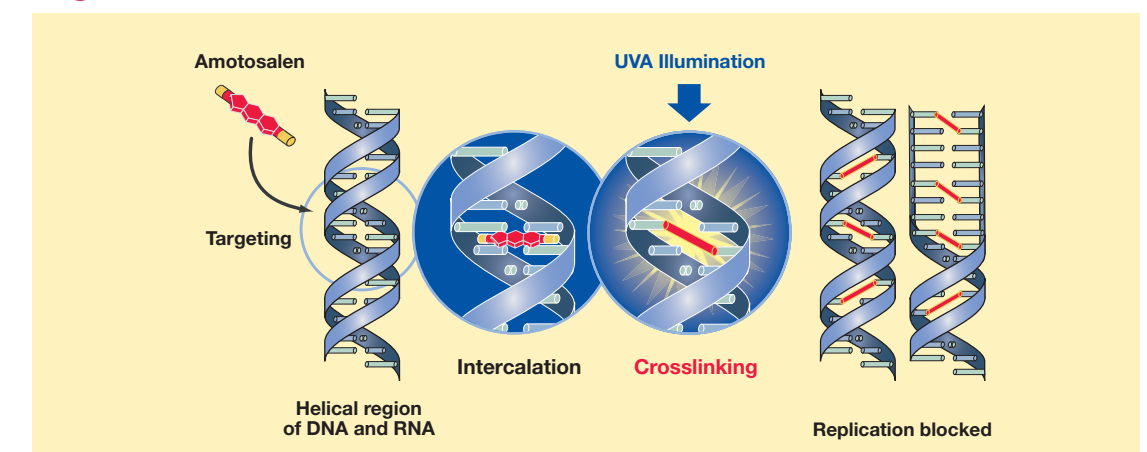
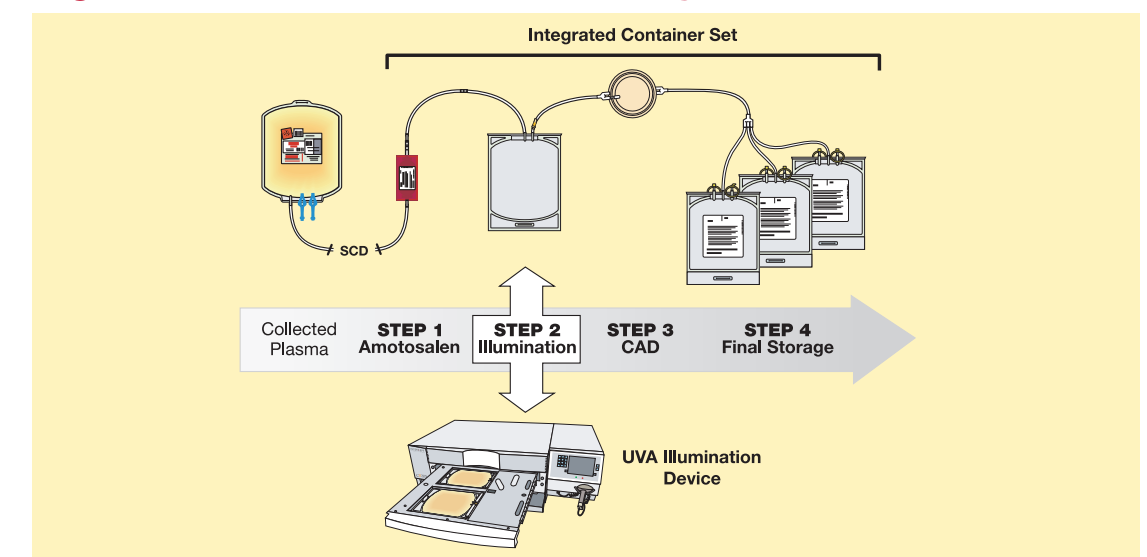


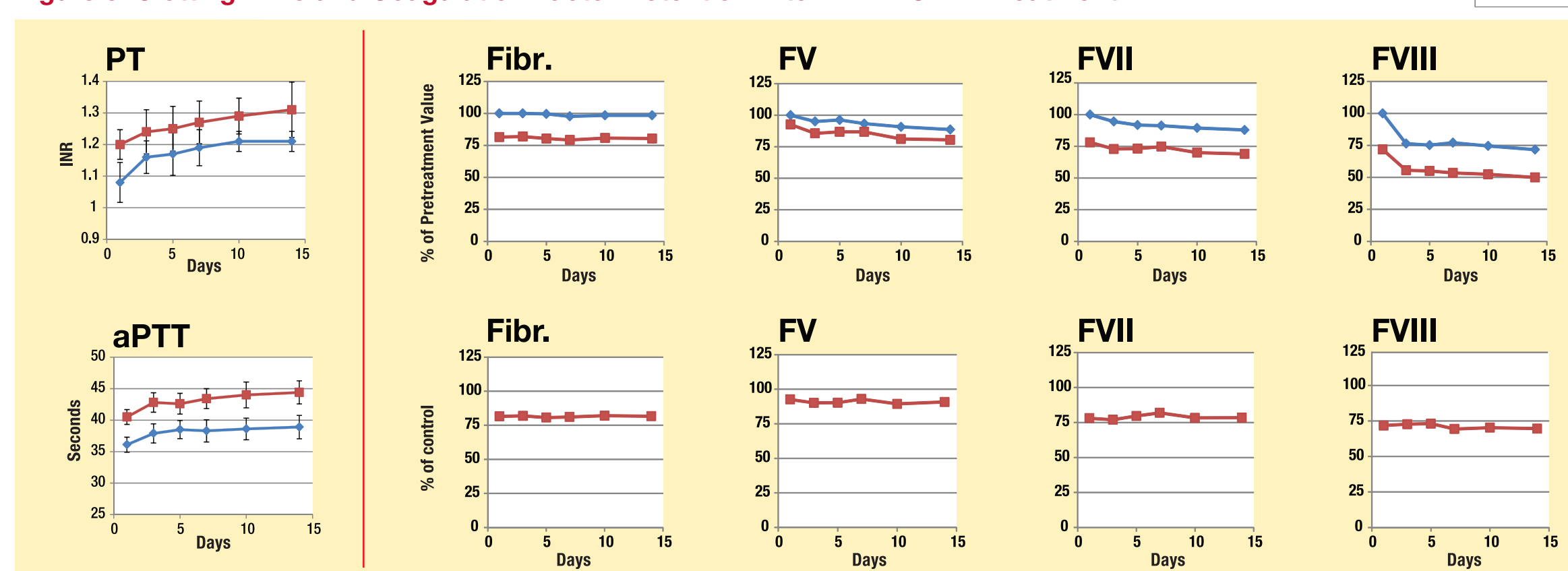
Figure 2: The INTERCEPT Blood System for Plasma



Results

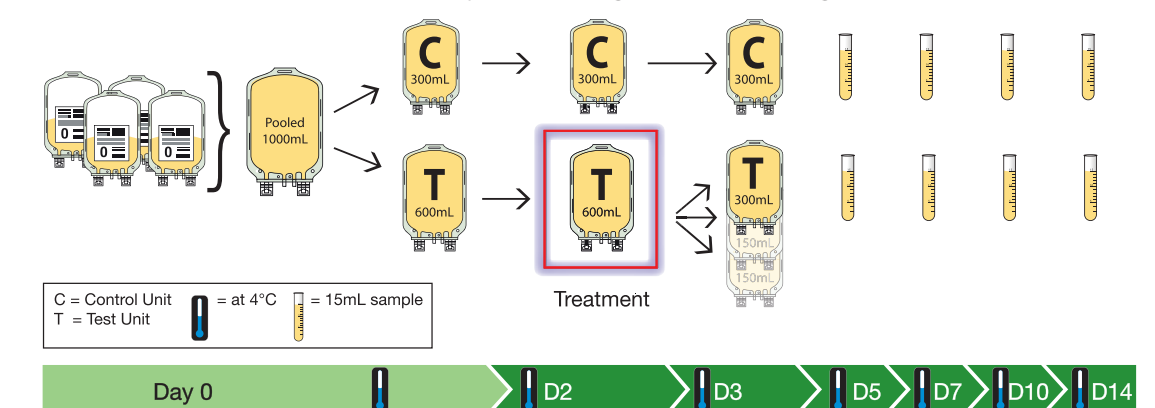
Overall the effect of INTERCEPT treatment to coagulation parameters immediately post treatment, was similar to that observed in previous studies (Figure 3). A slight elongation of PTT and aPTT (11-12%) was seen and FV, FVII and Fibrinogen were maintained at 93%, 78% and 82% of the pretreatment values (114%, 104% and 2.7 g/dL), while the labile FVIII was retained at 73% (pretreatment value: 0.76 KIE/L) (Figure 3). Factors were found to have similar storage stability to control liquid plasma over 14 days of storage, maintaining a constant activity ratio (Figure 3). On Day 7, the factor activities in treated liquid plasma were at levels of 87, 75 and 79% of pretreatment values respectively, while FVIII was at 54%. On Day 14 the factor activities in treated liquid plasma were still at levels of 80, 69 and 80% respectively, while FVIII was at 35%. When factors are above 50% of normal range, plasma has been shown to maintain hemostatic capacity^{1a}.

Figure 3: Clotting Time and Coagulation Factor Retention After INTERCEPT Treatment



Methods

The study was executed as shown in below, in 10 replicates. Briefly, 4 units of ABO matched plasma were pooled and distributed in two parts (Test (T) and Control (C)). The T unit was treated, the plasma transferred into a storage bag and samples were taken from both T and C units as indicated below, over 14 days of refrigerated storage.



References

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Conclusions

- Liquid plasma can be used to treat critically bleeding trauma patients and its use may also improve plasma utilization. Pathogen inactivation could address any increased pathogen risks associated with a non-frozen product.
- INTERCEPT treatment of liquid plasma results in 73% greater retention of the coagulation factors tested immediately post-treatment.
- Coagulation factors in treated liquid plasma have similar storage stability to control plasma and retain mean activity above 50% of pretreatment values for at least 7 days of refrigerated storage.