



VALIDATION OF HIV INACTIVATION CAPACITY OF THE THERAFLEX MB-PLASMA SYSTEM WITH HIGH SENSITIVITY

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BACKGROUND

It is known that the treatment of plasma to attenuate the viral load of HIV by methylene blue/ light is very effective. A fast reduction of infectious particles (infectious units; IU) to the limit of detection with the THERAFLEX MB-Plasma procedure has been reported previously. However, this limit of detection is in the range of abt. 1000 IU/ml (eq. to 1 log/ml of IU). Theoretically, residual infectious virus could be present below this threshold.

AIMS

Aim of this study was to investigate the reduction of infectious HIV particles by the THERAFLEX MB-Plasma procedure using a highly sensitive detection method (assay). Its limit of detection was set very low: in the range of or less than 100 IU/bag.

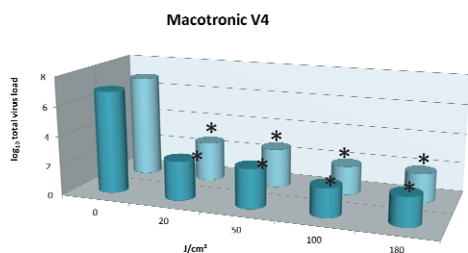
METHODS

This investigation was performed under the quality system Good Laboratory Practice (GLP). Plasma was transferred into the illumination bag of the THERAFLEX MB-Plasma system and was spiked with HIV stock solution (final volume: 315 ml, MB concentration approx. 0.8 µmol/l, virus titre 4.7 to 5.2 log₁₀ TCID₅₀/ml). The bag was subjected to the virus inactivation procedure using two different illumination devices (Macotronic V4: final dose 180 J/cm² and B2: final dose 120 J/cm²). The final dose is dependent on the correspondence of the wavelength to the absorption maximum of the MB. Samples were withdrawn at different light doses and monitored for virus by endpoint titration and by large volume plating on adequate indicator cells. The reduction factors achieved were calculated.

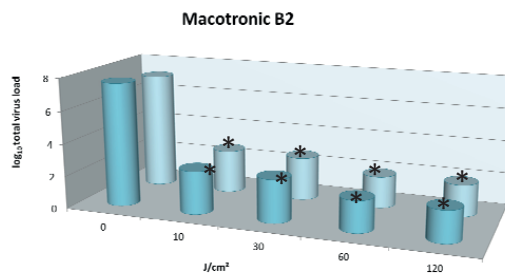


RESULTS

The virus was repeatedly reduced to the limit of detection already after illumination with one tenth of the final light dose regardless of the illumination device. The viral load after the full illumination dose was below 10^{-0.56} IU/ml equivalent to ≤ 1.94 log₁₀ per unit, i.e. less than 90 virus particles/ plasma bag.



*below limit of detection



*below limit of detection

Fraction	Log ₁₀ total virus load/unit Macotronic V4			Fraction	Log ₁₀ total virus load/unit Macotronic B 2		
	Run 1	Run 2	Run 3		Run 1	Run 2	Run 3
Load	6.93	6.93	6.87	Load	7.59	7.17	7.71
20 J/cm ²	≤2.65	≤2.65	-	10 J/cm ²	≤2.65	≤2.65	-
50 J/cm ²	≤2.65	≤2.65	-	30 J/cm ²	≤2.65	≤2.65	-
100 J/cm ²	≤1.94	≤1.94	-	60 J/cm ²	≤1.94	≤1.94	-
180 J/cm ²	≤1.94	≤1.94	≤1.94	120 J/cm ²	≤1.94	≤1.94	≤1.94
Hold	7.11	7.17	6.63	Hold	7.05	7.29	7.59
Log ₁₀ reduction factor (180 J/cm ²)	≥4.99	≥4.99	≥4.93	Log ₁₀ reduction factor (120 J/cm ²)	≥5.65	≥5.23	≥5.77

SUMMARY/CONCLUSIONS

The investigation shows that the THERAFLEX MB-Plasma procedure is robust and reproducible and that it has a high safety margin. Moreover, it was shown for the first time under GLP that this pathogen inactivation method is capable of reducing high initial loads of infectious HIV particles to very low levels which probably are insufficient to induce an apparent infection.