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BRIEF REPORT

TRANSFUSION

Inactivation of SARS-CoV-2 infectivity in platelet concentrates or plasma following treatment with ultraviolet C light or with methylene blue combined with visible light

Jody Hobson-Peters[1,2] | **Alberto A. Amarilla**[1] | **Lina Rustanti**[3] | **Denese C. Marks**[3] | **Eileen Roulis**[3] | **Alexander A. Khromykh**[1,2] | **Naphak Modhiran**[1] | **Daniel Watterson**[1,2] | **Stefan Reichenberg**[4] | **Frank Tolksdorf**[4] | **Chryslain Sumian**[5] | **Axel Seltsam**[6] | **Ute Gravemann**[7] | **Helen M. Faddy**[3,8]

[1]School of Chemistry and Molecular Biosciences, The University of Queensland, Brisbane, Queensland, Australia

[2]Australian Infectious Diseases Research Centre, Global Virus Network Centre of Excellence, Brisbane, Queensland, Australia

[3]Research and Development, Australian Red Cross Lifeblood, Brisbane, Queensland, Australia

[4]Macopharma International GmbH, Langen, Germany

[5]Macopharma, Tourcoing, France

[6]Bavarian Red Cross Blood Service, Nuremberg, Germany

[7]German Red Cross Blood Service NSTOB, Springe, Germany

[8]School of Health and Behavioural Sciences, University of the Sunshine Coast, Sunshine Coast, Queensland, Australia

Correspondence
Jody Hobson-Peters, School of Chemistry and Molecular Biosciences, The University of

Abstract

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is unlikely to be a major transfusion-transmitted pathogen; however, convalescent plasma is a treatment option used in some regions. The risk of transfusion-transmitted infections can be minimized by implementing Pathogen Inactivation (PI), such as THERAFLEX MB-plasma and THERAFLEX UV-Platelets systems. Here we examined the capability of these PI systems to inactivate SARS-CoV-2.

Study Design and Methods: SARS-CoV-2 spiked plasma units were treated using the THERAFLEX MB-Plasma system in the presence of methylene blue (~0.8 μmol/L; visible light doses: 20, 40, 60, and 120 [standard] J/cm^2). SARS-CoV-2 spiked platelet concentrates (PCs) were treated using the THERAFLEX UV-platelets system (UVC doses: 0.05, 0.10, 0.15, and 0.20 [standard] J/cm^2). Samples were taken prior to the first and after each illumination dose, and viral infectivity was assessed using an immunoplaque assay.

Results: Treatment of spiked plasma with the THERAFLEX MB-Plasma system resulted in an average ≥5.03 $\log_{10}$ reduction in SARS-CoV-2 infectivity at one third (40 J/cm^2) of the standard visible light dose. For the platelet concentrates (PCs), treatment with the THERAFLEX UV-Platelets system resulted in an average ≥5.18 $\log_{10}$ reduction in SARS-CoV-2 infectivity at the standard UVC dose (0.2 J/cm^2).

Jody Hobson-Peters and Alberto A. Amarilla joint first authors.

Queensland, Brisbane, Qld, Australia.
Email: j.peters2@uq.edu.au

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Conclusions: SARS-CoV-2 infectivity was reduced in plasma and platelets following treatment with the THERAFLEX MB-Plasma and THERAFLEX UV-Platelets systems, to the limit of detection, respectively. These PI technologies could therefore be an effective option to reduce the risk of transfusion-transmitted emerging pathogens.

KEYWORDS
emerging infectious disease, pathogen inactivation, plasma, platelets, safety, SARS-CoV-2, transfusion-transmission

1 | INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is characterized by fever, cough, headache, fatigue and breathing difficulties. As of 31st August 2022, there have been over 598 million confirmed cases worldwide and over 6.4 million deaths.[1] Infectious diseases may pose a risk to transfusion safety when they are transfusion-transmissible. SARS-CoV-2 RNA has been detected in the plasma from infected individuals,[2] however, based on donor follow-up studies, is unlikely to be a major transfusion-transmitted pathogen.[3,4] Nevertheless, investigation into methodologies to inactivate SARS-CoV-2 in blood products, as a model for other similar emergent viruses is warranted.

Pathogen Inactivation (PI) can play a role in minimizing the risk of transfusion-transmission through permanently reducing the ability of blood-borne pathogens to replicate.[5] A number of PI systems have been developed, several of which are in use for the treatment of plasma and platelets.[5] Macopharma has developed a PI method for plasma (THERAFLEX MB-plasma system) and a system for platelets (THERAFLEX UV-platelets system), both of which have been successfully investigated for the reduction of (re)emerging pathogens, such as Zika, Japanese encephalitis, dengue, chikungunya, and Ross River viruses.[6–9] This study investigated the efficacy of these systems to inactivate SARS-CoV-2 spiked into plasma and platelet components (PCs).

2 | MATERIALS AND METHODS

2.1 | Plasma and platelet concentrates

Plasma and platelet concentrates (PCs) were prepared as described previously.[7,8,10–12] Plasma components included in this study were collected prior to the COVID-19 pandemic. PCs were collected from donors residing in the state of Queensland, Australia, prior to widespread SARS-CoV-2 vaccination and when case numbers in the state were extremely low. As such, it was not necessary to test for the presence of anti-SARS-CoV-2 antibodies in these plasma units and PCs. Platelet count, unit volume, swirl, and pH, collectively referred to as platelet quality control (QC) parameters, were assessed as described previously.[12,13] This study had approval from the Australian Red Cross Lifeblood Ethics Committee (Reference number Marks21082020).

2.2 | Virus and viral production

SARS-CoV-2 hCoV-19/Australia/QLD02/2020 (QLD02) strain (GISAID Accession ID; EPI_ISL_407896, collected 30/01/2020)[14] was used for this study. The virus was grown by propagation in African green monkey kidney cells (Vero E6, ATCC#: CRL-1586) transduced with lentivirus containing puromycin-selectable codon-optimized human TMPRSS2 construct, as described previously,[14] harvested 2 days post-infection and clarified by centrifugation and stored at −80°C.

This study was approved by the Institutional Biosafety Committee of the University of Queensland (Approval number IBC/471Bv2/SCMB/2021). All experiments were performed in a biosafety level 3 facility at the School of Chemistry and Molecular Biosciences at the University of Queensland, Australia.

2.3 | Viral inactivation

Thawed plasma aliquots (~315 ml) were treated with the THERAFLEX MB-Plasma system as per the manufacturer's instructions. The plasma was spiked with SARS-CoV-2 to create a virus concentration of approximately 10^5–10^6 focus forming units (FFU)/ml. A sample of spiked plasma was stored in the dark at room temperature until the end of the viral inactivation process ('hold – no methylene blue (MB)' sample), while a second hold sample, which was also stored in the dark, was collected

following the addition of MB (~0.8 μmol/L; 'hold – MB'). The spiked plasma in the presence of MB was treated at multiple visible light cumulative doses (20, 40, 60, and 120 [standard] J/cm^2) as described previously.[8,11,12] PCs were treated with the THERAFLEX UV-Platelets system in accordance with the manufacturer's instructions, using a series of cumulative UVC doses (0.05, 0.10., 0.15, 0.20 [standard] J/cm^2) as described previously.[6,8] The same illumination bag was used for all treatment doses, whereby the bag was re-sealed after each post-illumination sample was collected. Three separate units of plasma and three separate PCs were spiked and treated.

2.4 | Evaluation of infectious virus

An immunoplaque assay, including a large volume plating approach whereby each sample was transferred to the washed cell monolayer (50 μl/well; $n = 48$ per treatment dose), was used to assess SARS-CoV-2 infectivity as previously described,[8,11,12,15] with the following modifications: incubation with Medium 199/2% carboxymethyl-cellulose (Sigma-Aldrich)/3% heat-inactivated FBS for 16 hours at 37 °C/5% CO_2; primary antibody: a murine anti-SARS-CoV-2 antibody CR3022 (50 μg/ml) for 1 h; secondary antibody: RDye® 800CW-Goat anti-mouse IgG (1:2500; LI-COR, Lincoln, NE) for 1 h.[15] Plaques were visualized using Image Studio software version 5.2 (LI-COR, Lincoln, NE), counted, and the FFU/ml were calculated. The concentration of SARS-CoV-2 was reported as $\log_{10}$ FFU/ml.

3 | RESULTS

SARS-CoV-2 infectivity was assessed following treatment of spiked plasma with the THERAFLEX MB-Plasma system at a range of visible light doses, up to 120 J/cm^2 (standard dose). We observed an average ≥3.83 $\log_{10}$ reduction in SARS-CoV-2 infectivity via the standard immunoplaque assay and ≥5.03 $\log_{10}$ as assessed via the large volume plating plaque method (Table 1, Figure 1). An average log reduction of −0.15 $\log_{10}$ was achieved for the hold sample without MB, while the hold sample containing MB resulted in an average 0.77 $\log_{10}$ reduction (Table 1).

The efficacy of the THERAFLEX UV-Platelets system to inactivate SARS-CoV-2 in PCs was investigated at a range of UVC doses up to 0.20 J/cm^2 (standard dose). Treatment resulted in the reduction of SARS-CoV-2 by an average of ≥3.98 $\log_{10}$, via the standard immunoplaque assay and ≥5.18 $\log_{10}$ as assessed via the large volume

TABLE 1 SARS-CoV-2 infectivity in plasma following treatment with the THERAFLEX MB-plasma system

	Pre-treatment titre ($\log_{10}$ FFU/ml)	10-fold serial dilution titre ($\log_{10}$ FFU/ml) log reduction Treatment dose (J/cm^2)						Large volume plating titre ($\log_{10}$ FFU/ml) log reduction Treatment dose (J/cm^2)		
		0 (HOLD; no MB)	0 (HOLD + MB)	20	40	60	120	40	60	120
Bag 1	5.18 ± 0.05	5.21 ± 0.07	4.1 ± 0.07	≤1.3[a]	≤1.3[a]	≤1.3[a]	≤1.3[a]	<0.1[a]	<0.1[a]	<0.1[a]
		−0.03	1.08	≥3.88	≥3.88	≥3.88	≥3.88	≥5.08	≥5.08	≥5.08
Bag 2	4.90 ± 0.21	5.30 ± 0.13	4.3 ± 0.06	≤1.3[a]	≤1.3[a]	≤1.3[a]	≤1.3[a]	<0.1[a]	<0.1[a]	<0.1[a]
		−0.4	0.6	≥3.60	≥3.60	≥3.60	≥3.60	≥4.8	≥4.8	≥4.8
Bag 3	5.30 ± 0.05	5.31 ± 0.05	4.69 ± 0.15	≤1.3[a]	≤1.3[a]	≤1.3[a]	≤1.3[a]	<0.1[a]	<0.1[a]	<0.1[a]
		−0.01	0.61	≥4	≥4	≥4	≥4	≥5.2	≥5.2	≥5.2
Avg.	5.13 ± 0.21	5.27 ± 0.10	4.36 ± 0.27	≤ 1.3[a]	≤ 1.3[a]	≤ 1.3[a]	≤ 1.3[a]	≤ 0.1[a]	≤ 0.1[a]	≤ 0.1[a]
		−0.15	0.77	≥3.83	≥3.83	≥3.83	≥3.83	≥5.03	≥5.03	≥5.03

[a]Virus detected below the limit of detection of the assay used (1.30 $\log_{10}$ FFU/ml for 10-fold serial dilutions; 0.1 FFU/ml for large volume plating).

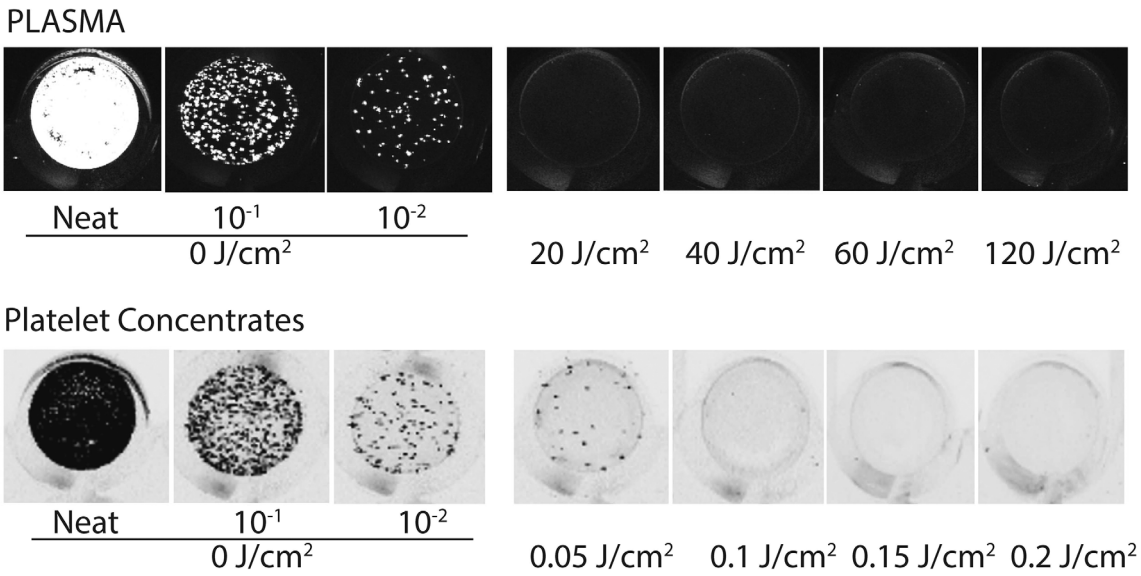

FIGURE 1 SARS-CoV-2 plaque formation before and after treatment with the THERAFLEX systems detected by immunoplaque assay on Vero cells. Representative plaques formed by SARS-CoV-2 at neat (undiluted), 1:10 and 1:100 viral dilutions for untreated samples and undiluted preparations for treated samples, in plasma treated with the THERAFLEX MB-plasma system using different illumination doses (top, plaques in white) and in PCs treated with the THERAFLEX UV-platelets system using different illumination doses (bottom, color inverted – Plaques in black)

TABLE 2 SARS-CoV-2 infectivity in platelet concentrates following treatment with the THERAFLEX UV-platelets system

	Pre-treatment titre (log_{10} FFU/ml)	10-fold serial dilution titre (log_{10} FFU/ml) log reduction Treatment dose (J/cm^2)					Large volume plating titre (log_{10} FFU/ml) log reduction Treatment dose (J/cm^2)		
		0 (HOLD)	0.05	0.10	0.15	0.20	0.10	0.15	0.20
Bag 1	5.34 ± 0.03	5.70 ± 0.09	2.61 ± 0.09	≤1.3[a]	≤1.3[a]	≤1.3[a]	1.40	≤0.1[a]	≤0.1[a]
		−0.36	2.73	≥4.04	≥4.04	≥4.04	3.94	≥5.24	≥5.24
Bag 2	5.21 ± 0.13	5.31 ± 0.04	1.82 ± 0.26	≤1.3[a]	≤1.3[a]	≤1.3[a]	≤0.1[a]	≤0.1[a]	≤0.1[a]
		−0.1	3.39	≥3.91	≥3.91	≥3.91	≥5.11	≥5.11	≥5.11
Bag 3	5.28 ± 0.05	5.13 ± 0.04	1.60 ± 0.27	≤1.3[a]	≤1.3[a]	≤1.3[a]	1.04	≤0.1[a]	≤0.1[a]
		0.12	3.68	≥3.98	≥3.98	≥3.98	≥4.24	≥5.18	≥5.18
Avg.	5.28 ± 0.09	5.38 ± 0.25	2.01 ± 0.49	≤ 1.3[a]	≤ 1.3[a]	≤ 1.3[a]	1.07	≤0.1[a]	≤0.1[a]
		−0.1 ± 0.26	3.27 ± 0.49	≥ 3.98	≥ 3.98	≥ 3.98	4.18	≥5.18	≥5.18

[a]Virus detected below the limit of detection of the assay used (1.30 log_{10} FFU/ml for 10-fold serial dilutions; 0.1 FFU/ml for large volume plating).

plating plaque assay (Table 2, Figure 1). For the large volume of plaque counts, the visible background in cell only negative controls containing no platelets (96 wells) was subtracted. For both plating methods, residual virus was detectable only at the lowest UV doses (0.05 J/cm^2 or 0.1 J/cm^2 for the large volume plating method). The average viral titre was stable in the hold sample (Table 2). All PCs showed acceptable platelet QC parameters, and each had a final platelet count and volume that met specifications for transfusion (platelet count: 0.8–1.4 × 10^9/ml; platelet unit volume: 325–375 ml; data not shown).

4 | DISCUSSION

PI is a proactive strategy to prevent transfusion-transmission of blood-borne pathogens. Although now believed not to be a significant risk of transfusion-transmissibility for SARS-CoV-2,[3] convalescent plasma has been used for the treatment of SARS-CoV-2 patients.[16] In this study, we demonstrate the potential for the THERAFLEX MB-Plasma, and the THERAFLEX UV-Platelets systems to inactivate SARS-CoV-2 in plasma, and PC, respectively. Our results are similar to those obtained using the Theraflex PI system for

SARS-CoV-1 inactivation (virus reduction factor ≥3.4 $\log_{10}$) and those investigating SARS-CoV-2 infectivity following treatment with other PI systems.[17–20]

The THERAFLEX MB-Plasma system was able to inactivate SARS-CoV-2 by ≥3.83 $\log_{10}$ using standard detection methods and by ≥5.03 $\log_{10}$ shown by the large volume plating method. Viral inactivation below the limit of detection (LOD) was evident at one-sixth of the standard visible light illumination dose (20 J/cm^2). The MB-Plasma system has been used to prepare convalescent plasma for clinical trials[21] and MB treatment has been shown to preserve the immunological properties of convalescent plasma.[22] It is therefore important that we demonstrate its effectiveness for inactivating SARS-CoV-2 in plasma as a model virus for other emergent pathogens and provide evidence for the breadth of viral pathogens inactivated by the THERAFLEX PI systems. Likewise, THERAFLEX UV-Platelets system reduced SARS-CoV-2 infectivity in PCs on average by ≥3.98 $\log_{10}$ at the standard dose of UVC light, whereas the large volume plating method resulted in ≥5.18 $\log_{10}$ reduction of the viral infectivity. This level of inactivation is greater than what was observed following treatment with UV light and riboflavin (plasma: ≥4.79 $\log_{10}$; platelets: ≥4.53 $\log_{10}$)[17] or amotosalen/UVA light (plasma: >3.32 $\log_{10}$; platelets: >3.2 $\log_{10}$),[18] although, as inactivation was achieved to the limit of assay detection in all studies, the greater inactivation observed herein is likely a reflection of the high pre-treatment spiked titres of SARS-CoV-2, in combination with the large volume plating assessment.

We note minimal change in SARS-CoV-2 infectivity in the hold sample from spiked PCs (−0.1 $\log_{10}$ reduction) or spiked plasma prior to the addition of MB (hold – no MB; −0.15 $\log_{10}$ reduction). However, we saw a reduction (average 0.77 $\log_{10}$) in SARS-CoV-2 infectivity in the hold sample that contained MB. This is similar to previous studies,[23] suggesting a small amount of viral inactivation through the addition of MB alone, likely due to the effect of ambient light. Although samples were kept in the dark, it is possible they were exposed to small amounts of ambient light during the experimental procedure. Moreover, MB alone has been shown to inactivate SARS-CoV-2, as well as bovine coronavirus (BCoV), although in both studies, MB in combination with light showed marked increases in pathogen inactivation as compared to MB alone.[24,25]

This study extends the list of pathogens inactivated by the THERAFLEX PI systems and provides strong evidence as a model system of inactivation for other similar emergent infectious agents in the future. While in this study, SARS-CoV-2 served as a model virus, and it is acknowledged that no related coronavirus or respiratory virus has been shown to be transfusion transmissible, it is important to investigate whether these PI systems are effective against a variety of emergent pathogens with a possible risk to blood transfusion safety.

AUTHOR CONTRIBUTIONS

Jody Hobson-Peters, Alberto Amarilla and Naphak Modhiran performed the experimental work and analyzed the data. Lina Rustanti performed plasma pooling and PCs preparations. Helen Faddy prepared the first draft of the manuscript. All authors contributed to the study design, data interpretation, and manuscript editing. All authors approved the final manuscript.

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CONFLICT OF INTEREST

Jody Hobson-Peters, Lina Rustanti, Helen M. Faddy, Denese C. Marks, and Daniel Watterson received partial funding for this study from Macopharma. Stefan Reichenberg, Frank Tolksdorf and Chryslain Sumian are employed by the company that developed the THERAFLEX UV-Platelets and THERAFLEX MB-Plasma systems, Macopharma (Tourcoing, France). Ute Gravemann and Axel Seltsam work for blood donation centers that collaborates with Macopharma on the development of pathogen inactivation systems for platelets and plasma. Alberto A Amarilla, Naphak Modhiran, Alexander A Khromykh and Eileen Roulis report no conflict of interest.

ORCID

Jody Hobson-Peters https://orcid.org/0000-0003-0139-9829
Lina Rustanti https://orcid.org/0000-0001-6385-1580
Denese C. Marks https://orcid.org/0000-0002-3674-6934
Eileen Roulis https://orcid.org/0000-0001-6824-5432

Axel Seltsam https://orcid.org/0000-0001-5858-5097
Ute Gravemann https://orcid.org/0000-0001-9050-1295
Helen M. Faddy https://orcid.org/0000-0002-3446-8248

REFERENCES

1. World Health Organization. Weekly epidemiological update on COVID-19 - 31 August 2022 https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---31-august-2022
2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan. China Lancet. 2020;395:497–506.
3. Cappy P, Candotti D, Sauvage V, Lucas Q, Boizeau L, Gomez J, et al. No evidence of SARS-CoV-2 transfusion transmission despite RNA detection in blood donors showing symptoms after donation. Blood. 2020;136:1888–91.
4. Muench MO, Jin J, Chaflets D, Darst O, Hui A, Townsend R, et al. Lack of infectivity of SARS-CoV2 RNA+ donor plasma, In 2022 plenary, Oral, and poster abstract presentations. Transfusion. 2022;62:9A–274A.
5. Devine DV, Schubert P. Pathogen inactivation technologies: the advent of pathogen-reduced blood components to reduce blood safety risk. Hematol Oncol Clin North Am. 2016;30:609–17.
6. Faddy HM, Fryk JJ, Prow NA, Watterson D, Young PR, Hall RA, et al. Inactivation of dengue, chikungunya, and Ross River viruses in platelet concentrates after treatment with ultraviolet C light. Transfusion. 2016;56:1548–55.
7. Fryk JJ, Marks DC, Hobson-Peters J, Watterson D, Hall RA, Young PR, et al. Reduction of Zika virus infectivity in platelet concentrates after treatment with ultraviolet C light and in plasma after treatment with methylene blue and visible light. Transfusion. 2017;57:2677–82.
8. Rustanti L, Hobson-Peters J, Colmant AMG, Hall RA, Young PR, Reichenberg S, et al. Inactivation of Japanese encephalitis virus in plasma by methylene blue combined with visible light and in platelet concentrates by ultraviolet C light. Transfusion. 2020;60:2655–60.
9. Eickmann M, Gravemann U, Handke W, Tolksdorf F, Reichenberg S, Muller TH, et al. Inactivation of three emerging viruses - severe acute respiratory syndrome coronavirus, Crimean-Congo haemorrhagic fever virus and Nipah virus - in platelet concentrates by ultraviolet C light and in plasma by methylene blue plus visible light. Vox Sang. 2020;115:146–51.
10. Johnson L, Hyland R, Tan S, Tolksdorf F, Sumian C, Seltsam A, et al. In vitro quality of platelets with low plasma carryover treated with ultraviolet C light for pathogen inactivation. Transfus Med Hemother. 2016;43:190–7.
11. Seghatchian J, Struff WG, Reichenberg S. Main properties of the THERAFLEX MB-plasma system for pathogen reduction. Transfus Med Hemother. 2011;38:55–64.
12. Seghatchian J, Tolksdorf F. Characteristics of the THERAFLEX UV-platelets pathogen inactivation system - an update. Transfus Apher Sci. 2012;46:221–9.
13. Ravanat JL, Douki T, Cadet J. Direct and indirect effects of UV radiation on DNA and its components. J Photochem Photobiol B. 2001;63:88–102.
14. Amarilla AA, Sng JDJ, Parry R, Deerain JM, Potter JR, Setoh YX, et al. A versatile reverse genetics platform for SARS-CoV-2 and other positive-strand RNA viruses. Nat Commun. 2021;12:3431.
15. Amarilla AA, Modhiran N, Setoh YX, Peng NYG, Sng JDJ, Liang B, et al. An optimized high-throughput Immuno-plaque assay for SARS-CoV-2. Front Microbiol. 2021;12:625136.
16. Klassen SA, Senefeld JW, Senese KA, Johnson PW, Wiggins CC, Baker SE, et al. Convalescent plasma therapy for COVID-19: a graphical mosaic of the worldwide evidence. Front Med. 2021;8:684151.
17. Ragan I, Hartson L, Pidcoke H, Bowen R, Goodrich R. Pathogen reduction of SARS-CoV-2 virus in plasma and whole blood using riboflavin and UV light. PLoS One. 2020;15:e0233947.
18. Azhar EI, Hindawi SI, El-Kafrawy SA, Hassan AM, Tolah AM, Alandijany TA, et al. Amotosalen and ultraviolet a light treatment efficiently inactivates severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in human plasma. Vox Sang. 2021;116:673–681.
19. Hindawi SI, El-Kafrawy SA, Hassan AM, Badawi MA, Bayoumi MM, Almalki AA, et al. Efficient inactivation of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) in human apheresis platelet concentrates with amotosalen and ultraviolet a light. Transfus Clin Biol. 2022;29:31–6.
20. Santa Maria F, Huang Y-JS, Vanlandingham DL, Bringmann P. Inactivation of SARS-CoV-2 in all blood components using Amotosalen/ultraviolet a light and Amustaline/glutathione pathogen reduction technologies. Pathogens. 2022;11:521.
21. Alemany A, Millat-Martinez P, Corbacho-Monne M, Malchair P, Ouchi D, Ruiz-Comellas A, et al. High-titre methylene blue-treated convalescent plasma as an early treatment for outpatients with COVID-19: a randomised, placebo-controlled trial. Lancet Respir Med. 2022;10:278–88.
22. Kostin AI, Lundgren MN, Bulanov AY, Ladygina EA, Chirkova KS, Gintsburg AL, et al. Impact of pathogen reduction methods on immunological properties of the COVID-19 convalescent plasma. Vox Sang. 2021;116:665–72.
23. Cagno V, Medaglia C, Cerny A, Cerny T, Zwygart AC, Cerny E, et al. Methylene blue has a potent antiviral activity against SARS-CoV-2 and H1N1 influenza virus in the absence of UV-activation in vitro. Sci Rep. 2021;11:14295.
24. Svyatchenko VA, Nikonov SD, Mayorov AP, Gelfond ML, Loktev VB. Antiviral photodynamic therapy: inactivation and inhibition of SARS-CoV-2 in vitro using methylene blue and Radachlorin. Photodiagnosis Photodyn Ther. 2021;33:102112.
25. Zhukhovitsky V, Shevlyagina N, Zubasheva M, Russu L, Gushchin V, Meerovich G, et al. Infectivity and morphology of bovine coronavirus inactivated In vitro by cationic photosensitizers. Viruses. 2022;14:1053.

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