British Journal of Pharmacy

https://doi.org/10.5920/bjpharm.1178

British Journal of Pharmacy

www.bjpharm.hud.ac.uk

Proceedings of the 13th APS International PharmSci 2022

Characterizing RAPID™ platelet and leukocyte-rich plasma gels – an autologous, point-of-care medicine for diabetic foot ulcer treatment.

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ARTICLE INFO

Received: 16/06/2022
Accepted: 07/07/2022
Published: 04/11/2022

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KEYWORDS: platelet-rich plasma; wound healing; diabetic foot ulcers; diabetes

SUMMARY

In 2017/18 wound healing cost the NHS 8.3 billion pounds. There is an urgent need for more effective, accessible, and safe treatments. Platelet-rich plasma (PRP) therapies have been emerging since the early 2000s, currently they are used across various medical fields treating conditions from cosmetic procedures through burn treatments to wound healing. RAPID™ gel is a product for the treatment of diabetic foot ulcers that is currently in stage 2b of clinical trials. This project aims to better understand the properties of the gel and how these are affected by the manufacturing process. The PRP gels were characterized physiochemically by exploring the gel time, exudate release and growth factor content. These data provide a baseline for future studies exploring how variations in manufacturing conditions affect the gel properties.

INTRODUCTION

Platelet-rich plasma (PRP), a blood derivative has been used successfully to treat various medical conditions. Initially patented in 1985 (Knighton et al., 1986), it gained popularity in maxillofacial surgery in the late 1990s (Marx, 2004). PRP-based products are potentially potent and safe regenerative medicine treatments. Being easy to manufacture and use, they are being utilized in various medical fields. One of the more accepted and successful uses is treating diabetic foot ulcers (DFU) (Martinez-Zapata et al., 2016).

RAPID™ gel has been developed specifically for DFU patients, showing promising results in preventing amputations in pilot studies (14 out of 15)(Martin T, Kyriakides CK, Sarkar S, 2015). This project aims to characterise gels physico-chemically as a step towards investigating potential critical processing parameters in the manufacturing process.

MATERIALS AND METHODS

Ethical approval was obtained through King's College London Ethical Committee.

RAPID™ gel manufacture

Standard Biotherapy Services protocol was followed to manufacture the RAPID™ gels (Fig 1.).

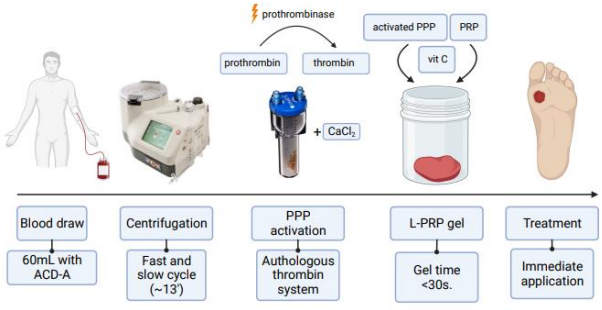

Fig. 1. *RAPID™ gel manufacture protocol.*

Sixty millilitres of whole blood were separated in an Angel blood centrifuge (Arthrex Angel™ Systems). A

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thrombinator (Arthrex GmbH) was used to produce autologous thrombin by activating platelet-poor plasma. To form the RAPID™ gel, vitamin C, activated platelet-poor plasma (rich in autologous thrombin) and PRP were combined in a plastic cup.

Gel characterization

Platelet counts of whole blood and PRP were carried out by 1:100 dilution of samples in Stromatol (Mascia Brunelli S.p.A.) followed by resuspension in a haemocytometer (Marienfeld) for counting. Gelling time was noted and each gel was weighed at the point of manufacture. Exudate release was measured over time by collection of exudate. A human VEGF ELISA kit (OmniKine™, Assay Biotech) was used to quantify growth factor content.

Data analysis

All data was analysed in Microsoft Excel (version 16.61.1) and GraphPad Prism 9.

RESULTS AND DISCUSSION

Eight RAPID™ gels were manufactured and characterized. An average gel weighed 8.90 ± 1.41 g; gel time was 33.09 ± 10.30 s. Gel dimensions in a standard plastic cup measured 0.8x5 cm (height x diameter). Exudate release was measured every five minutes to obtain an exudate release profile (Fig. 2.).

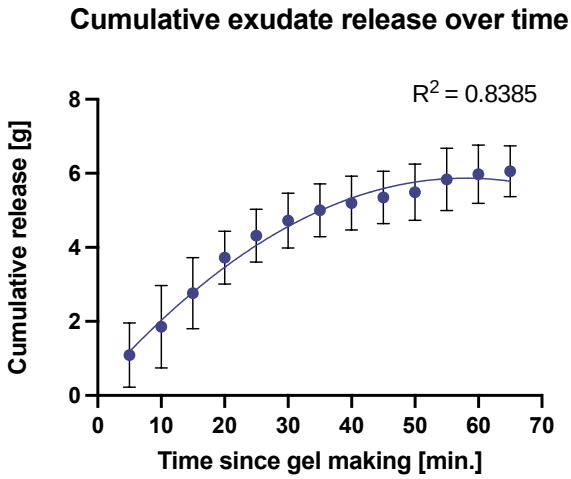

Fig. 2. *Exudate release profiles from RAPID™ gels measured as cumulative mass released over time (n=3).*

No statistical significance in the growth factor content was observed between the unactivated PRP and exudate (Table 1), which is consistent with previous findings (data not shown) which only found a difference in growth factor release after longer times.

Table 1. *VEGF content for unactivated PRP and exudate samples (at 60 min) from different gels.*

Sample	VEGF concentration [pg/mL]	Sample	VEGF concentration [pg/mL]
PRP #1	172.22	Exudate #1	122.11
PRP #2	69.82	Exudate #2	235.94
PRP #3*	946.28	Exudate #3*	821.20
PRP #4	597.00	Exudate #4	429.70
PRP #5	266.75	Exudate #5	295.85

*Sample frozen 3 hours following gel manufacturing

CONCLUSION

Gel weight and time was consistent across the manufacturing runs. Exudate release was plateaued over time, with greater variability in rate at the beginning. The average growth factor content was 410.4 pg/mL and 381.5 pg/mL for PRP and exudate, respectively. Further studies will explore how variations in manufacturing conditions affect the gel properties.

ACKNOWLEDGEMENTS

This work was supported by a BBSRC LIDo iCASE studentship with Biotherapy Services Ltd.

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