PHARMACEUTICS 27.06.22: Review 1

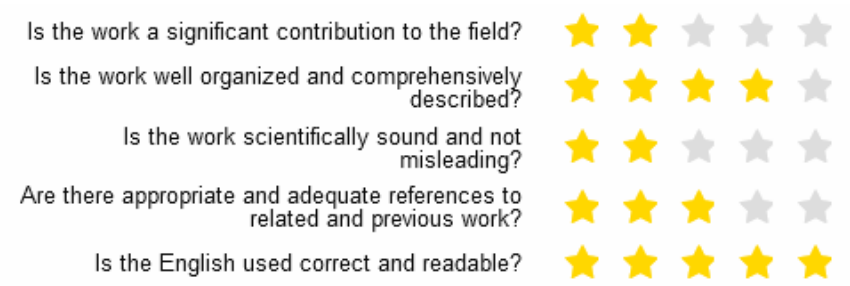
Answers to Reviewer 2

Open Review

(x) I would not like to sign my review report
( ) I would like to sign my review report

English language and style

( ) Extensive editing of English language and style required
( ) Moderate English changes required
(x) English language and style are fine/minor spell check required
( ) I don't feel qualified to judge about the English language and style



Comments and Suggestions for Authors

- The authors Gomri et al. who are all affiliated with the firm Regen Lab SA describe the scientific thought on the development and quality control of their products that deliver platelet-rich plasma. Moreover, they reviewed and summarized literature that depicted data using their technique to gain platelet-rich plasma. They show results using different in vitro assays to e.g. assess the influence of platelet-rich-plasma on enhancing amounts of adipose-derived stem cells, gaining regenerative function of fibroblasts and endothelial cells. They conclude that their technology "provides a solution to the challenge of standardizing PRP preparations intended for therapeutic uses".

- Overall, to be scientifically sound, other technical approaches in regenerative medicine and even regarding platelet-rich plasma must be introduced and discussed more thorougly.

To meet this reviewer's comment, we have slightly modified the text by citing embryonic, stem or differentiated cell-related regenerative approaches. We also propose to add The Table 1 describing the other technical approaches that are currently used to produce PRP, with examples of devices on the market. We have also enriched the text regarding the other PRP preparation technologies.

Table 1: Examples of medical devices for PRP preparation

Technology	Examples of devices	Blood vol.	PRP vol.	Platelet conc. factor	Biological product	Remarks
Low force centrifugation in tubes or syringes	BTI PRGF Endoret	8 mL	1-2 mL	2-3 X	**Plasma PRP (LP-PRP)**	Devices with no physical separation of platelet rich plasma from red and white blood cells. **Operator dependent results**
	Arthrex ACP double syringe	15 mL	4-6 mL	1.6-2 X		
High force centrifugation in hourglass shaped devices	Tozai Holdings Prosys	25 mL	2 mL	6-8 X	**Buffy coat PRP (LR-PRP)**	
High force centrifugation in devices with floating buoy or shelf	Biomet GPS III	27-54 mL	3-6 mL	6-9X	**Buffy coat PRP (LR-PRP)**	Devices with physical separation of platelet rich plasma from red and white blood cells. **Device dependent results**
	Harvest SmartPrep2	27-54 mL	3-7 mL	3-8 X		
Variable force centrifugation in computer aided systems	Arthrex Angel	40-180 mL	variable	1-18 X	**Setting dependent product**	
	Arteriocyte Magellan	26-52 mL	6 mL	3-7 X		
High force centrifugation in tubes with separating gel	RegenTubes	10 mL	5-6 mL Can be reduced to 1.5 mL	1.6-1.7 X Up to 4 X by PPP removal	**Plasma PRP (LP-PRP)**	

Blood Vol. : Volume of blood PRP vol. : Volume of PRP; Platelet conc. factor : Platelet concentration factor

- In detail, the close affiliation and sole description of in vitro studies depicting research conducted with Regen Lab platelet-rich plasma bears high risk that the conclusion is misleading.

The in vitro studies were already published in per-reviewed renowned journals (Tissue Engineering, Biomedicines, Scientific Reports). Copyright permissions were obtained for sharing the contents in this particular article. We refer the reviewer and future readers to those publications where results of other in vitro studies are thoroughly discussed.

Moreover, almost all *in vitro* studies cited in our publications are not dealing with non-activated fresh PRP but platelet lysates or supernatant released after the coagulation process, containing a batch of growth factors in a serum mixture but no living platelets or other cell entities.

- Strong examples are the findings in Figures 6-8 because 10% FBS solution is not an ideal (positive) control to compare to the influence of platelet-rich plasma in vitro whereas a growth medium formulation should have been used to compare these findings.

Those studies aimed at presenting PRP as an ideal autologous supplement to replace xenogenic sera in the development of cell expansion protocols for future cell therapy purposes. Therefore, we and others (Anitua et al. 2022) believe that the classical culture medium containing 10% FBS is an ideal control.

- The approach explaining the development and quality control of the products is interesting and English is fine.

We thank the reviewer for this comment.

References

Anitua, E., M. Zalduendo, M. Troya, M. H. Alkhraisat, and L. A. Blanco-Antona. 2022. 'Platelet-Rich Plasma as an Alternative to Xenogeneic Sera in Cell-Based Therapies: A Need for Standardization', Int J Mol Sci, 23.