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### Corresponding author:

João Silva

drjoacolussi@gmail.com

### Author Affiliation:

School of Health and Life Sciences,  
Pontifícia Universidade Católica do  
Rio Grande do Sul. Porto Alegre,  
Brazil.

Silva, JAC<sup>1</sup>; Warmeling, M<sup>2</sup>; Pagnoncelli, RM<sup>3</sup>.

### ADMINISTRATIVE INFORMATION

**Support** - None.

**Review Stage at time of this submission** - Preliminary searches.

**Conflicts of interest** - None declared.

**INPLASY registration number:** INPLASY202380005

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 01 August 2023 and was last updated on 01 August 2023.

### INTRODUCTION

**Review question / Objective** The aim of this systematic review is to comprehensively explore the existing literature on the use of platelet-rich fibrin as a drug delivery system. The primary objective is to assess the current state of knowledge in this area. The specific objectives are as follows:

- Identify and summarize the relevant information in the literature, including author names, publication titles, and publication years.
- Document the drugs used in conjunction with platelet-rich fibrin, along with their concentrations.
- Investigate the methods employed to fabricate platelet-rich fibrin.
- Analyze the applied volume and pharmaceutical presentation of platelet-rich fibrin.
- Examine the incorporation methods utilized for drugs within platelet-rich fibrin.
- Assess the physical characteristics of platelet-rich fibrin before drug incorporation.

- Evaluate the stability of the preparation after drug incorporation.

- Explore the release profile of drugs from platelet-rich fibrin over time.

- Investigate the antimicrobial activity of platelet-rich fibrin in comparison to other drug delivery systems.

To achieve these objectives, the proposed scoping review will address the following question: Can platelet-rich fibrin sustain drug release over time and elicit distinct responses in cells, microorganisms, and tissues when compared to other drug delivery systems?

**Rationale** Platelet-rich fibrin can be easily produced, making it cost-effective. Additionally, it can be combined with various types of molecules, thereby enhancing healing, regeneration, and antimicrobial activity.

**Condition being studied** Platelet-rich fibrin as a drug delivery system.

## METHODS

**Search strategy** The data bases will be searched as follows: MEDLINE (Pubmed) - we will do a search utilizing this Mesh, entry terms and other relevance terms in one section of search: (((((((((((("platelet-rich fibrin"[MeSH Terms]) OR ("platelet-rich fibrin"[Title/Abstract])) OR (platelet rich fibrin[Title/Abstract])) OR (Fibrin, Platelet-Rich[Title/Abstract])) OR (Platelet Rich Fibrin[Title/Abstract])) OR (L-PRF[Title/Abstract])) OR (Leukocyte-[Title/Abstract] AND Platelet-Rich Fibrin[Title/Abstract])) OR (Leukocyte[Title/Abstract] AND Platelet Rich Fibrin[Title/Abstract])) OR (PRF[Title/Abstract])) OR (LPRF[Title/Abstract])) OR (L-PRF[Title/Abstract])) OR (Advanced Platelet Rich Fibrin[Title/Abstract])) OR (Advanced PRF[Title/Abstract])) OR (A-PRF[Title/Abstract])) OR (APRF[Title/Abstract]), and then make another search in other section utilizing this Entry Terms: (((((((((((("drug delivery systems"[MeSH Terms]) OR (drug delivery systems[Title/Abstract])) OR ("Drug Targeting"[Title/Abstract])) OR ("Targeting, Drug"[Title/Abstract])) OR ("drug carriers"[Title/Abstract]) OR "drug carriers"[MeSH Terms]) OR ("Drug Carrier"[Title/Abstract])) OR (Delivery Systems, Drug[Title/Abstract])) OR (Delivery System, Drug[Title/Abstract])) OR (Drug Delivery System[Title/Abstract])) OR (System, Drug Delivery[Title/Abstract])) OR (Systems, Drug Delivery[Title/Abstract])) OR (Drug Targeting[Title/Abstract])) OR (Drug Targetings[Title/Abstract])) OR (Targeting, Drug[Title/Abstract])) OR (Targetings, Drug[Title/Abstract]). And then do another search in other section utilize #1 AND #2. EMBASE: 'platelet-rich fibrin'/exp OR 'L-PRF' OR 'leukocyte- and platelet-rich fibrin' OR 'leukocyte-PRF' OR 'P-PRF' OR 'pure platelet-rich fibrin' OR 'pure PRF' OR 'thrombocyte-rich fibrin' OR 'platelet-rich fibrin' and this search in another section, 'drug delivery system'/exp OR 'delivery system, drug' OR 'drug delivery' OR 'drug delivery systems' OR 'drug delivery system', before we will utilizing the COMBINE button utilizing and AND function. Cochrane Library:(platelet rich fibrin):ti,ab,kw AND ("drug delivery system"):ti,ab,kw. Science Direct: Title, abstract or author-specified, with this keywords: ("platelet rich fibrin" OR "PRF" OR "Advanced Platelet Rich Fibrin" OR "LPRF" OR "IPRF") AND ("drug delivery system" OR "drug targeting" OR "drug carrier"). Web of Science: All fields "platelet rich fibrin" OR "PRF" OR "Advanced Platelet Rich Fibrin" OR "LPRF" OR "IPRF" AND "drug delivery system" OR "drug targeting" OR "drug carrier". Scopus: TITLE-ABS-KEY ( ("platelet rich fibrin" OR "PRF" OR "Advanced Platelet Rich Fibrin" OR "LPRF" OR "IPRF" ) AND ( "drug delivery system" OR "drug

targeting" OR "drug carrier" ) ). BVS/LILACS: title, abstract, subject ("platelet rich fibrin" OR "PRF" OR "Advanced Platelet Rich Fibrin" OR "LPRF" OR "IPRF") AND ("drug delivery system" OR "drug targeting" OR "drug carrier").

We will do a search in the GREY LITERATURE. Google Scholar: only in the title of article, utilizing in the field "with all of the words" the term drug and in the field "with the exact phrase" the term platelet rich fibrin. PROQUEST: noft("platelet rich fibrin" OR "PRF" OR "Advanced Platelet Rich Fibrin" OR "LPRF" OR "IPRF") AND noft("drug delivery system" OR "drug targeting" OR "drug carrier"). Biblioteca Digital Brasileira de Teses e Dissertações: "platelet rich fibrin". OMNIS library of Pontifícia Universidade Católica: "any field" / with / ("platelet rich fibrin" OR "PRF" OR "Advanced Platelet Rich Fibrin" OR "LPRF" OR "IPRF") AND "any field"/ with / ("drug delivery system" OR "drug targeting" OR "drug carrier").

**Participant or population** Platelet-rich fibrin and Injectable platelet-rich fibrin.

**Intervention** Platelet-rich fibrin or Injectable platelet-rich fibrin with a drug.

**Comparator** Other type of drug delivery system or a drug by it's own.

**Study designs to be included** In vitro studies.

**Eligibility criteria** All types of revisions, letters, short communications, in vivo studies and prospectives or retrospectives will be excluded from this review. Also, studies with other types of platelet concentrates or those they put something to prevent natural clotting of platelet-rich fibrin.

**Information sources** The data bases that will be searched are: MEDLINE (Pubmed), EMBASE, Cochrane Library, Science Direct, Web of Science, Scopus, BVS/LILACS. Grey literature will be also searched: Google Scholar, PROQUEST, Biblioteca Digital Brasileira de Teses e Dissertações and OMNIS library of Pontifícia Universidade Católica.

**Main outcome(s)** Explore the release profile of drugs from platelet-rich fibrin over time ( $\mu\text{g/mL}$ ).

**Data management** Data from the databases will be extracted and imported into the ZOTERO bibliographic software. Duplicates will be removed. Firstly, titles and abstracts will be screened, and the papers will be categorized into folders named: added, uncertain, excluded. Papers in the uncertain folder will be fully read, and then they will be moved to either the excluded or added folder.

Sub-folders will be created in the "excluded folder" to document the main reasons for exclusion.

**Quality assessment / Risk of bias analysis** OHAT Risk-of-Bias Tool for In Vitro studies.

**Strategy of data synthesis** The data will be summarized in a spreadsheet, created in the google docs. All the results will be described in a narrative analysis.

**Subgroup analysis** Subgroup analysis will not be performed.

**Sensitivity analysis** Subgroup analysis will not be performed.

**Language restriction** Portuguese and English.

**Country(ies) involved** Brazil.

**Keywords** Platelet-Rich Fibrin; Drug Delivery Systems; Blood Platelets; Systematic Review.

**Dissemination plans** The results will be disseminated through publication in a peer-reviewed journal. This ensures that the findings undergo rigorous evaluation and scrutiny by experts in the field before they are made publicly available.

#### **Contributions of each author**

Author 1 - João Silva.

Email: drjoacolussi@gmail.com

Author 2 - Matheus Warmeling.

Email: matheusws@live.com

Author 3 - Rogerio Pagnoncelli.

Email: rogerio.pagnoncelli@puhrs.br

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