

## Formulation of a Submicron Delivery System including a Platelet Lysate to Be Administered in Damaged Skin

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**Abstract :** The prevalence of people with chronic wounds has increased dramatically by many factors including smoking, obesity and chronic diseases, such as diabetes, that can slow the healing process and increase the risk of becoming chronic. Because of this situation, the improvement of chronic wound treatments is a necessity, which has led to the scientific community to focus on improving the effectiveness of current therapies and the development of new treatments. The wound formation is a physiological complex process, which is characterized by an inflammatory stage with the presence of proinflammatory cells that create a proteolytic microenvironment during the healing process, which includes the degradation of important growth factors and cytokines. This decrease of growth factors and cytokines provides an interesting strategy for wound healing if they are administered externally. The use of nanometric drug delivery systems, such as polymer nanoparticles (NP), also offers an interesting alternative around dermal systems. An interesting strategy would be to propose a formulation based on a thermosensitive hydrogel loaded with polymeric nanoparticles that allows the inclusion and application of a platelet lysate (PL) on damaged skin, with the aim of promoting wound healing. In this work, NP were prepared by a double emulsion-solvent evaporation technique, using polylactic-co-glycolic acid (PLGA) as biodegradable polymer. Firstly, an aqueous solution of PL was emulsified into a PLGA organic solution, previously prepared in dichloromethane (DCM). Then, this disperse system (W/O) was poured into a polyvinyl alcohol (PVA) solution to get the double emulsion (W/O/W), finally the DCM was evaporated by magnetic stirring resulting in the NP formation containing PL. Once the NP were obtained, these systems were characterized by morphology, particle size, Z-potential, encapsulation efficiency (%EE), physical stability, infrared spectrum, calorimetric studies (DSC) and in vitro release profile. The optimized nanoparticles were included in a thermosensitive gel formulation of Pluronic® F-127. The gel was prepared by the cold method at 4 °C and 20% of polymer concentration. Viscosity, sol-gel phase transition, time of no flow solid-gel at wound temperature, changes in particle size by temperature-effect using dynamic light scattering (DLS), occlusive effect, gel degradation, infrared spectrum and micellar point by DSC were evaluated in all gel formulations. PLGA NP of  $267 \pm 10.5$  nm and Z-potential of  $-29.1 \pm 1$  mV were obtained. TEM micrographs verified the size of NP and evidenced their spherical shape. The %EE for the system was around 99%. Thermograms and in infrared spectra mark the presence of PL in NP. The systems did not show significant changes in the parameters mentioned above, during the stability studies. Regarding the gel formulation, the transition sol-gel occurred at 28 °C with a time of no flow solid-gel of 7 min at 33°C (common wound temperature). Calorimetric, DLS and infrared studies corroborated the physical properties of a thermosensitive gel, such as the micellar point. In conclusion, the thermosensitive gel described in this work, contains therapeutic amounts of PL and fulfills the technological properties to be used in damaged skin, with potential application in wound healing and tissue regeneration.

**Keywords :** growth factors, polymeric nanoparticles, thermosensitive hydrogels, tissue regeneration

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