Degradation, intra-articular biocompatibility, drug-release and bioactivity of tacrolimus-loaded poly(DL-lactide-PEG)-b-poly(L-lactide) multiblock copolymers based monospheres

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Supporting information:

3 pages

3 figures (S.1, S.2, S.3)

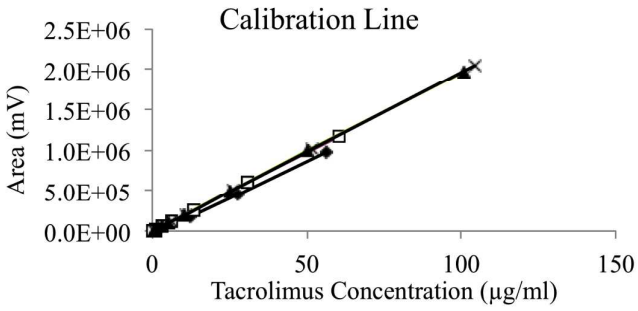

Figure S.1 *Extraction and HPLC method for tacrolimus quantification after extraction. Quantification and drug extraction method were developed based on literature [39]. HPLC method showed high linearity and reproducibility between 0 – 100 µg/mL of Tacrolimus.*

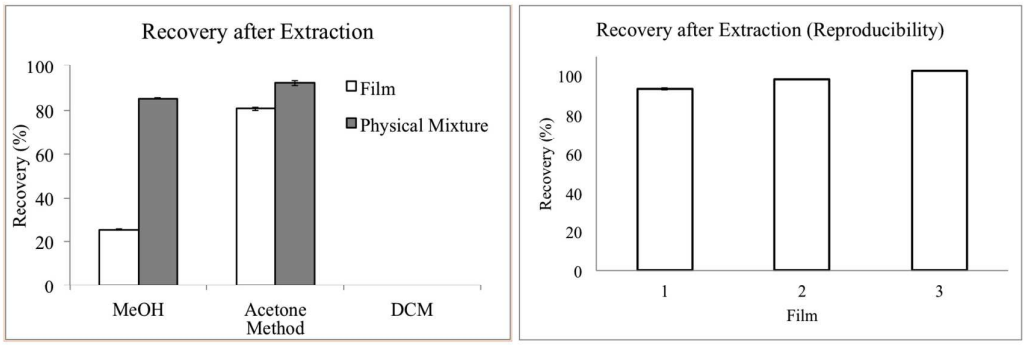

Figure S.2 *Three different organic solvents (methanol, acetone and dichloromethane) were tested for their suitability for extraction of tacrolimus from the polymer matrix. Physical blends and films of xx[PDLA-PEG$_{1000}$]-yy[PLLA] multiblock co-polymers and tacrolimus (1wt. %) were prepared in triplicate for the extraction tests. Acetone was finally selected because it showed the higher recovery and good reproducibility among the samples evaluated.*

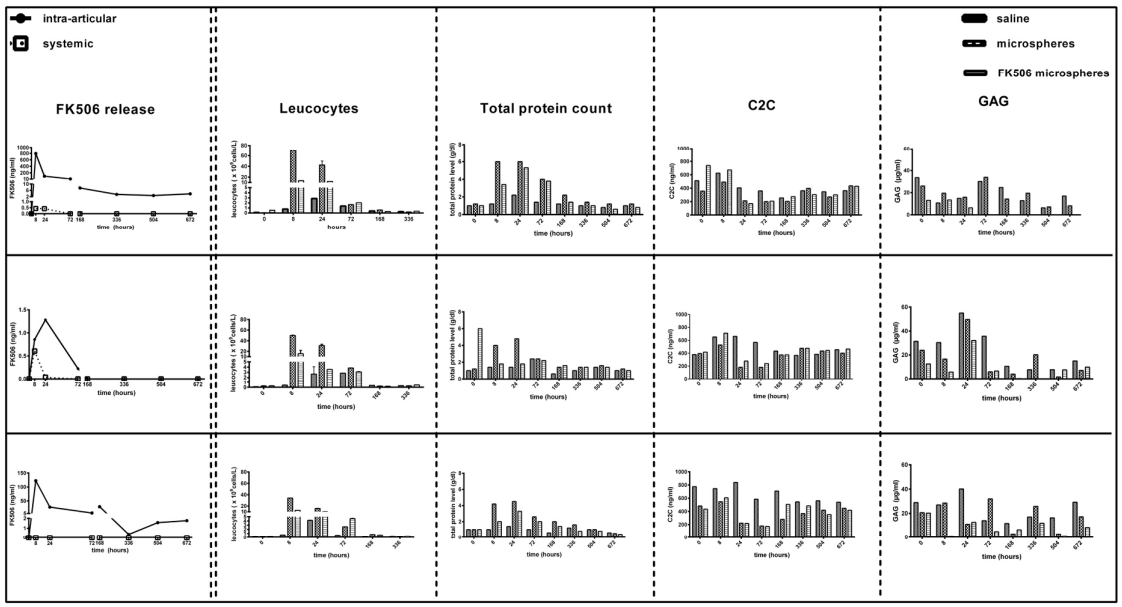

Figure S.3 *Tacrolimus concentrations in synovial fluid (intra-articular) and plasma (systemic) after intra-articular administration of tacrolimus loaded monospheres over time per individual horse (left). Right: for the same horse the amount of intra-articular leucocytes and total protein, measures of inflammatory reaction, for joints injected with saline (negative control), unloaded monospheres (positive control) and tacrolimus loaded monospheres. Also C2C and GAG content of the synovial fluid (indicative for cartilage breakdown) are shown. Neither of these two markers where elevated, indicating that neither the inflammation, nor the injection of FK-506 loaded monospheres led to cartilage breakdown during the study period.*