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## A pH and thermo-sensitive targeted nanogel as a possible treatment for rheumatoid arthritis

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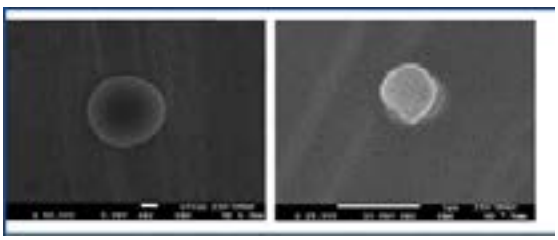
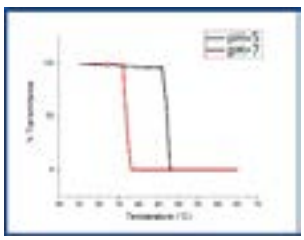
**Statement of the Problem:** Rheumatoid arthritis is a chronic, autoimmune and inflammatory disease that affects almost 1.0% of the world population. The current treatment used is based on the administration of Disease-Modifying Antirheumatic Drugs (DMARDs) like methotrexate (MTX), which is the first-choice medication. Unfortunately, DMARDs based therapies aren´t satisfactory, because of the kidney and medullar damage they cause, associated with the non- specificity of the drugs to a target tissue. Here, it is proposed the development of a targeted, pH and thermosensitive nanogel that ensure MTX´s delivery only at arthritic joints.

**Methodology:** Nanogel particles were made by the radical polymerization of N-isopropylacrylamide, 1- vinylimidazole and N'N-methylenebisacrylamide in water. The obtained system was coated with a hyaluronic acid film in order to get an active target mechanism. An amount of MTX was loaded at the coated nanogel particles by physical adsorption. The system´s structure was characterizated by FTIR and NMR. The size and morphology of the particles were studied with DLS and SEM (Figure 1). The thermo and pH sensibility of the system were getting by turbidimetry techniques. An *in vitro* drug delivery was made to quantify the MTX´s delivery.

**Results:** It was found that 90.5% of NIPAM, 7.5% of VI and 2% of MBA are required to obtain stable nanogel particles that swell at 36.5°C at pH 7 and at 42°C at pH 5 (Figure 2). It was demonstrated the adsorption of a therapeutic amount of MTX according a *Langmuir- Freundlich* isotherm. *In vitro* essays show that MTX loaded is delivered at arthritic joints conditions in 10 hrs., whereas at physiological health conditions, it is required more than 36 hrs. for its complete delivery (Figure 3).

**Conclusion and Significance:** The obtained system has special characteristics to deliver MTX specifically at arthritic joints, so it could help to reduce the adverse effects that affect the life condition of patients.





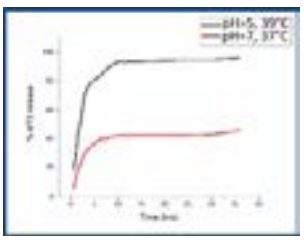


**Figure 1.** Nanogel and coated nanogel images obtained by SEM.

**Figure 2.** Turbidimetry analysis shows the thermo and pH sensitive of the system

**Figure 3.** *In vitro* drug delivery of MTX-adsorbed nanogel

**Recent Publications**

1. Jeffery, R. (2014) Clinical features of rheumatoid arthritis. Medicine. 45; 231-236
2. Zampeli, E., *et al.* (2015) Treatment of rheumatoid arthritis: Unraveling the conundrum. Journal of Autoimmunity. 65: 1-18
3. Wilsdon, T., *et al.* (2017) Managing the drug treatment of rheumatoid arthritis. Australian Prescriber, 40(2): 51-58
4. Strang, A., *et al.* (2004) Methotrexate toxicity induced by acute renal failure. Journal of the Royal Society of Medicine, 97(11) 536
5. Yang, M., *et al.,* (2016) Nanotherapeutics relieve rheumatoid arthritis. Journal of Controlled Release, 252; 108-124.

**Biography**

Mayra Martínez-Peláez is dedicated at the design and development of novel drug delivery systems. Because of her knowledge in chemistry, pharmacology and pharmacokinetics, she has experience in preformulation and formulation of drugs, but also, she is familiar with regulatory and marketing affairs. She was graduated with honors by the Universidad Autonoma de Mexico in Mexico City and right now she is about to obtain a chemistry master's degree.

**Notes:**