

Study of drug release on smart nano-sized hydrogels based on *N*-isopropyl acrylamide by High Performance Liquid Chromatography

X. Hervías¹, L.G. Guerrero¹, S. Nuño-Donlucas², L.C. Cesteros¹, L. Sanz¹, I. Katime¹

1) Grupo de Nuevos Materiales y Espectroscopia Supramolecular. Facultad de Ciencia y Tecnología. Universidad del País Vasco (UPV/EHU). Campus de Lejona, Apartado. 644

Bilbao, España. E-mail: issa.katime@ehu.es

2) Universidad de Guadalajara. Departamento de Ingeniería Química. CUCEI. Guadalajara (Jalisco, México).

A novel method to measure the drug release of 5-Fluorouracil (5-FU) on smart nano-sized hydrogels based on *N*-isopropyl acrylamide has been developed using a High Performance Liquid Chromatography (HPLC) technique. The employ of polymeric materials such a hydrogels in drug release, generates o lot of possibilities in specific drug delivery systems [1]. The release of the active agent may be constant over a long period, it may be cyclic over a long period, or it may be triggered by the environment or other external events [2]. The nanoparticles were synthesized by inverse microemulsion polymerization using a method previously reported [3]. The release speed of a drug is virtually controlled by the polymer properties and some factors such the pH of the release medium [4]. The behaviour of this nanoparticles show a selective swelling-collapse response to external pH changes [5]. It is known that the incorporation of pH sensitive groups into polymer grid, can modify the original behaviour of this macromolecules [6] changing the pH response value. The use of these materials is an important application in delivery and administration of drugs due to incorporation of polymeric systems advantages [7]. Nanohydrogels were charged with 5-FU by the dispersion of the nanoparticles in a phosphate buffer solution (pH 7.4) in which 5-FU was previously added. Purification process of the charged nanohydrogels was carried out by washing the samples with ultra purified water. The HPLC equipment was conditioned using KH_2PO_4 0.01 M as a mobile phase and the optimal flow rate for the system was obtained in 1 mL/min, the wavelength UV detector was located at 254 nm. The 5-FU concentration released by the nanogels was calculated after calibrating equipment with 5-FU standards by integrating the peak area in each case. UV-visible spectroscopic experiments were performed to corroborate the kinetic curve obtained by HPLC. These experiments were carried out using a peristaltic pump coupled with a Peltier Power Supplied Thermocell to keep constant the flow rate and the concentration gradient. The measurements made by UV-visible spectroscopy confirm the values obtained by HPLC.

References:

- [1] Katime, I., Katime, O. and Katime, D. “**Los materiales inteligentes de este Milenio: los hidrogeles polímeros**”. Universidad del País Vasco. Bilbao 2004
- [2] Brannon-Peppas L., **Medical Plastics and Biomaterials Magazine** (1997)
- [3] Katime I., Guerrero L.G., Cesteros L.C. and Nuño Donlucas S. **IV World Congress on Biomimetics, Artificial Muscles and Nano-Bio 2007**. Pag. 43.
- [4] Sáez V., Hernáez E. and Sanz Angulo L., **Revista Iberoamericana de Polímeros**, Vol. 5 (2004), 55-70.
- [5] Heller J., Pangburn S.H., and Penhale D.W.H., **Controlled-Release Technology, Pharmaceutical Applications**, ACS Symposium Series, (1987) pp 172–187,
- [6] Vert M., Li S., and Garreau H., **Journal of Controlled Release**, Vol. 16 (1991), 15–26.
- [7] Buckpitt A.R., Boyd M.R., **Analytical Biochemistry**, Vol. 106, 432-437.

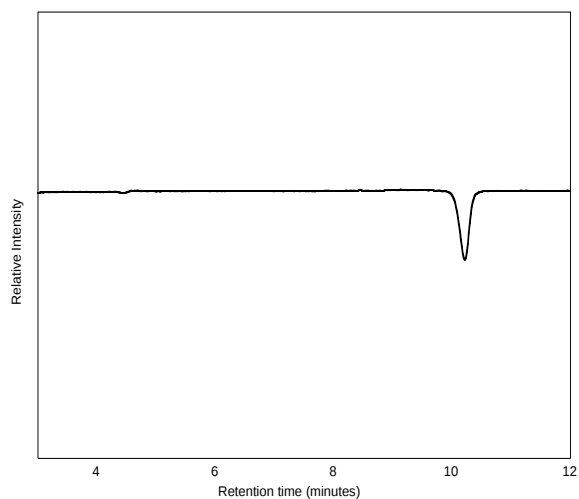
Figures:

Figure 1. HPLC measurement of the drug release in smart nanohydrogels at pH 7.4.

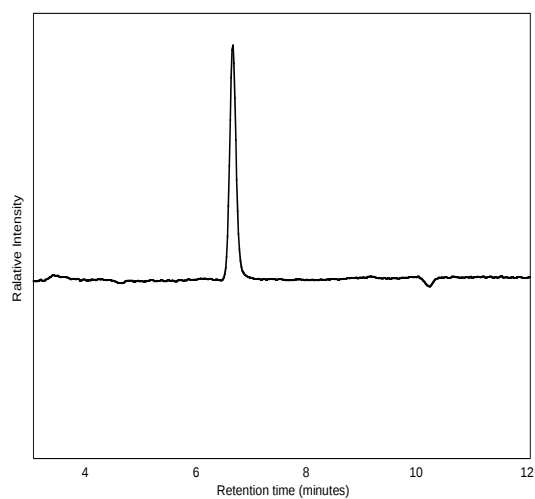


Figure 2. HPLC measurement of the drug release in smart nanohydrogels at pH 4.0.

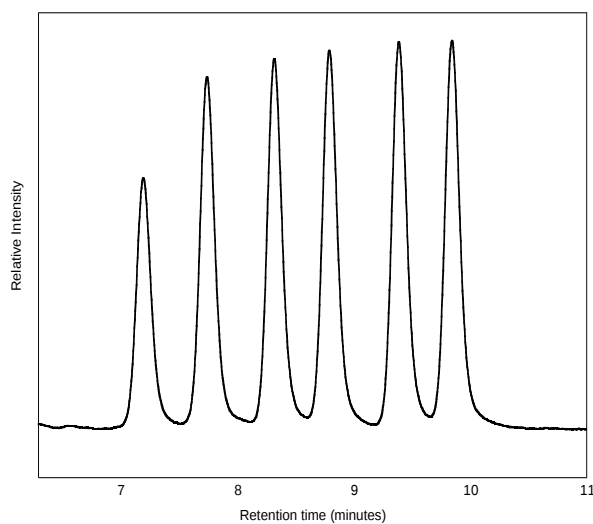


Figure 3. Drug release kinetics in smart nanohydrogels charged with 5-FU at pH 4.0.