

Supplementary Information

Water-soluble gold nanoparticles based on imidazolium gemini amphiphiles for delivery of piroxicam

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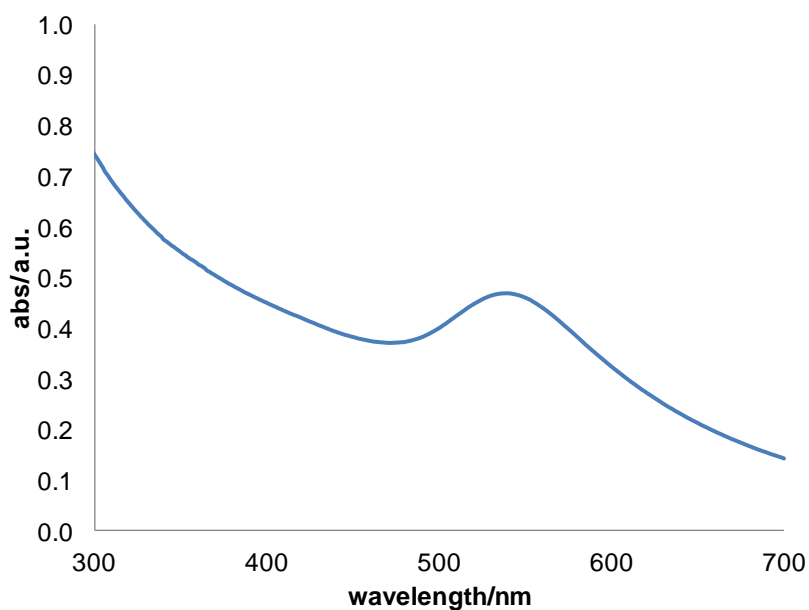


Figure S1: UV-vis spectra of **1•GNP**, showing the typical SPR peak around 533 nm.

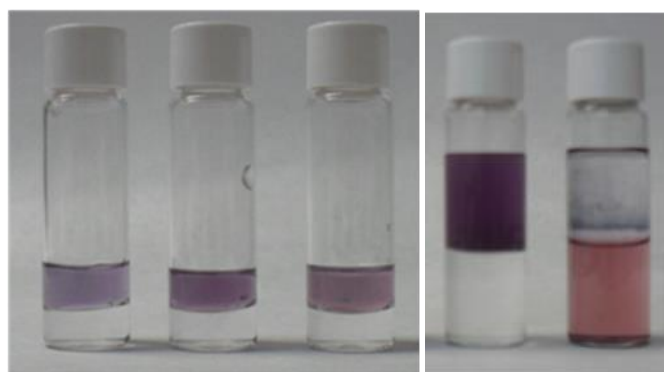


Figure S2: From left to right: GNP from experiments 2 to 4 (in Table 1) in aqueous phase (organic dichloromethane phase below without any GNP). GNP from experiment 4 (after centrifugation to concentrate them) and from experiment 1 (transferred to organic dichloromethane phase).

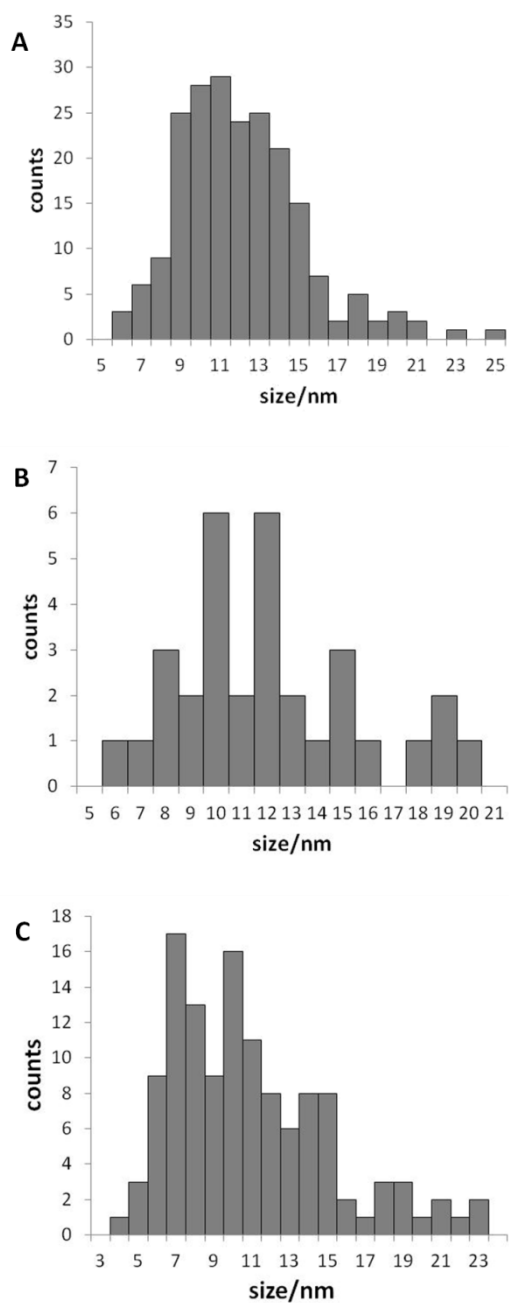


Figure S3: Histograms corresponding to the size distributions (measured in the TEM micrographs) for the GNP from experiment 2 (A), experiment 3 (B) and experiment 4 (C).

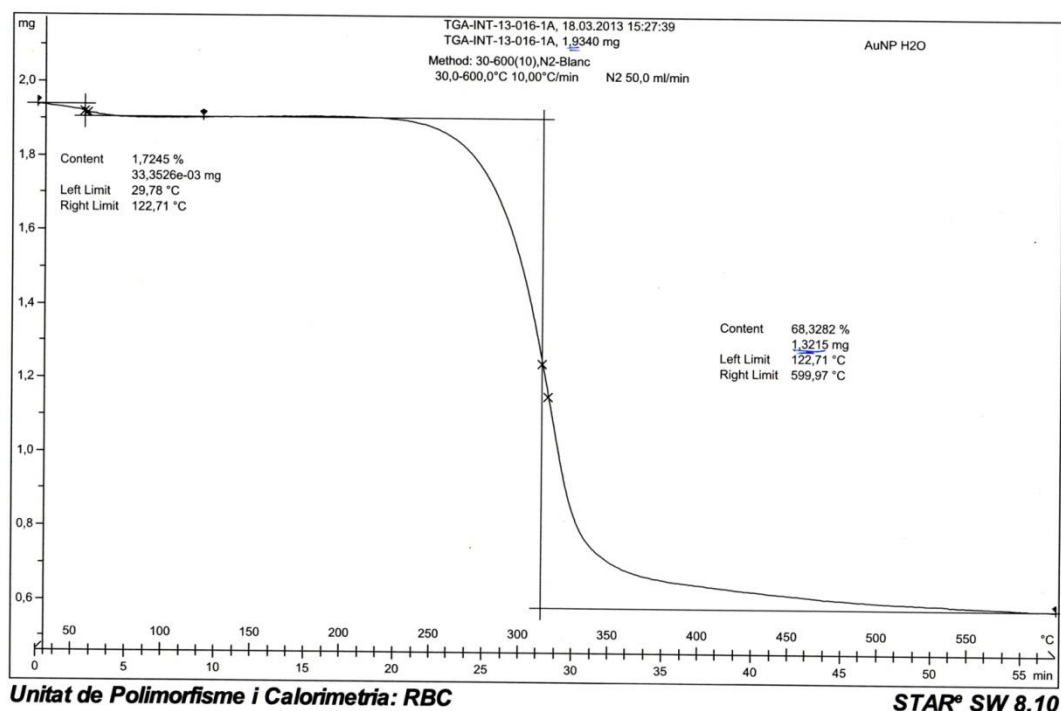


Figure S4 Thermogravimetry curve obtained for the 1·GNP

Table S1

Thermogravimetry results and calculations of amount of ligand per NP and per area of NP surface based on the ratio of ligand to gold present in the GNP and their gold core size obtained by TEM.

Sample	Total mass (mg)	Ligand mass (mg)	Ligand: Au (mmol)	Average diameter (nm)	Moles Au/NP	Ligand/NP	Ligand/nm ²
1·GNP	1.8605	1.2861	0.62969	11.6	8.0x10 ⁻²⁰	30255	71.57
GNP ¹	5.8230	3.1521	0.32610	8.8	3.5 x10 ⁻²⁰	6840	28.12

¹ L. Casal-Dujat, M. Rodrigues, A. Yagüe, A. C. Calpena, D. B. Amabilino, J. González-Linares, M. Borràs and L. Pérez-García, *Langmuir*, 2012, **28**, 2368-2381

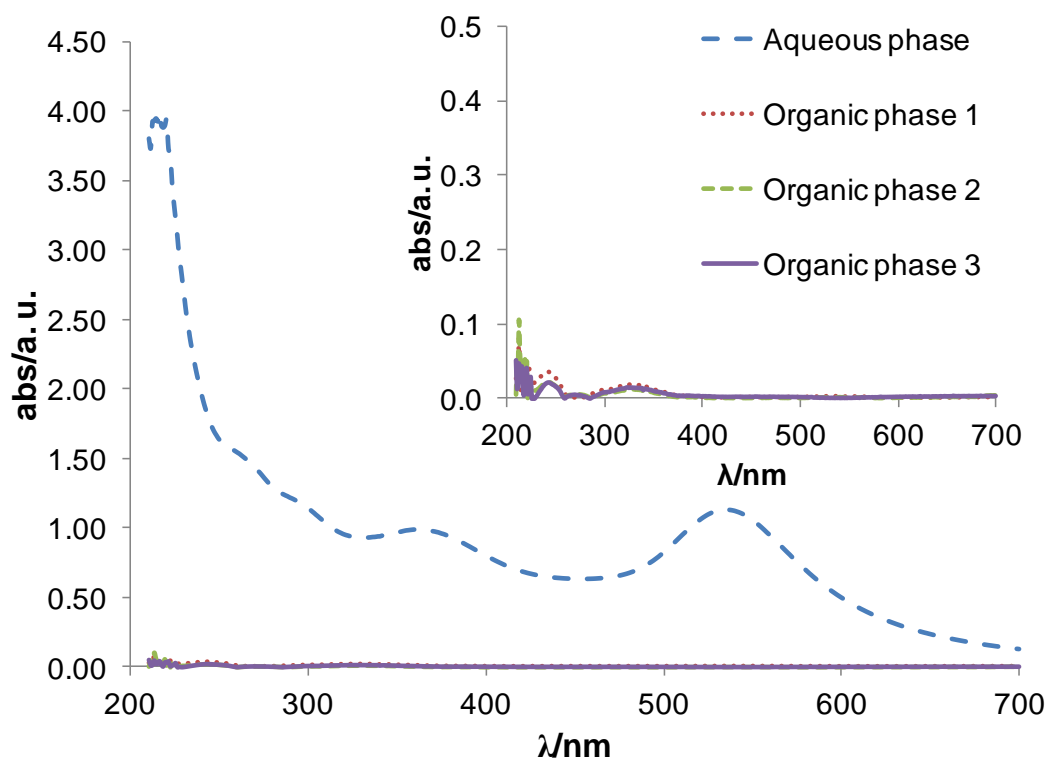


Figure S5: UV/Vis spectrum of the **1•GNP** after extraction of piroxicam, presenting the peak corresponding to piroxicam at 360 nm and the SPR of the GNP, and the organic phases (amplified scale included).

Table S2:

Kinetic models used to fit the data for the release of Piroxicam from **1•GNP**, and the respective AIC parameter

Kinetic model	Equation	AIC	
		pH 5.5	pH 7.4
Zero order	$Qt/Q_{\infty} = K_0 * t$	-77.2	-95.1
First order	$Qt/Q_{\infty} = 1 - e^{-K_1 * t}$	-77.1	-107.7
One phase exponential	$Qt/Q_{\infty} = 1 + (S/P) * e^{-Kt}$	-96.1	-128.2
Higuchi	$Qt/Q_{\infty} = KH * t^{1/2}$	-72.1	-101.4
Weibull	$Qt/Q_{\infty} = 1 - e^{-(t/td)^{\beta}}$	-89.0	-118.0
Korsmeyer-Peppas	$Qt/Q_{\infty} = K * t^n$	-80.7	-102.0

Q_t is the amount of drug released at time t

Q_{∞} is the total amount of drug released

Q_t/Q_{∞} is the fraction of drug released at time t

K is the release rate constant

P is the Plateau (Q at t_{∞}) and S is the Span (the difference between Q_0 and P)

n is the diffusion release exponent that could be used to characterize the different release mechanism ($n \leq 0.43$ (Fickian diffusion), $0.43 < n < 0.85$ (anomalous transport), and ≥ 0.85 (case II transport; i.e. zero order release))

t_d is the time in which the 63.2% of the drug is released and β is the shape parameter

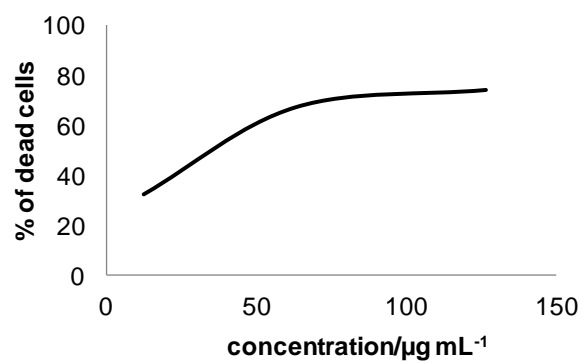


Figure S6: Effect of the **1•GNP** on the viability of Caco-2 cells, by the MTT method.

Table S3:

COX activity in cells exposed to **1•GNP**, **1•GNP** with piroxicam (**1•GNP-pxc**) and **1•GNP** with piroxicam and LPS (**1•GNP-pxc + LPS**). LPS is used to induce inflammation.

	$t_{\text{exposure}}/\text{days}$	Optical density		Activity/ $\text{U}^{\text{a}} \text{mL}^{-1}$		% activity	
		COX-total	COX-II	COX-total	COX-II	COX-I	COX-II
1•GNP	1	0.156	0.158	9.915	10.042	-1.3	101.3
	10	0.39	0.356	24.788	22.627		91.3
1•GNP-pxc	1	0.141	0.145	8.962	9.216	-2.8	102.8
	10	0.312	0.286	19.831	18.178	8.3	91.7
1•GNP-pxc + LPS	1	0.155	0.159	9.852	10.106	-2.6	102.6
	3	0.193	0.18	12.267	11.441	6.7	93.3
	5	0.271	0.271	17.225	17.225	0.0	100.0
	8	0.351	0.31	22.309	19.703	11.7	88.3
	10	0.361	0.345	22.945	21.928	4.4	95.6

^aUnits of enzymatic activity