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Supporting Information

Laser light triggered smart release of Silibinin from a PEGylated-PLGA gold nanocomposite

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NMR analysis

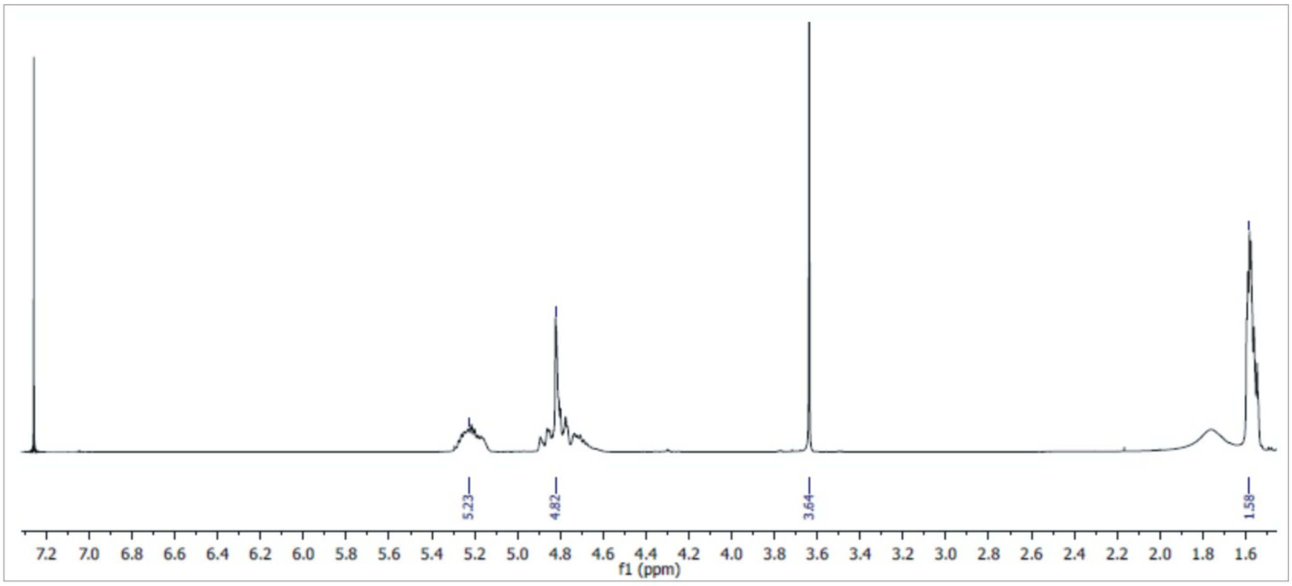

Fig. S1: ^{1}H-NMR of PEG-PLGA copolymer in $CDCl_3$.

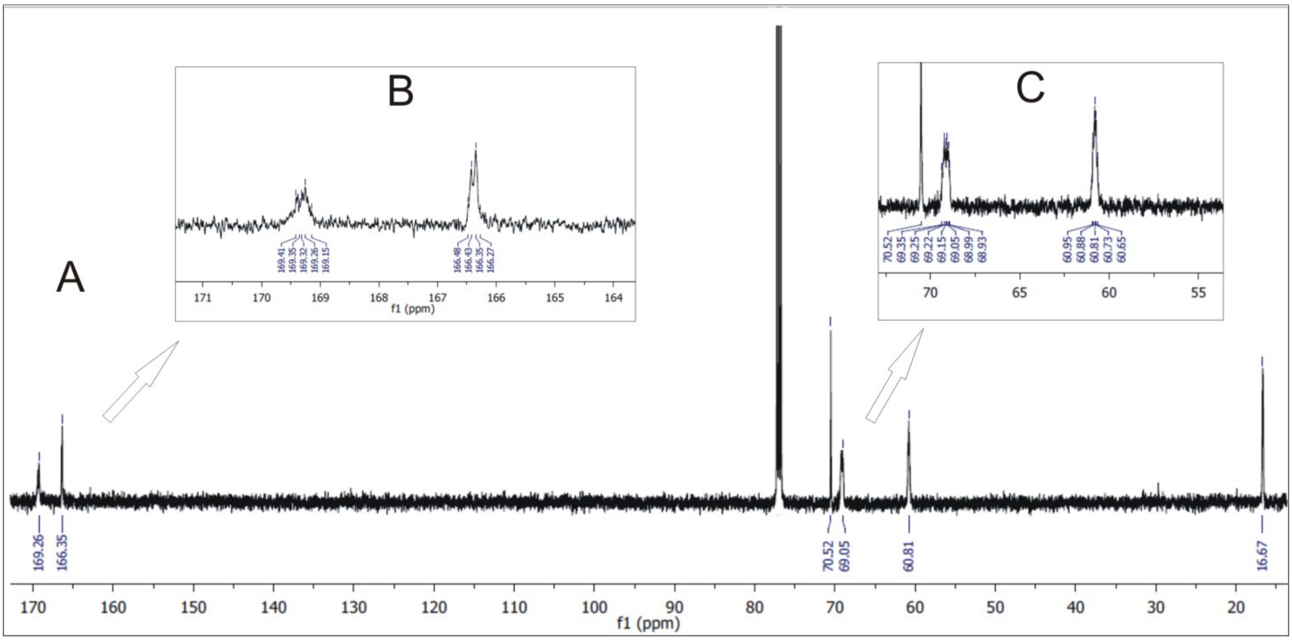

Fig. S2: A) ^{13}C-NMR of PEG-PLGA copolymer in $CDCl_3$. Inserted figures (B) and (C) are the magnifications of the carbonyl and aliphatic regions, respectively.

Static Light Scattering analysis

Static Light Scattering (SLS) measurements were carried out, at room temperature, using the Horiba SZ-100 nanoparticle analyzer. The scattered light intensity of the polymeric solution is proportional to the product of the weight-average molecular weight and the concentration of the solution (I α ($M_w \cdot C$). This is called a Debye plot (KC/R_θ versus C) and allows for the determination of absolute molecular weight and 2nd virial coefficient (A_2) values. Therefore, a plot of KC/R_θ versus C gives a straight line whose intercept at zero concentration is 1/M and whose gradient is A_2: $KC/R_\theta = (1/M + 2A_2C)$. In Fig. S3 the Debye plot of the PEG-PLGA copolymer is shown. Moreover, the SLS measured molecular weight of the PLGA and PEG precursors were evaluated and are 28400 and 7500 KDa, respectively.

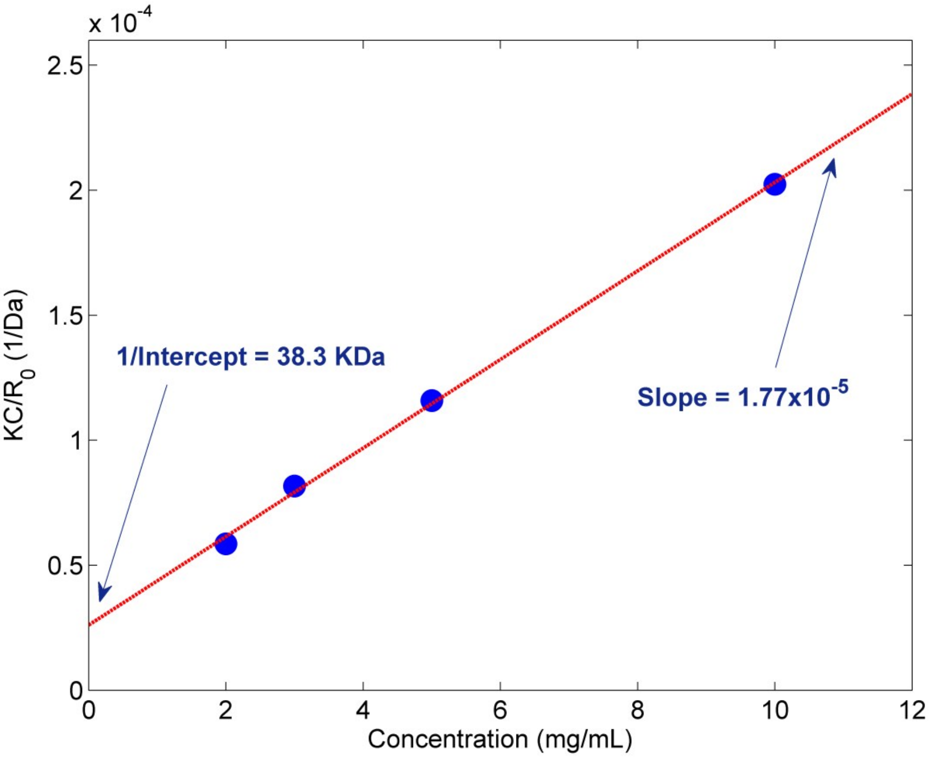

Fig. S3: Debye plot of the PEG-PLGA copolymer.

Thermogravimetric (TGA) analysis

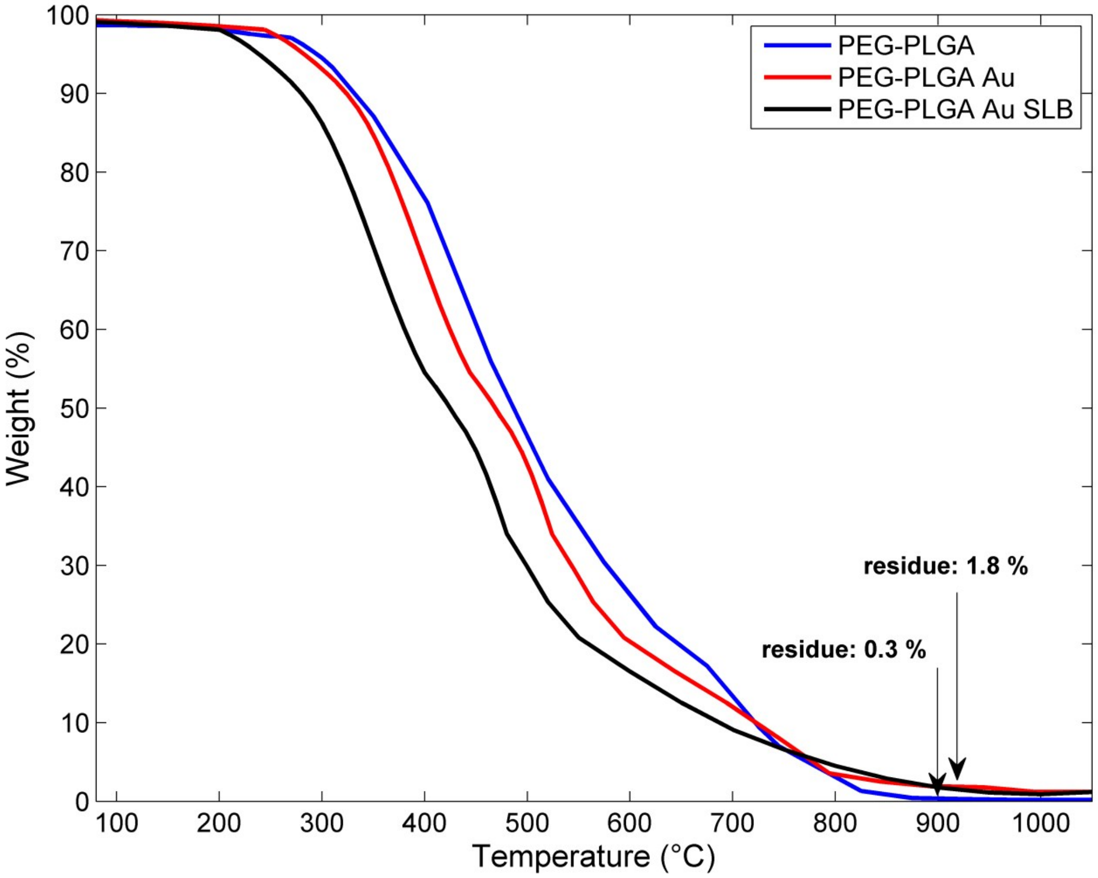

Fig. S4: TGA curves for the investigated systems.

UV-vis optical absorption analysis

Unlike the chemical approaches, adopting the pulsed laser ablation (PLAL), the amount of the prepared products cannot be estimated directly by weighing. The PLAL technique consists in the mass removal by coupling laser energy to a target material. When the laser radiation is focused on the surface of a solid target, pulsed-laser radiation can be absorbed through various energy transfer mechanisms, leading to thermal and non-thermal heating, melting, and finally ablation of the target. Laser ablation is one of the most efficient physical methods for micro, and more recently, nanofabrication, due to the high resolution capability, low heat deposition in the target and high level of flexibility. The ablation of the target yields to an ejection of its constituents and to the formation of nanoclusters and nanostructures which, when the target is ablated in liquids, are dispersed in the solvent.

Therefore, the gold amount in the water solution was indirectly calculated by analyzing UV–vis spectra and taking into account microscopy results. As it has been demonstrated by Link and El Sayed [*Link S, El-Sayed MA. Spectral properties and relaxation dynamics of surface plasmon electronic oscillations in gold and silver nanodots and nanorods. J. Phys. Chem. B 1999; 103, 8410–8426.*], in the particle size range of our experiments, the width variation with size is difficult to appreciate. Nevertheless, the concentration of the water Au nanocolloids in the PEG-PLGA system was calculated from the plasmon resonance position and taking into account NPs size estimated by TEM analysis. Particularly, we consider the linear relationship of the peak plasmon resonance wavelength λ_{max} as a function of the gold molar fraction f_{Au}, as determined by Link et al. Such linear relationship has been verified both with experimental results from XPS analysis obtained considering the Au $_{4f}$ core signals as well as a comparison with nanocolloids produced during simultaneous reduction of the gold ions by sodium citrate in the same solution [*E. Messina, L. D'Urso, E. Fazio, C. Satriano, M.G. Donato, C. D'Andrea, O.M. Maragò,P.G. Gucciardi, G. Compagnini, F. Neri, Tuning the structural and optical properties of gold/silver nano-alloys prepared by laser ablation in liquids for optical limiting, ultra-sensitive spectroscopy, and optical trapping. Journal of Quantitative Spectroscopy & Radiative Transfer 113 (2012) 2490–2498 ; Link S, Wang ZL, El-Sayed MA. Alloy formation of gold–silver nanoparticles and the dependence of the plasmon absorption on their composition. J. Phys. Chem. B 1999; 103, 3529–33; Peng Z, Spliethoff B, Tesche B, Walther T, Kleinermanns K. Laser-assisted synthesis of Au–Ag alloy nanoparticles in solution. J. Phys. Chem. B 2006; 110, 2549–54; Compagnini G, Messina E, Puglisi O, Nicolosi V. Laser synthesis of Au/Ag colloidal nano-alloys: exploring the optical properties for an accurate analysis. Appl Surf Sci 2007; 254, 1007–11*].

As shown in Fig. S5, the Au Surface Plasmon Resonance (SPR) characteristic peak is well distinguishable in the freshly prepared gold solutions. On the other hand, the SPR feature is less evident when the Au NPs are loaded in the co-polymers. This behavior is explained taking into account the relatively low Au NPs content within the polymers, so that the Au SPR signal is overlapped by the polymers absorption response. On the overall, the estimated concentration of the Au colloid in the copolymer is about 1.0×10^{-6} M, assuming an average molar extinction coefficient of 2.5×10^{4} $M^{-1}cm^{-1}$.

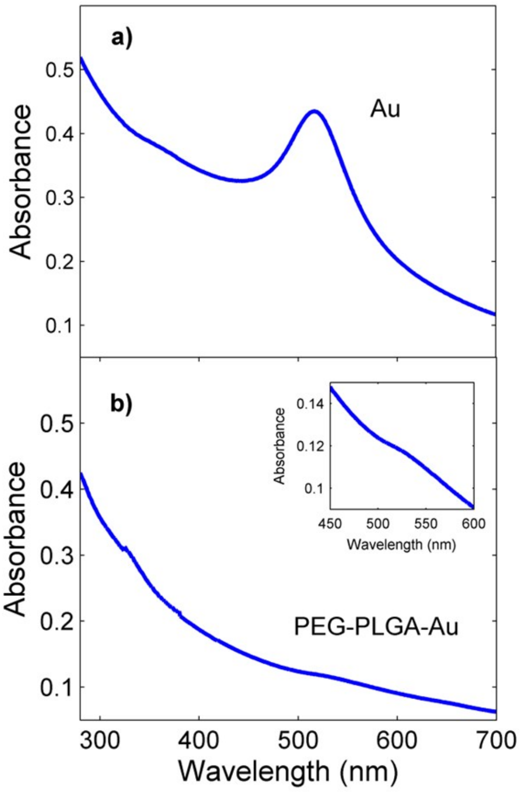

Fig. S5: Absorption spectra of (a) Au nanocolloids and (b) PEG-PLGA_Au nanocomposite dispersed in PBS/DMSO (1:99).

Drug release mechanism

The classic model used to explain the diffusion phenomena, due to local concentration gradients (Fick's law), was adopted to explain the increment of the drug release from the polymer matrix, taking into account the polymeric structural configuration change, and considering spherical 200 nm sized polymeric structure. The diffusion law is:

$$\frac{M_t}{A} = \left[D(2c_0 - c_s)c_s t\right]^{1/2} \quad \text{per } c_0 > c_s$$

where M_t is the cumulative drug content released in the time, A is the area of the nanocomposite exposed to the medium in which the drug is released, D is the diffusion coefficient, c_0 and c_s are, respectively, the concentration of the loaded drug and the solubility of the drug in the polymer. The diffusion law can be expressed, in a simplified expression, as proportional to the square of the time:

$$\frac{M_t}{M_\infty} = Kt^{1/2}$$

where M_∞ is the drug content released in an infinite time (which, really, is the loaded drug content) and K is a constant which takes into account the nanocomposite structural properties [*J. Siepmann, N.A. Peppas, Advanced Drug Delivery Reviews 48 (2001) 139–157*].