Evaluation of the release kinetics of hydrophilic and lipophilic compounds from lipid-polymer hybrid nanoparticles: Supplementary material

Juan P. Carmona-Almazán[1,2], Ana B. Castro-Ceseña[1,3,*], and Sergio A. Aguila[2,**]

[1]Departamento de Innovación Biomédica, Centro de Investigación Científica y de Educación Superior de Ensenada, Baja California (CICESE), Carretera Ensenada-Tijuana No. 3918, Zona Playitas, C.P. 22860, Ensenada, Baja California, México. for Scientific Research and Higher Education
[2]Centro de Nanociencias y Nanotecnología, Universidad Nacional Autónoma de México (CNyN-UNAM), Km 107 Carretera Tijuana-Ensenada. Ensenada, Baja California
[3]CONAHCYT- Departamento de Innovación Biomédica, Centro de Investigación Científica y de Educación Superior de Ensenada, Baja California (CICESE), Carretera Ensenada-Tijuana No. 3918, Zona Playitas, C.P. 22860, Ensenada, Baja California, México.
[*]Corresponding author at: Departamento de Innovación Biomédica, Centro de Investigación Científica y de Educación Superior de Ensenada (CICESE). E-mail address: abcastroca@conacyt.mx
[**]Corresponding author at: Centro de Nanociencias y Nanotecnología, Universidad Nacional Autónoma de México (CNyN-UNAM). E-mail address: aguila@ens.cnyn.unam.mx

1 Load efficiency after purification, proposed mathematical determination

It is important to clarify that this is an approximation and not a model, as it has not been proven or tested yet. Future works may undertake the validation of this approximation. With that noted, we propose a mathematical expression to approximate the loading efficiency, which quantifies the amount of drug encapsulated within the LPHNPs after purification. This approach could be useful for calculating the efficiency of the purification method and obtaining a more accurate estimate of the actual quantity of compound loaded in the nanoparticles. The following assumptions were made to develop this approximation:

1. To simplify, after synthesis, the initial mass of the compound may either remain encapsulated or become free. Therefore, we define the mass of encapsulated compound q_{ce} in the polymeric nanoparticles as the initial mass of compound used in synthesis q_{ci} minus the mass of non-encapsulated compound q_{cn}.

$$q_{ce} = q_{ci} - q_{cn} \tag{1}$$

2. We assume that eventually, 100% of the encapsulated compound will be released. Therefore, at infinite time, the amount of released compound q_{cl} will equal the total amount of encapsulated compound after purification q_{ep}.

$$q_{ep} = \lim_{t\to\infty} q_{cl}(t) \tag{2}$$

3. Assuming that a quantity of nanoparticles is lost during purification, some compound would also be lost, so this amount of lost compound $q_{c\pi}$ should be subtracted from the amount of encapsulated compound.

$$q_{ep} = q_{ci} - q_{cn} - q_{c\pi} \tag{3}$$

With these assumptions in place, encapsulation efficiency ξ can be defined as the ratio of encapsulated compound to the initial amount of compound. This concept can be expressed in terms of both encapsulated and non-encapsulated compound

$$\xi = \frac{q_{ce}}{q_{ci}} \tag{4}$$

$$\xi = \frac{q_{ci} - q_{cn}}{q_{ci}} = 1 - \frac{q_{cn}}{q_{ci}} = 1 - \frac{q_{cn}}{q_{ce} + q_{cn}} \tag{5}$$

We can define the yield ϵ as the fraction of purified encapsulated compound q_{ep} with respect to the amount of encapsulated compound, also, considering assumption 3, could be rewritten in terms of the compound lost during purification $q_{c\pi}$

$$\epsilon = \frac{q_{ep}}{q_{ce}} \tag{6}$$

$$q_{c\pi} = q_{ci} - q_{cn} - q_{ep} = q_{ce} - q_{ep} \tag{7}$$

$$\epsilon = \frac{q_{ce} - q_{c\pi}}{q_{ce}} = 1 - \frac{q_{c\pi}}{q_{ce}} \tag{8}$$

By rearranging equation (8) and substituting it into equation (5), we obtain an expression that relates both efficiencies, which are the only data obtained experimentally

$$\frac{q_{c\pi}}{q_{ce}} = 1 - \epsilon \tag{9}$$

$$q_{c\pi} = (1 - \epsilon)(q_{ce}) \tag{10}$$

$$q_{ce} = \frac{q_{c\pi}}{1 - \epsilon} \tag{11}$$

$$\xi = 1 - \frac{q_{cn}}{\frac{q_{c\pi}}{1-\epsilon} + q_{cn}} \tag{12}$$

Furthermore, we derive an expression that mathematically describes the amount of compound lost during purification in terms of the loading efficency and yield.

$$1 - \xi = \frac{q_{cn}}{\frac{q_{c\pi}}{1-\epsilon} + q_{cn}} \tag{13}$$

$$q_{cn} = (1 - \xi)(\frac{q_{c\pi}}{1 - \epsilon} + q_{cn}) = (1 - \xi)\frac{q_{c\pi}}{1 - \epsilon} + q_{cn}(1 - \xi) \tag{14}$$

$$q_{cn} - q_{cn}(1 - \xi) = (1 - \xi)\frac{q_{c\pi}}{1 - \epsilon} \tag{15}$$

$$q_{cn}[1 - (1 - \xi)] = q_{cn}\xi = (1 - \xi)\frac{q_{c\pi}}{1 - \epsilon} \tag{16}$$

$$q_{c\pi} = \frac{q_{cn}\xi(1 - \epsilon)}{1 - \xi} \tag{17}$$

Now, we define a new term R_c as the fraction of compound mass to polymer mass q_p

$$R_c = \frac{q_{ci}}{q_p} \tag{18}$$

$$q_{ci} = R_c q_p \tag{19}$$

By substituting equations (17) and (19) into equation (3)

$$q_{ep} = R_c q_p - q_{cn} - q_{cn}\xi\frac{(1 - \epsilon)}{1 - \xi} = R_c q_p - q_{cn}[1 + \xi\frac{(1 - \epsilon)}{1 - \xi}] \tag{20}$$

If we rearrange 5 and substitute (19) into it, then we obtain an expression that define q_{cn} in terms of the mass of the polymer and encapsulation efficiency

$$\frac{q_{cn}}{q_{ci}} = (1 - \xi) \tag{21}$$

$$q_{cn} = q_{ci}(1 - \xi) = R_c q_p (1 - \xi) \tag{22}$$

By substituing 22 into 20, and regrouping themrs, we obtain a general equation to calculate the mass inside the LPHNPs after purification

$$q_{ep} = R_C \cdot q_p - R_C \cdot q_p \cdot (1 - \xi)[1 + \xi \frac{(1 - \epsilon)}{1 - \xi}] \tag{23}$$

$$q_{ep} = R_C \cdot q_p [1 - (1 - \xi)(1 + \frac{1 - \epsilon}{1 - \xi} \cdot \xi)] \tag{24}$$

$$q_{ep} = R_C \cdot q_p [1 - [(1 - \xi) + \xi(1 - \epsilon)]] \tag{25}$$

$$q_{ep} = R_C \cdot q_p [1 - (1 - \xi + \xi - \xi\epsilon)] \tag{26}$$

$$\boxed{q_{ep} = R_C \cdot q_p \cdot \xi \cdot \epsilon} \tag{27}$$

If we divide that quantity by the initial mass q_{ci}, we can obtain an approximation of the loading efficiency after purification E_f of the LPHNPs with this specific synthesis method

$$\boxed{E_f =_{ep} / q_{ci}} \tag{28}$$

2 Antioxidant activity of gelatine aerogels and LPHNPs embedded in gelatine

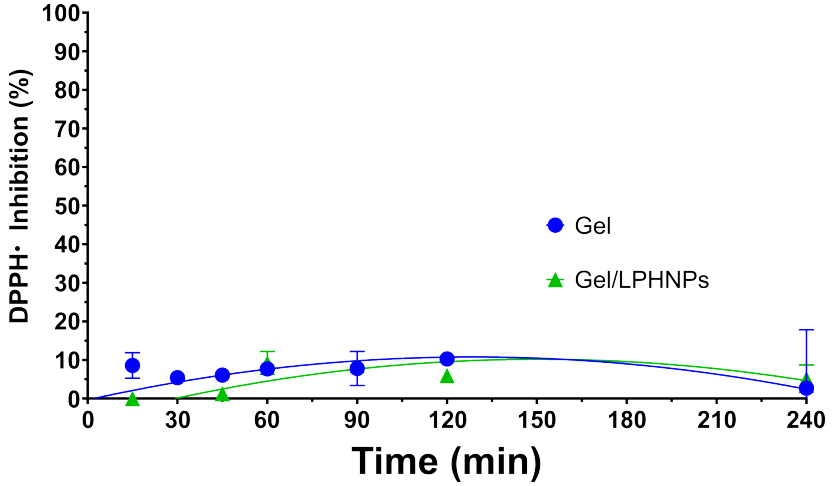

Figure S1: Antioxidant activity of gelatin aerogels and lipid/polymer hybrid nanoparticles (LPHNPs) embedded in gelatin aerogels, determined by inhibition of DPPH• radical.

3 Determination of the DPPH• inhibition technique sensibility

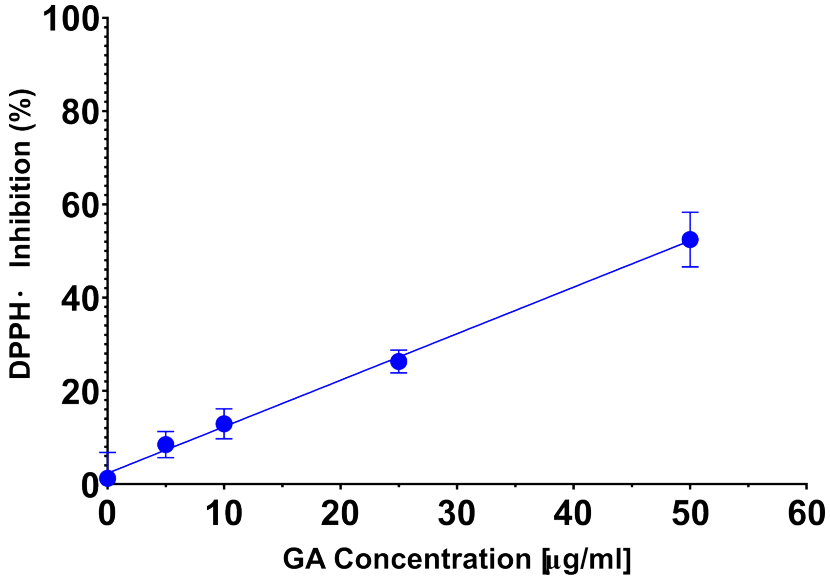

Figure S2: Preliminary calibration curve of DPPH• radical inhibition by the antioxidant activity of gallic acid (GA), made to determine the method's sensitivity to low concentrations.

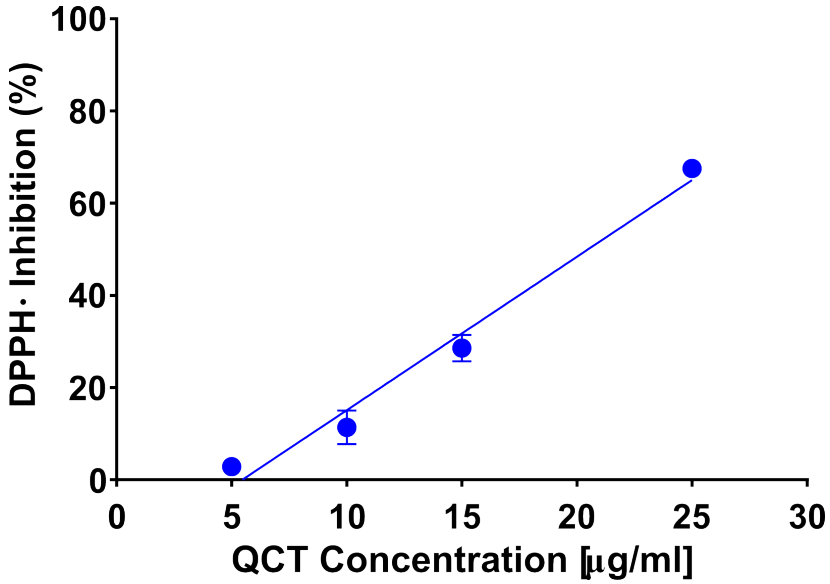

Figure S3: Preliminary calibration curve of DPPH• radical inhibition by the antioxidant activity of quercetin (QCT), made to determine the method's sensitivity to low concentrations.

4 Quercetin Release Assays Under Different Ethanol Concentration Conditions

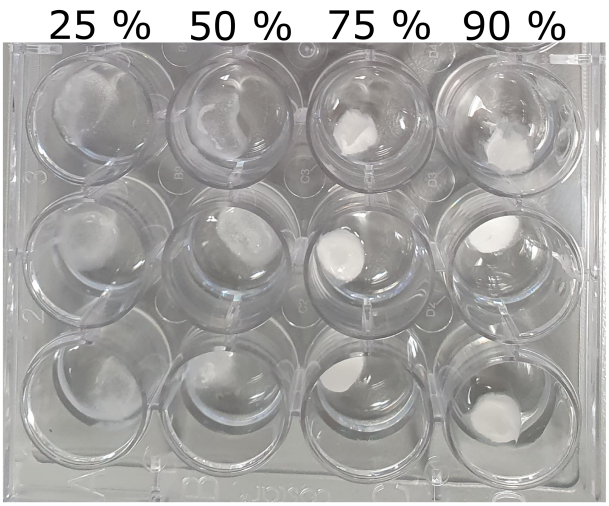

Figure S4: Behavior of gelatin aerogels subjected to different ethanol concentrations (25%, 50%, 75%, and 90%) after 2 hours. The image illustrates that in higher ethanol concentrations (75% and 90%) the aerogels shrunk while those in lower concentrations swelled as in aqueous conditions (25% and 50%).

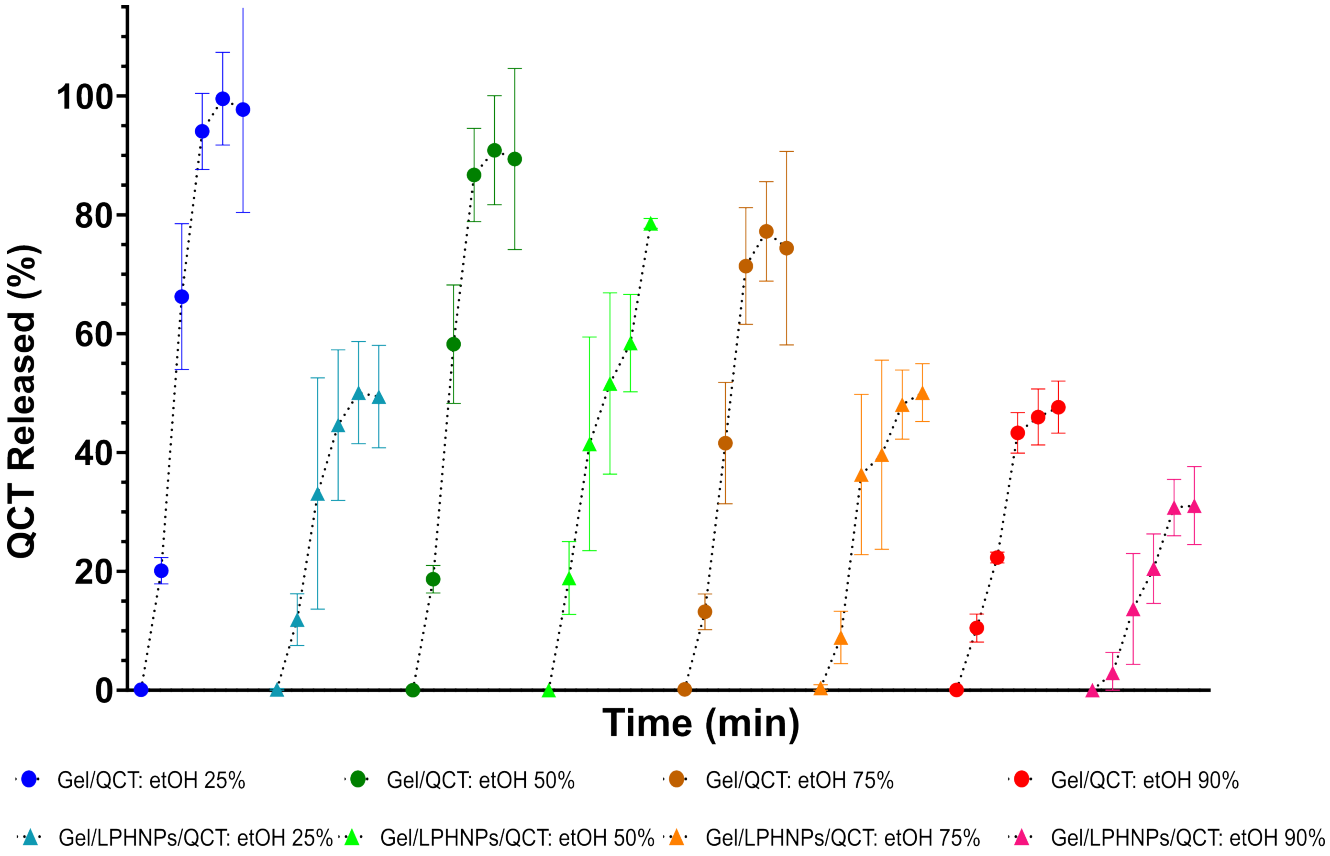

Figure S5: Release profile (from 0 to 40 min) of quercetin (QCT) from gelatin aerogels (Gel/QCT) and from LPHNPs embedded in gelatin aerogels (Gel/LPHNPs/QCT) in different ethanol conditions (25%, 50%, 75%, and 90%). The optimal concentration for QCT release is 50%, as it allows the highest quantity of compound release in a sustained form. The lowest concentration of ethanol (25%) allows some release of QCT from aerogels but shows poor release from Gel/LPHNPs. The highest concentrations (75% and 90%) result in poor release from both Gel and Gel/LPHNPs.