Supporting information for

Combining Olaparib and Ascorbic acid on nanoparticles to enhance the drug toxic effects in pancreatic cancer

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S1. AA quantification by UV-Vis spectroscopy

The cromophore group of Ascorbic Acid (AA) exhibited a high absorption peak in the UV region at 265 nm (Figure S1a). Taking into account the high intensity of AA signal, we carried out a calibration curve ranging from 0 to 12 ppm AA concentrations in ultrapure water (Figure S1b). Data were performed in triplicates. The fitting parameter for this calibration curve is:

$$Abs = 0.0731[AA] + 1.256 \cdot 10^{-4} \qquad R^2 = 0.999$$

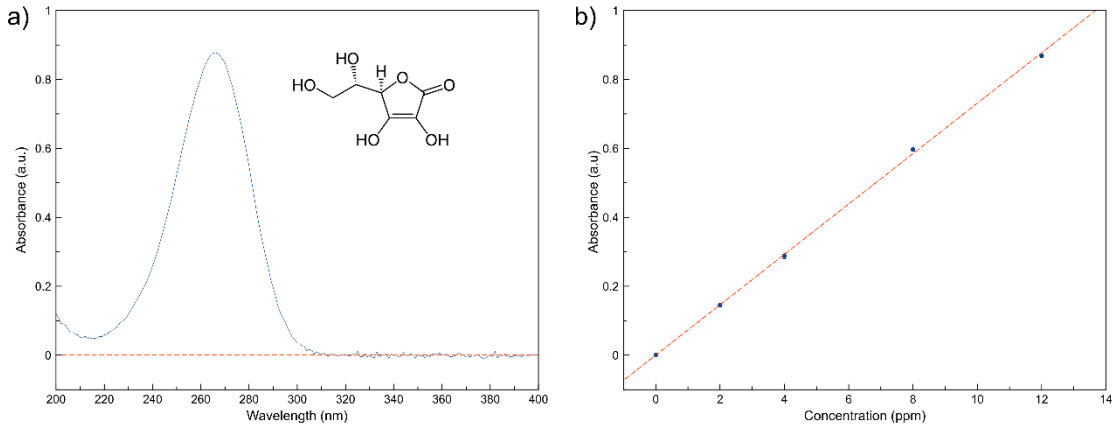

Figure S1: (a) UV-Vis spectrum with the maximum at 265 nm and (b) calibration curve of Ascorbic Acid in H_2O. Dashed line represents the best fits of the experimental data.

The loading capacity, i.e., adsorbed amount of AA (mg) per mg of NP-ACP-AA or NP-ACP-OLA-AA was obtained subtracting the mass of the stock AA solution and non-adsorbed AA.

$$Loading\ capacity\ (\%) = \frac{Stock\ AA\ (mg) - non\ adsorbed\ AA(mg)}{NP\ (mg)} \cdot 100$$

The efficiency capacity was calculated according to the following equation:

$$Efficiency\ capacity\ (\%) = \frac{Stock\ AA\ (mg) - non\ adsorbed\ AA(mg)}{Stock\ AA\ (mg)} \cdot 100$$

Where “stock AA” solution is an aliquot from the AA solution used to functionalize nanoparticles with AA, NP is referred to nanosystems (NP-ACP-AA or NP-ACP-OLA-AA) and “non-adsorbed AA” is the mass of AA in the supernatant collected after the adsorption.

S2. OLA and AA release kinetic in PBS media quantified by UV-Vis spectroscopy.

The delivery of AA and OLA molecules from nanoparticles was simultaneously monitored by UV-Vis spectroscopy during 72h, the entire time of in vitro cell experiments.

As previous commented, Ascorbic Acid (AA) exhibited a high absorption peak in the UV region at 265 nm (Fig. S1). However, a loss of that intensity is produced when ascorbic acid starts degrading.

On the other hand, OLA is a complex molecule with several chromophore groups on the UV spectrum, being the maximum absorbance at 254 nm. However, this maximum is quite near from

AA signal and tends to be overlapped (Fig. S2a). Then, we decided to make the calibration curve for OLA at 311 nm (Fig. S2b), obtaining the following fitting parameter:

$$Abs = 0.0092[OLA] + 0.0109 \qquad R^2 = 0.998$$

Considering the overlapping of the absorption bands of OLA and AA, AA release from the NPs was calculated subtracting the contribution of OLA signal at 265nm to experimental 265 nm values. First at all, we obtained a 311nm/(265nm experimental) constant value that indicates absorbance only came from OLA signal. Secondly, we obtained calculated OLA data at 265 nm by multiplying that constant to absorbance values at 311 nm (calculated 265 nm values). Then, we subtract the calculated 265 nm values to 265 nm experimental values and the result was AA acid contribution.

All data were performed in triplicates and represented with relative absorbance.

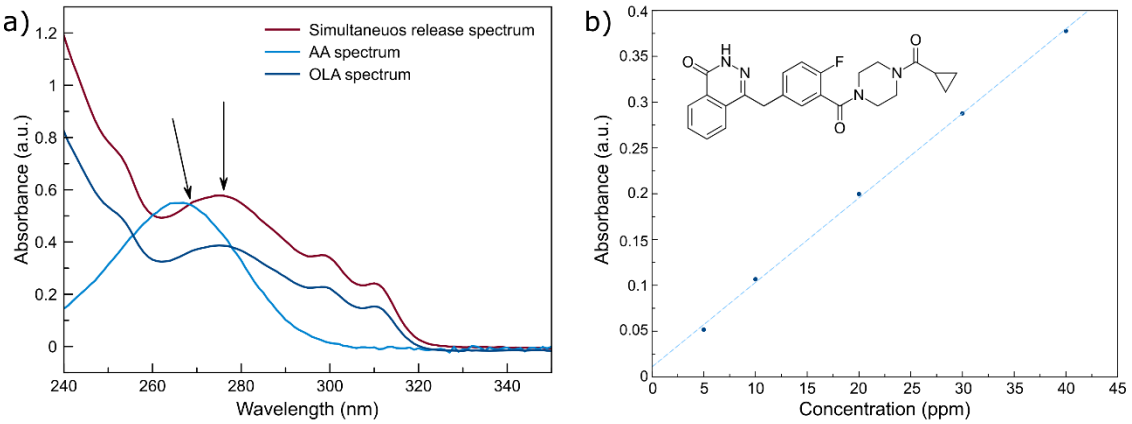

Fig S2: (a) UV-Vis spectrum of free OLA, free AA and their simultaneous release from NP-ACP-OLA-AA, (b) Calibration curve of OLA at 311nm.

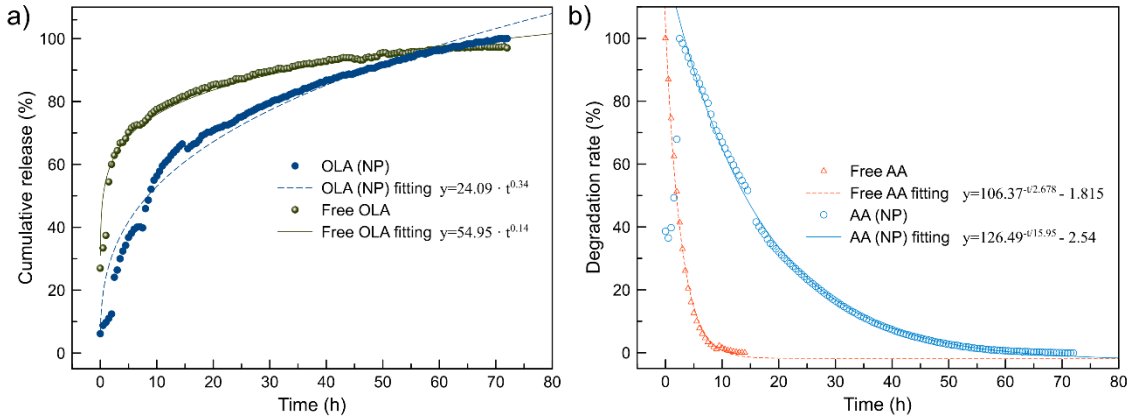

Fig S3: Release kinetic of (a) OLA and (b) AA from the NP-ACP-OLA-AA (blue) in comparison with their free molecules (red). Note that free OLA in (a) is under a slow dissolution process whereas free AA (b) followed an exponential decay.