Supplementary Material for

A Self-Assembled *α*-Synuclein Nanoscavenger for Parkinson's Disease

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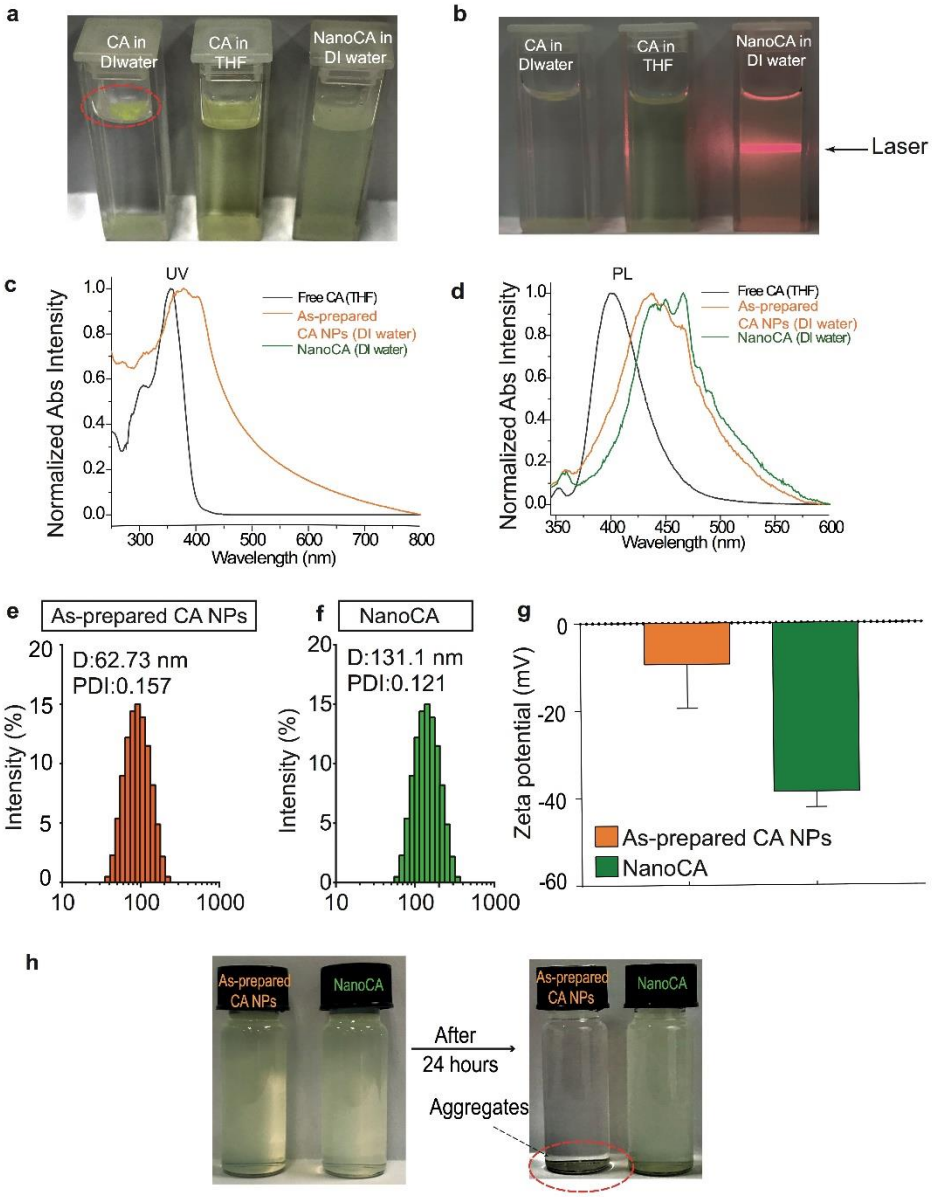
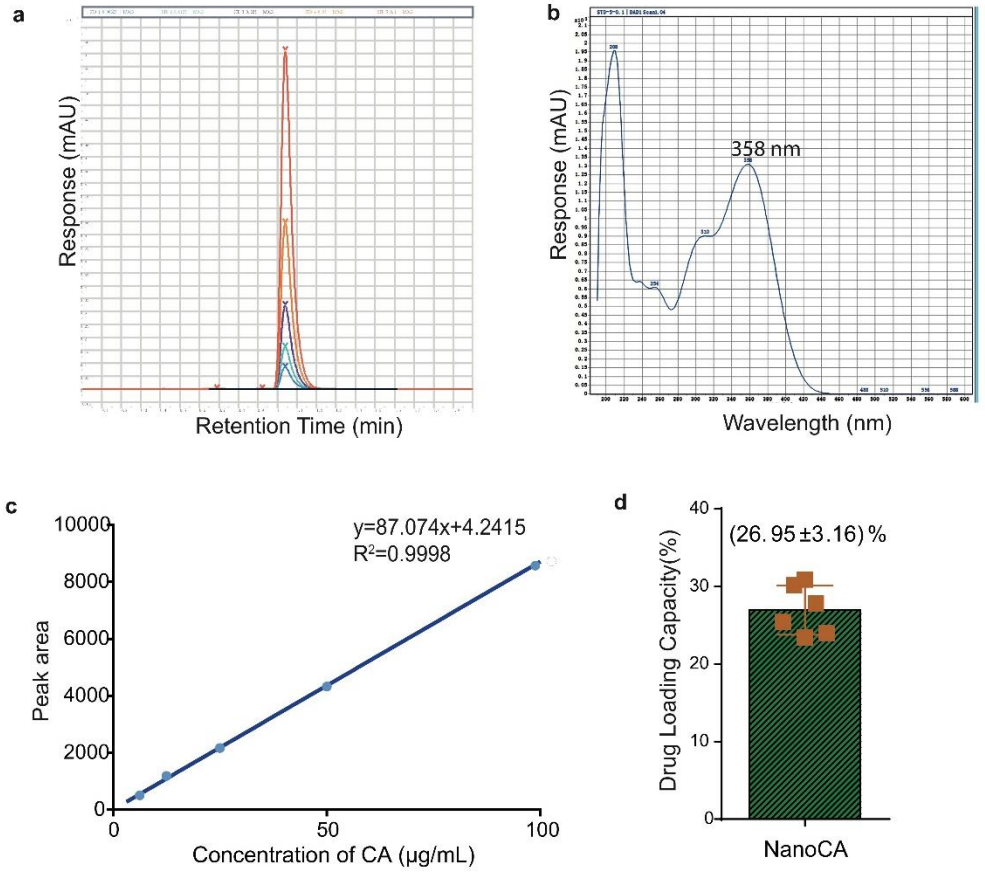
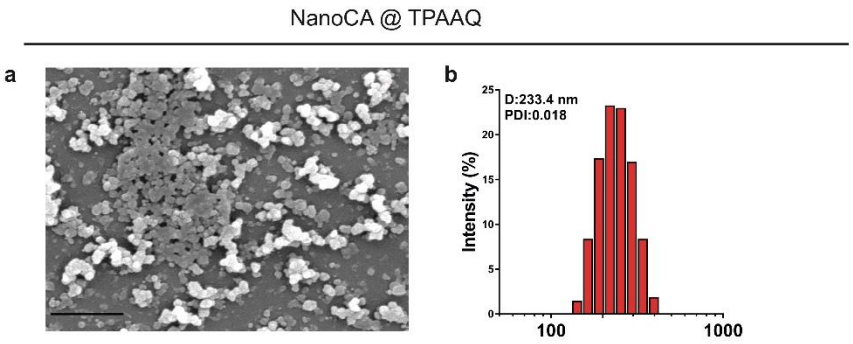


Supplementary Figure 1. Characteristics of as-prepared CA nanoparticles and NanoCA. (a) Digital images showing CA molecules undissolved in water, CA molecules dissolved in THF and NanoCA dispersed in water; (b) Digital images of a beam of green laser shining through the samples showing scattering from the NanoCA *via* the Tyndall effect Besides; (c) UV absorption and (d) Fluorescence spectra of CA molecules in THF, as-prepared CA nanoparticles in water and NanoCA in water, respectively; (e) Dynamic light scattering measurement (DLS) showing a hydrodynamic diameter of 62.73 nm and a polydispersity index (PDI) value of 0.157 of as-prepared CA NPs; (f) DLS showing a hydrodynamic diameter of 131.1 nm and a PDI value of 0.121 of NanoCA. (g) DLS showing the average zeta potential of as-prepared CA NPs and NanoCA were -9.42 and -38.6 mV, individually. (h) Digital images showing the rapid aggregation of as-prepared CA NPs compared to the stable

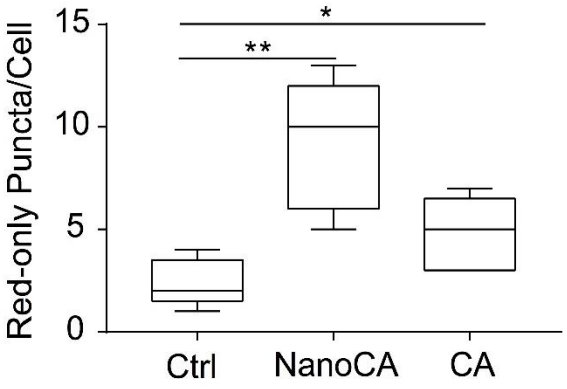
dispersion of NanoCA in water after 24 h.



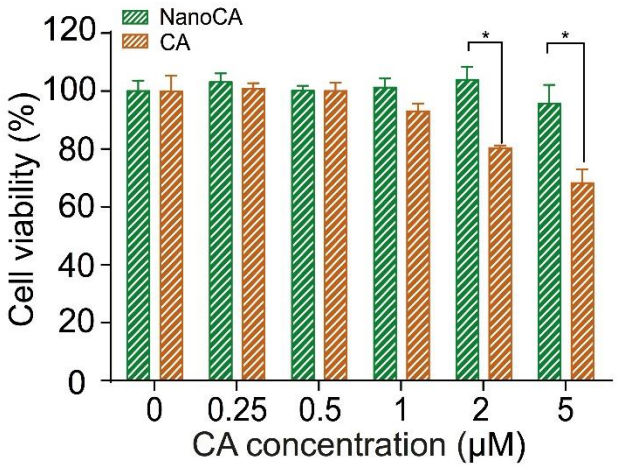
Supplementary Figure 2. Determination of Drug Loading Capacity (DLC) of NanoCA. (a) LC spectra of Standard solutions of CA dissolved in ethanol at concentrations of 6.25, 12.5, 25, 50 and 100 μg/mL determined by Agilent 1290 UPLC equipment; (b) UV spectra showing 358 nm is the maximum UV absorption wavelength of CA; (c) Standard curve of CA solutions; (d) DLC of NanoCA. DLC was calculated according to the following formulae: DLC (wt%) = (weight of loaded drug/weight of NanoCA) × 100%. The average DLC of 26.95±3.16% is calculated from six batches of NanoCA.



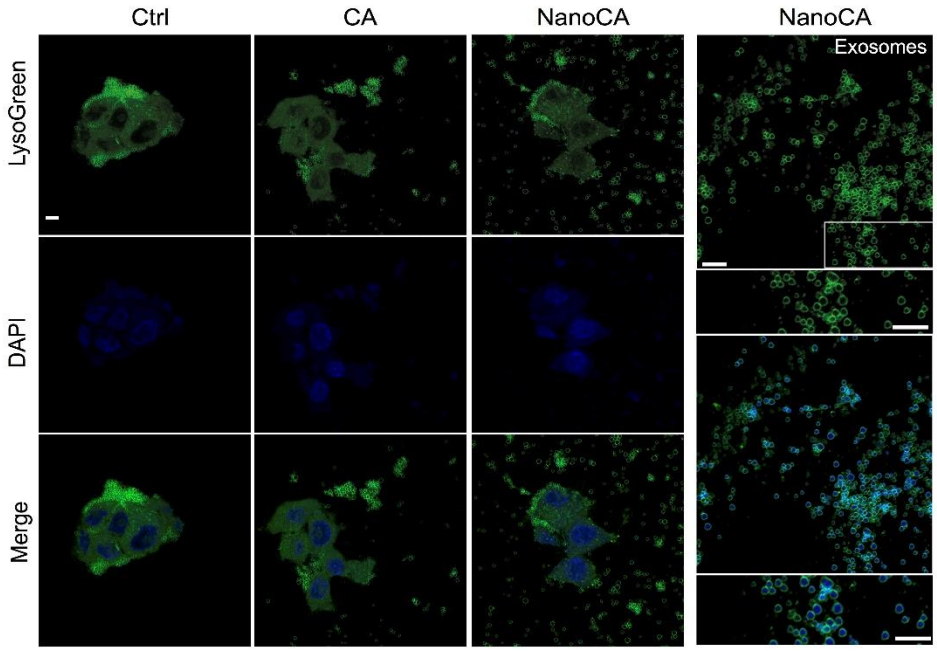
Supplementary Figure 3. Characteristics and cellular uptake of NanoCA@TPAAQ. (a) SEM images of NanoCA@TPAAQ; (b) DLS showing a hydrodynamic diameter of 233.4 nm and a PDI value of 0.018 of as-prepared CA NPs. Scale bar represent 1 μm (a).



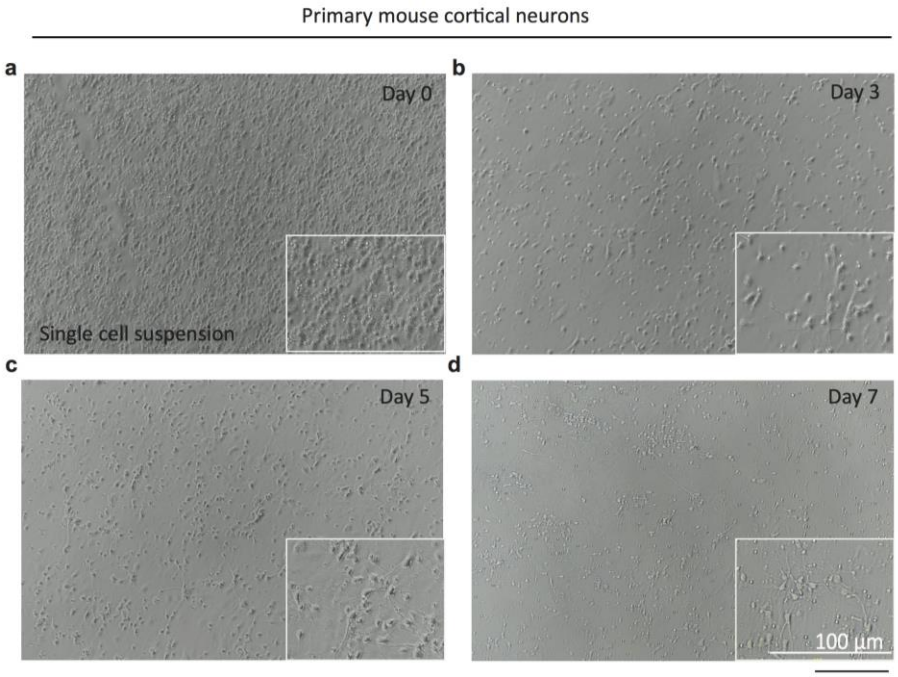
Supplementary Figure 4. Quantification of numbers of red-only puncta in Neuro-2a cells stably expressing GFP-RFP-LC3. Cells were treated with NanoCA (1 μM) or CA (in 0.1% DMSO, 1 μM) for 24 h. Quantifications were from eight random fields. Experiments were repeated three times. *p<0.05, **p<0.01, One-way analysis of variance (ANOVA).



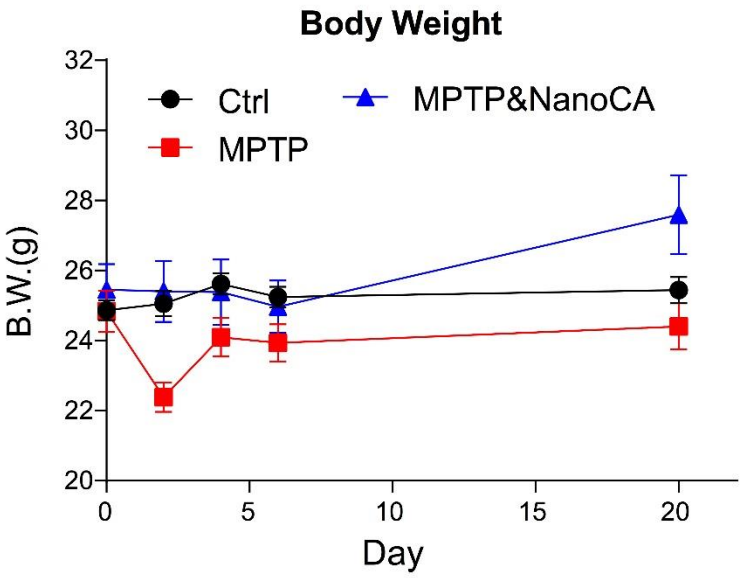
Supplementary Figure 5. Effect of NanoCA or CA on the viability of PC12 cells assessed by MTT assay. Cells were treated with different concentrations of NanoCA (calculated by CA content) or CA (dissolved in 0.1%DMSO) for 24h, respectively, then performed a standard MTT assay.



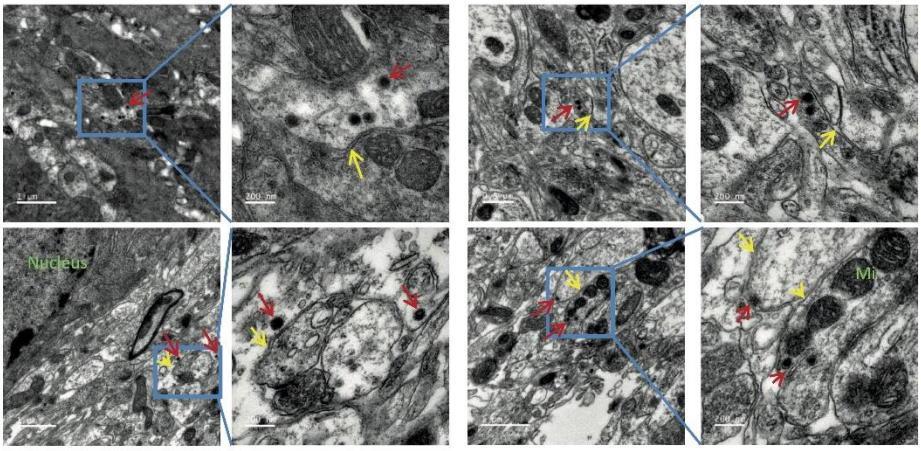
Supplementary Figure 6. NanoCA promotes exosome release from iPC12 cells. Representative images showing iPC12 cells treated with PBS, NanoCA (1 µM) or CA (1 µM) for 24 h. Imaging was performed using a confocal laser scanning microscopy (Zeiss LSM880). The cell nuclei and lysosomes were stained with DAPI (blue signal) and LysoGreen (red signal), respectively. Magnification images showing exosomes around cells treated with NanoCA that containing acidic components (green) and nucleic acids (blue). Scale bar represents 20 µm.



Supplementary Figure 7. Primary culture of mouse cortical neurons. Mice primary cortical neurons were cultured and differentiated over 7 days. Morphological examinations were performed on Day 0 (a), Day 3 (b), Day 5 (c) and Day 7 (d) under a Nikon Ti-U Microscope. Enlarged images showed the morphology of primary neurons. Scale bar represents 100 µm.



Supplementary Figure 8. Body weight of mice in all groups. Body weight of mice in all groups were evaluated during the whole experiment. n= 6 animals for each group**.**



Supplementary Figure 9. Bio-TEM images of brain tissues after intranasal administration of NanoCA (5 mg/kg). Mi, Mitochondria. Yellow arrows indicate membrane structures; Red arrows indicate NanoCA.