**Supporting Information**

# Sugar-Terminated Nanoparticle Chaperones Are $10^2$-$10^5$ Times Better Than Molecular Sugars in Inhibiting Protein Aggregation and Reducing Amyloidogenic Cytotoxicity

Nibedita Pradhan,[†] Shashi Shekhar,[‡] Nihar R. Jana[‡,*] and Nikhil R. Jana[†,*]

[†]Centre for Advanced Materials, Indian Association for the Cultivation of Science, Kolkata-700032, India

[‡]Cellular and Molecular Neuroscience Laboratory, National Brain Research Centre, Manesar, Gurgaon-122051, India

*Corresponding authors E-mail: nihar@nbrc.ac.in and camnrj@iacs.res.in

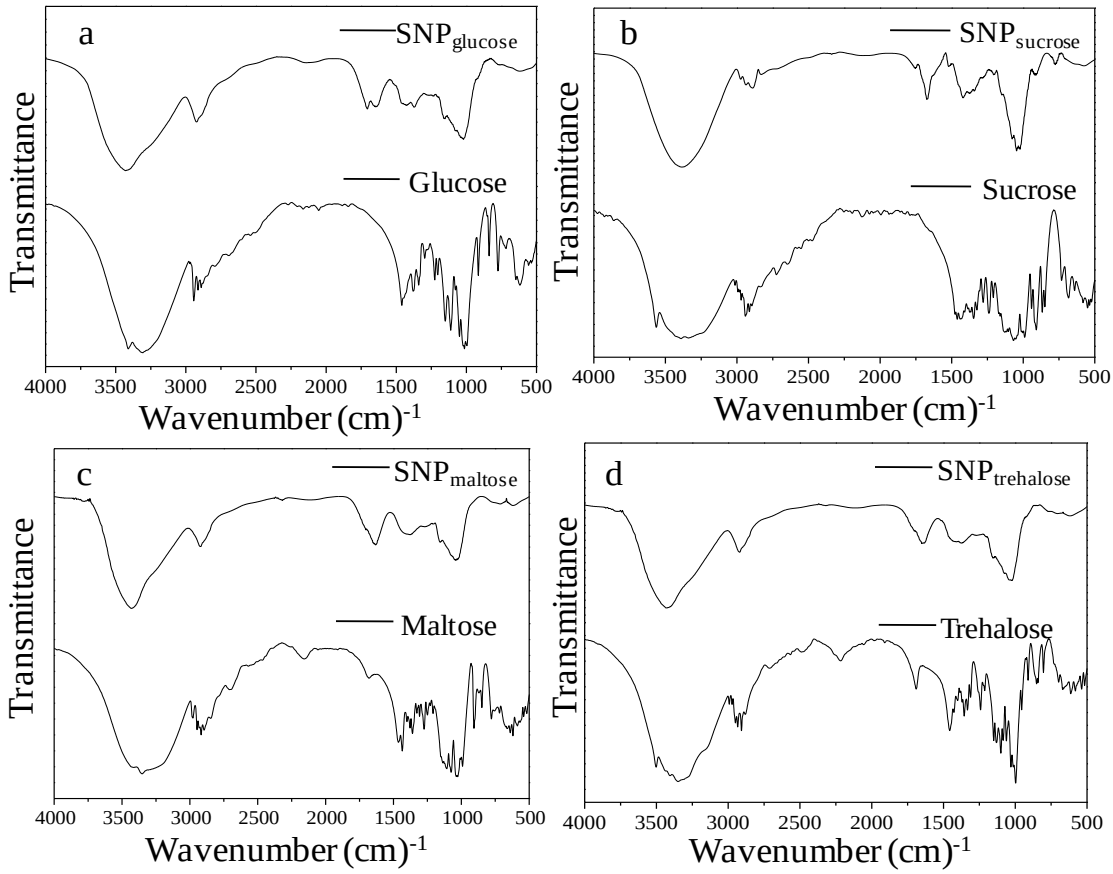


**Figure S1.** FTIR spectra of $SNP_{glucose}$(a)/$SNP_{sucrose}$(b)/$SNP_{maltose}$(c)/$SNP_{trehalose}$(d) with respective molecular sugars. Vibrational stretching bands of hydroxyl groups at 3100-3500 $cm^{-1}$ and CH stretching bands at 3000 $cm^{-1}$ are observed for nanoparticles, suggesting the similarity of functional groups as of sugars.

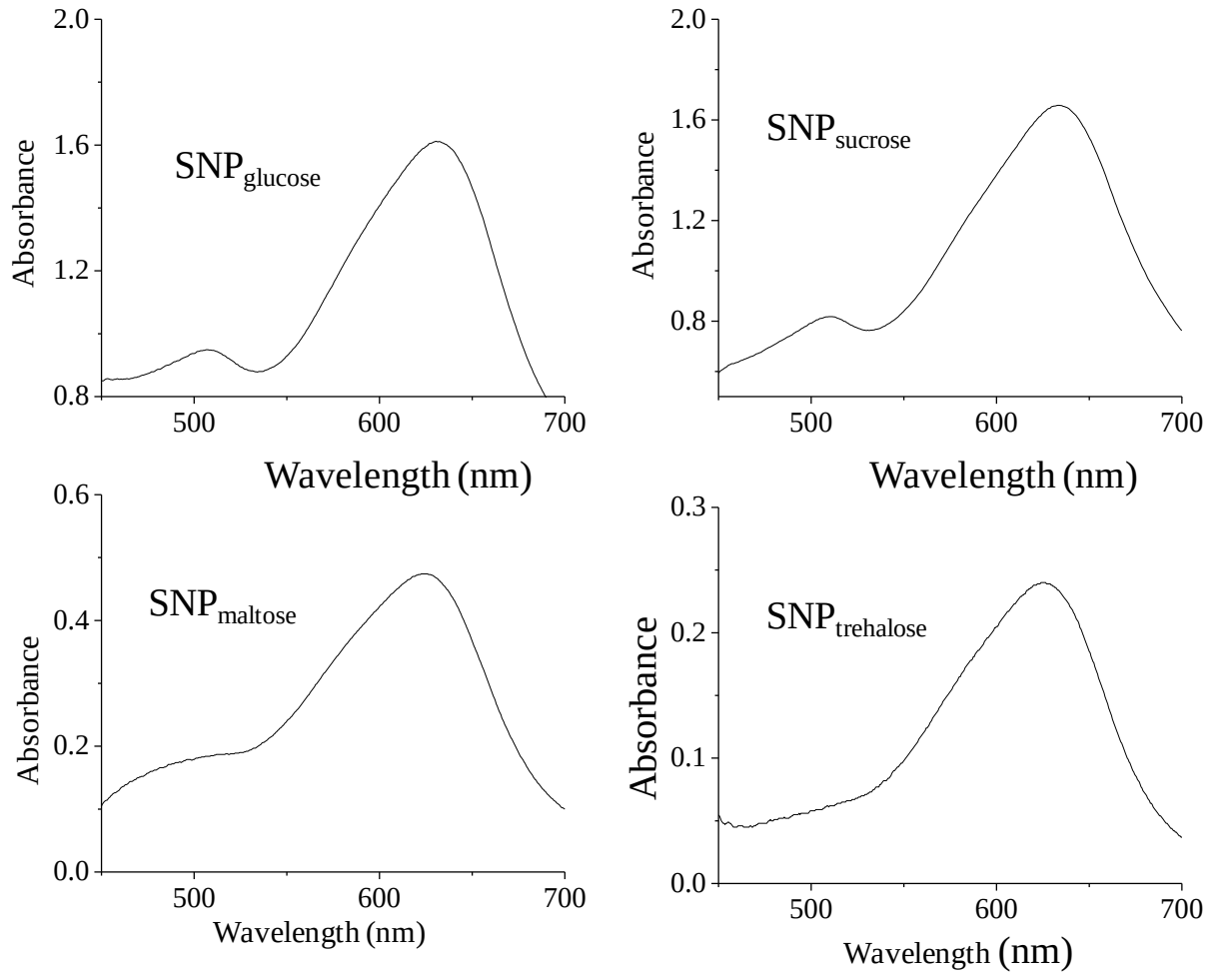


**Figure S2.** Anthrone test result showing the UV-visible spectra of solutions involving all the four nanoparticles. Strong green absorbance at 600-650 nm indicates the positive anthrone test.

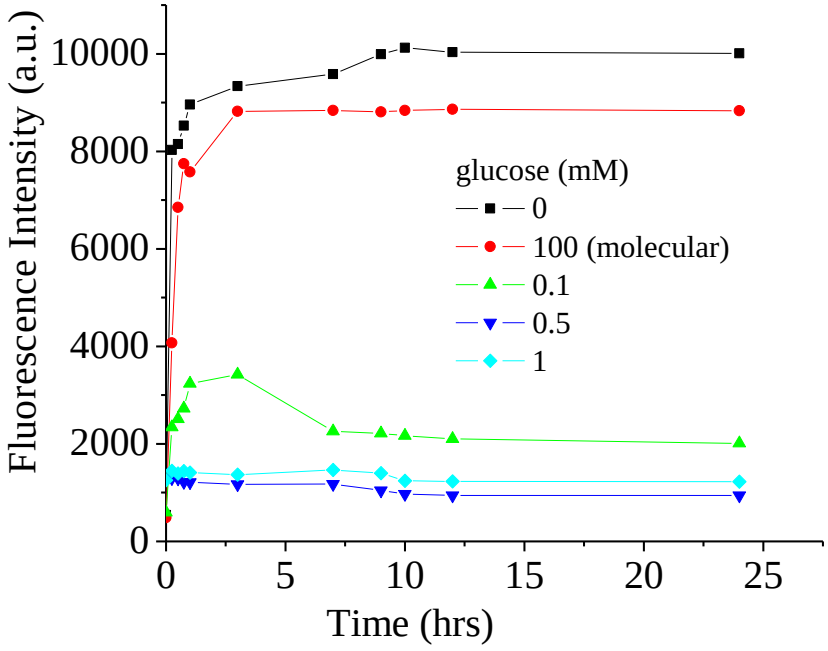


**Figure S3.** Inhibition of insulin fibrillation studied by ThT based titration, showing that $SNP_{glucose}$ is > $10^3$ times effective than glucose molecule.

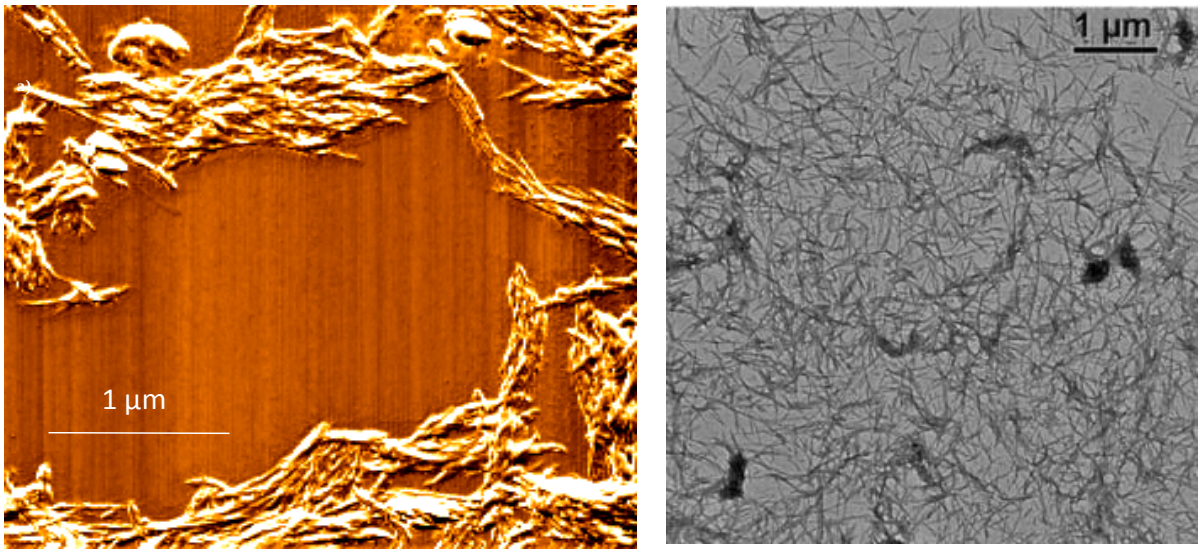


**Figure S4.** Typical AFM image of lysozyme fibril (left panel) and TEM image of lysozyme fibril (right panel) prepared under standard conditions.

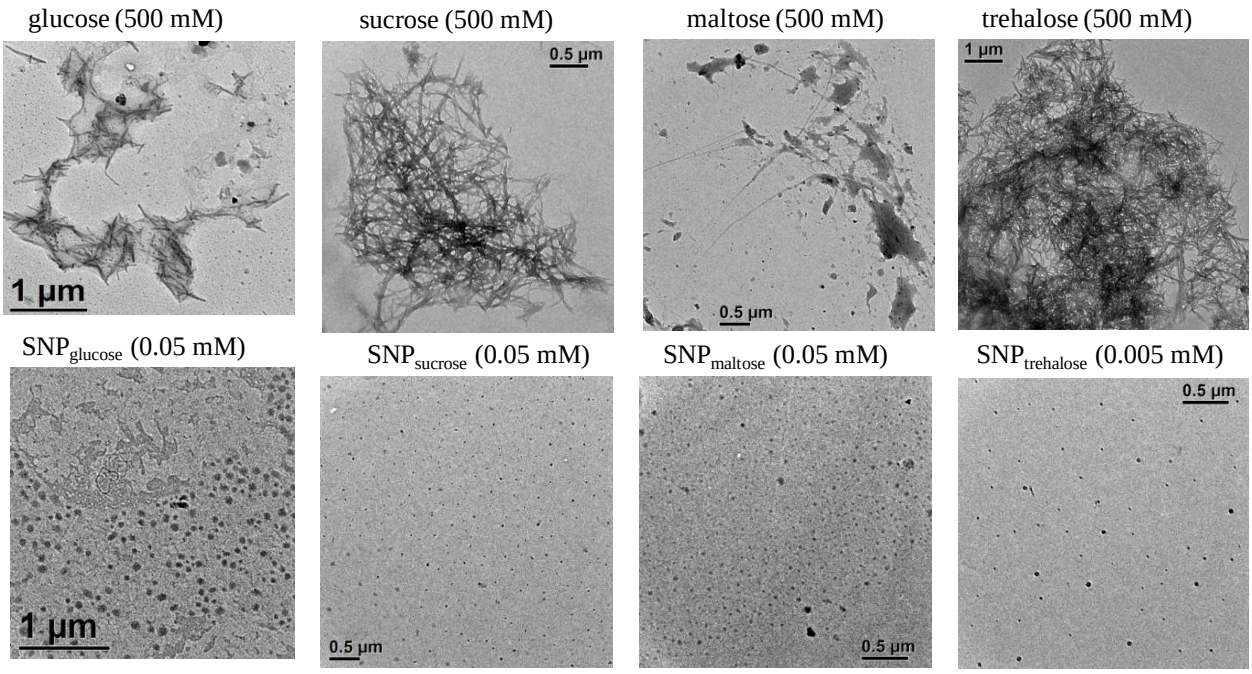


**Figure S5.** Representative TEM image of amyloid fibrils/aggregates formed in presence of 500 mM molecular glucose/sucrose/maltose/trehalose or 0.05/0.005 mM $SNP_{glucose}$/ $SNP_{sucrose}$/$SNP_{maltose}$/$SNP_{trehalose}$. Results show that molecular forms at 500 mM are partially efficient in inhibiting amyloid fibrillation but nanoparticle form can induce near complete inhibition of amyloid fibrillation at 0.05/0.005.0 mM concentration, meaning that nanoparticles are $10^4$-$10^5$ times efficient than molecular sugars.

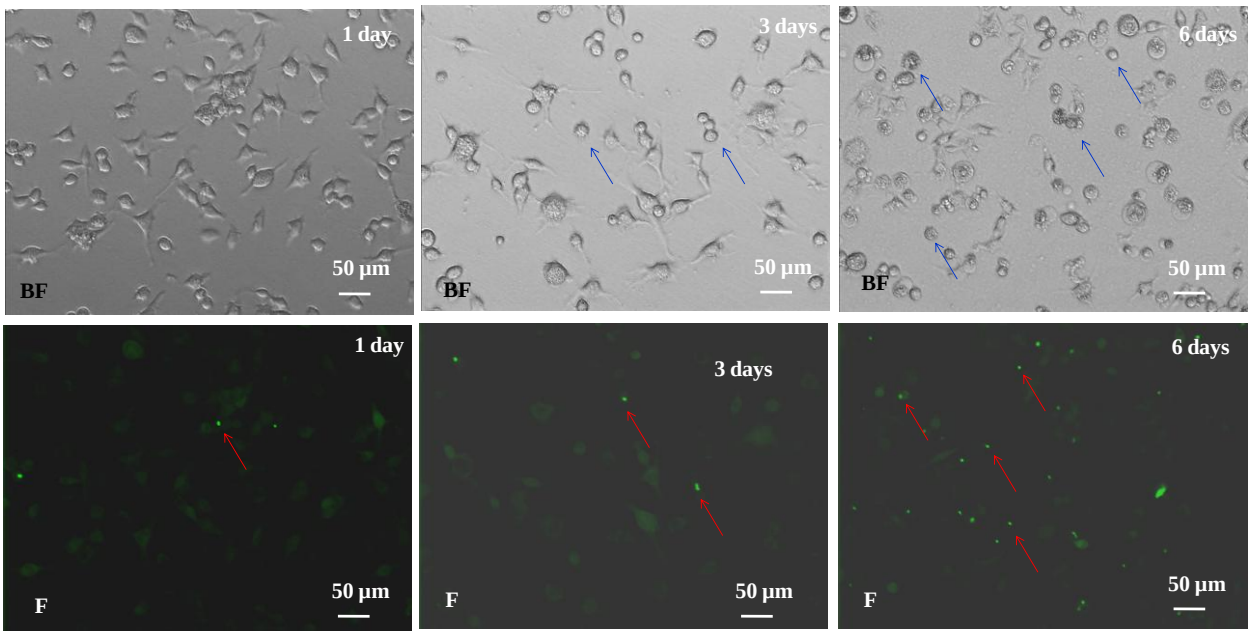


**Figure S6.** Bright field (BF) and fluorescence (F) image of HD150Q cells at different days after exposed with ponasterone A inducer and $SNP_{trehalose}$ corresponding to 0.1 mM trehalose. Formation of mutant huntingtin aggregates (seen as green fluorescent dot, shown as red arrows) and cell death (shown as blue arrows) are delayed by 2 to 3 days.

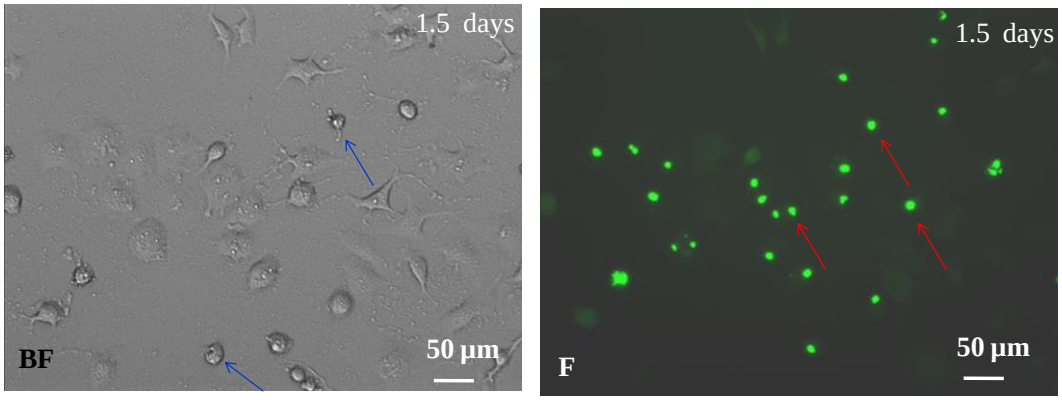


**Figure S7.** Bright field (BF) and fluorescence (F) image of HD150Q cells at 1.5 days after exposed with ponasterone A inducer and 50 mM trehalose. Results show that formation of mutant huntingtin aggregates (seen as green fluorescent dot, shown as red arrows) and cell death (shown as blue arrows) cannot be stopped.

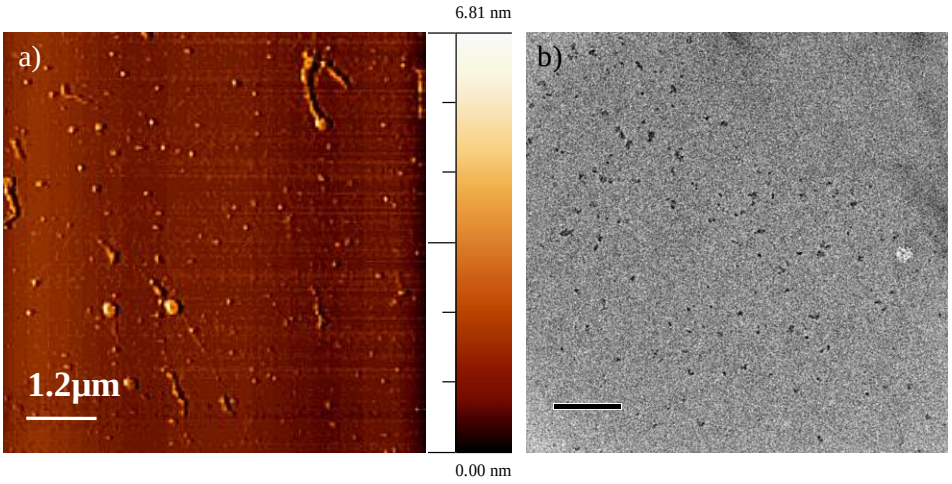


**Figure S8.** AFM (a) and HRTEM (b) image of lysozyme oligomer used in toxicity study. It shows non-fibrillar morphology and semi-spherical aggregates. At 30 mins time point of protein fibrillation a part of solution was collected as oligomer. After 30 min the reaction was stopped using ice cold water. Then the solution was centrifuged at 5000 rpm and dialyzed at 4 °C in 12 KDa dialysis membrane to remove salts. Protein solution was collected for further study after 3 consecutive changes of dialysis water.

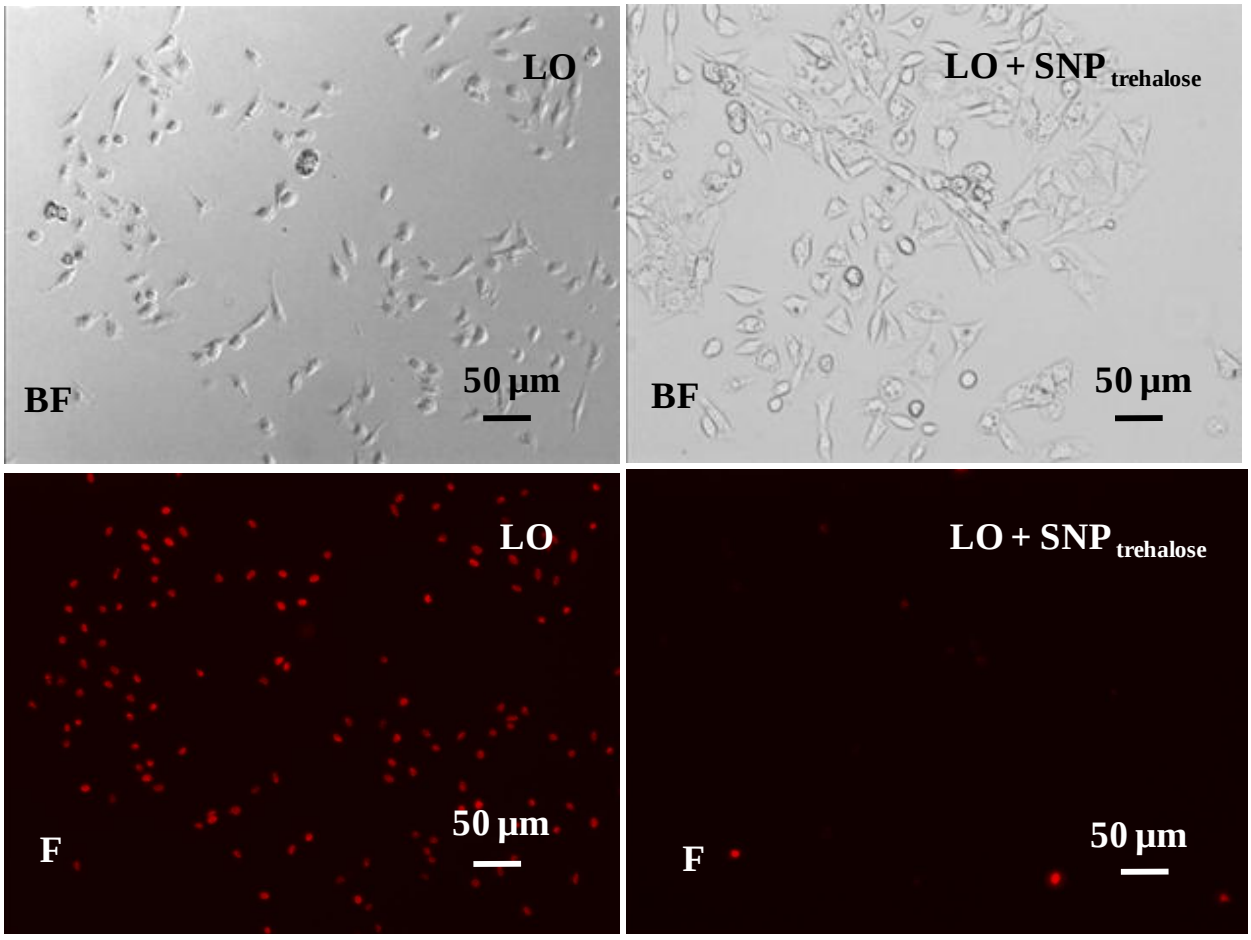


**Figure S9.** Propidium iodide (PI) staining experiment showing that lysozyme oligomer (LO) damage cell membranes but presence of $SNP_{trehalose}$ inhibit cell membrane damage. CHO cells are treated with $SNP_{trehalose}$ (0.5 mM) and then exposed with LO (0.4 mg/mL) for 24 hrs at 37 ºC.

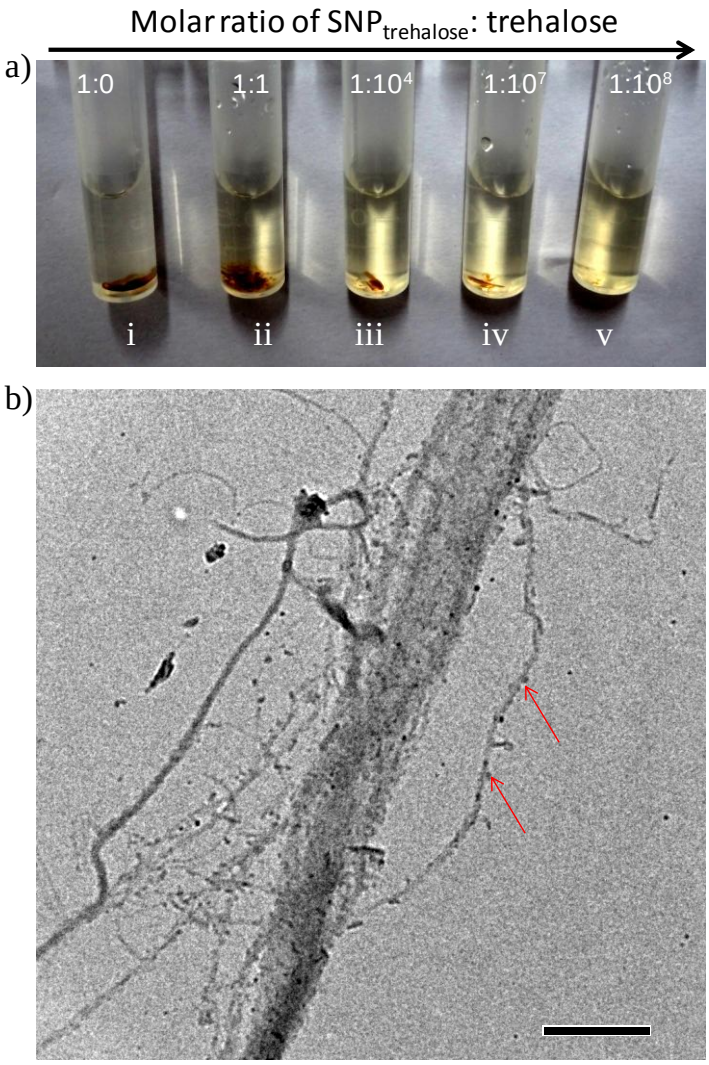


**Figure S10.** a) Evidence that sugar terminated nanoparticle binds with protein fibril > $10^4$ times stronger than sugar molecule. Typically, lysozyme fibril (0.2 mg/mL) is mixed with a mixture of $SNP_{trehalose}$ and molecular trehalose where concentration of lysozyme fibril and $SNP_{trehalose}$ are kept the same but concentration of molecular trehalose is varied. Lysozyme fibril binds with brown color $SNP_{trehalose}$ particles and observed as brown precipitate within 2-3 h. However, if there is free molecular trehalose typically > $10^4$ times than trehalose in $SNP_{trehalose}$, this precipitation is inhibited. In all the sets concentration of lysozyme fibril is 0.2 mg/mL and $SNP_{trehalose}$ corresponding to trehalose concentration is 0.1 mM. Molecular trehalose concentration is kept at 0 mM, 0.1 mM, 100 mM, 1M, 10M for sets i, ii, iii, iv and v respectively. b) TEM evidence of extensive binding of $SNP_{trehalose}$ with lysozyme fibrils. (some of these bindings are shown in red arrows)