

# Supplementary Materials: Design of Polycation-Functionalized Resveratrol Nanocrystals for Intranasal Administration

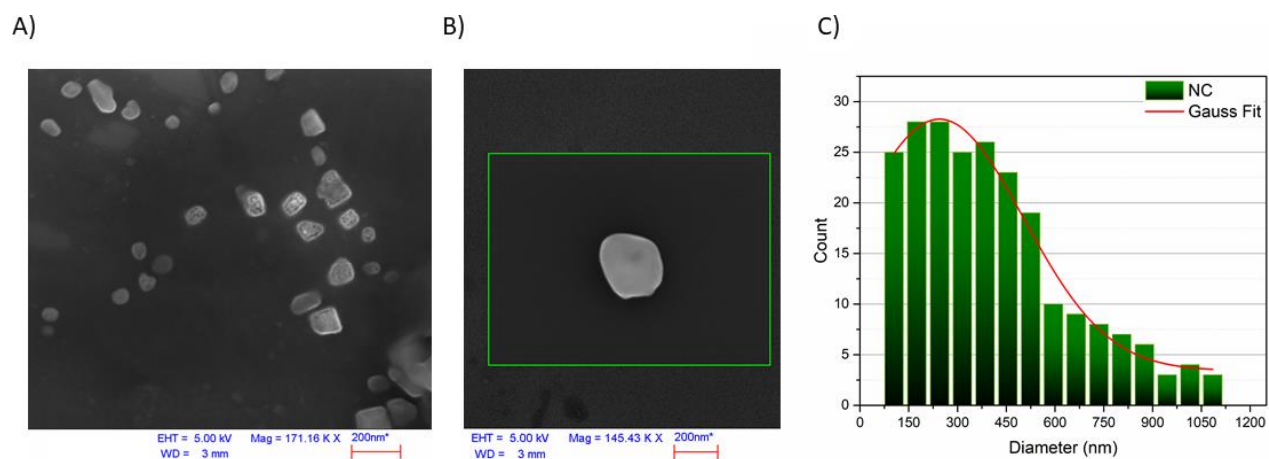
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**Table S1.** Combination of independent variables in RSV NC experimental runs prepared according to I-Optimal design.

| Run | Stabilizer conc. (%w/v) | S/AS ratio (v/v) | Stabilizer type |
|-----|-------------------------|------------------|-----------------|
| 1   | 1                       | 1:2              | Tween 80        |
| 2   | 1                       | 1:2              | Tween 80        |
| 3   | 2                       | 1:1              | Tween 80        |
| 4   | 2                       | 1:5              | Pluronic F127   |
| 5   | 1                       | 1:2              | Tween 80        |
| 6   | 1                       | 1:2              | Tween 80        |
| 7   | 0.5                     | 1:5              | Pluronic F127   |
| 8   | 0.5                     | 1:2              | Pluronic F127   |
| 9   | 1                       | 1:5              | Pluronic F127   |
| 10  | 2                       | 1:2              | Tween 80        |
| 11  | 1                       | 1:1              | Pluronic F127   |
| 12  | 1                       | 1:1              | Tween 80        |
| 13  | 0.5                     | 1:1              | Tween 80        |
| 14  | 2                       | 1:2              | Pluronic F127   |
| 15  | 1                       | 1:2              | Pluronic F127   |
| 16  | 2                       | 1:5              | Tween 80        |
| 17  | 0.5                     | 1:5              | Tween 80        |

**Table S2.** RSV NC optimization.

| Factors and Response     | Goal         | Lower limit    | Upper limit |
|--------------------------|--------------|----------------|-------------|
| Stabilizer conc. (% w/v) | maximize     | 0.5            | 2           |
| S/AS ratio (v/v)         | in the range | 1:1            | 1:5         |
| Type of stabilizer       | equal to     | Pluronic®F-127 |             |
| Mean size (nm)           | minimize     | 200            | 500         |
| PDI                      | minimize     | 0.261          | 1.00        |
| ZP (mV)                  | minimize     | -17.5          | +1.97       |



**Figure S1.** (a) SEM micrograph showing the overall morphology of the NC; (b) SEM detail showing the morphology of a single particle; (c) Diameter distribution histogram (green bars) obtained by averaging different SEM images, fitted with a Gaussian function (red line).