Supporting Information

Porphyrin Armored Gold Nanospheres Modulate the Secondary Structure of α-Synuclein and Arrest its Fibrillation

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Figure S1: UV-vis spectra of TPPS@AuNPs prepared at different molar ratio of Au(III) salt and TPPS. The concentration of KAuCl₄ is maintained constant at 500 μM and TPPS concentration is varied in the range (163-1000 μM); 1: 0.33 (black trace), 1:1 (red trace) and 1:2 (blue trace). The red colored AuNPs suspension with lowest SPR peak maxima is obtained with 1: 0.33 molar ratios.
Figure S2: Kinetics of TPPS@AuNPs formation, 24 h (black trace), 48 h (red trace), 72 h (blue trace) and 96 h (dark cyan). Concentration of TPPS and KAuCl4 is 163 μM and 500 μM respectively.
**Figure S3:** Zeta Potential (ζ) distribution curve of the bio-synthesized TPPS functionalized AuNPs dispersed in aqueous medium.
Figure S4: UV-vis spectrum of Au(III) salt (0.24 mM) in a 10 mM aqueous phosphate buffer medium, pH ~ 6.8, at room temperature.
Fluorescence Study

The classic view of Stern-Volmer equation is \( \frac{F_0}{F} = 1 + K_{sv}[Q] \), which is generally used in case of collisional or dynamic fluorescence quenching studies. However, quenching can also occur as a result of the formation of a non-fluorescent ground-state complex between the fluorophore and quencher. This is called static quenching. In this case Stern-Volmer equation can be represented as \( \frac{F_0}{F} = 1 + K_a[Q] \), where \( K_a \) is known as association constant.

Now, by using Stern-Volmer equation,

\[
\frac{F_0}{F} = 1 + K_a[Q] \quad \text{...(1)}
\]

\[
\frac{F}{F_0} = \frac{1}{1 + K_a[Q]}
\]

\[
1 - \frac{F}{F_0} = 1 - \frac{1}{1 + K_a[Q]}
\]

\[
\frac{\Delta F}{F_0} = \frac{K_a[Q]}{1 + K_a[Q]}
\]

\[
\frac{F_0}{\Delta F} = \frac{1}{K_a[Q]} + 1 \quad \text{...(2)}
\]

Classical Stern-Volmer equation (equation 1 & 2) is only used when 100% of the fluorophores are accessible to quencher. But, in our case TPPS fluorescence is not fully quenched by Au(III) ions (Figure 4A). Some of the fluorophores are being inaccessible or buried to quencher. This fluorescence is called residual fluorescence. Thus, it needs the modification of the S-V equation to plot the experimental data.

\[
\frac{F_0}{\Delta F} = \frac{1}{fK_a[Q]} + \frac{1}{f} \quad \text{......... (3)}
\]

Where ‘\( f \)’ is the fraction of fluorescence that is accessible to the quencher and which is nothing but the ratio \( \Delta F_{\text{max}} \) to \( F_0 \).\(^{1,2} \) Equation (3) is called the modified Stern-Volmer equation. In the present case \( f \) is found to be 0.44 i.e. only 44% of the TPPS fluorescence is accessible to Au(III) ion & remaining 56% fluorescence is the residual fluorescence. We used the modified Stern-Volmer equation to calculate the binding constant or association constant and the obtained value
is $2.1 \times 10^3 \text{ M}^{-1}$. However we have also calculated the association constant by using classic Stern-Volmer equation and it appeared as $1.1 \times 10^4 \text{ M}^{-1}$.

Thus, the obtained association constant value, calculated by S-V equation and modified S-V equation are different. The experimental data is better fitted in modified S-V equation ($R^2 = 0.99$) compared to classic Stern-Volmer equation ($R^2 = 0.98$) and therefore we have used $\frac{F_0}{\Delta F}$ vs. $\frac{1}{[Q]}$ to calculate accurate value of binding/association constant.

**Figure S5:** Stern–Volmer graphical plot obtained by using the intrinsic fluorescence of TPPS at 645 nm and in presence of the different known concentrations of Au(III) salt ($\sim 0$ to 0.24 mM).
Figure S6: Time resolved fluorescence decay of TPPS in aqueous phosphate buffer medium (pH ~ 7.0, 10 mM) and in the presence of different concentration of Au(III) ion. ‘Prompt’ is the laser pulse profile.
**Figure S7:** UV-Visible spectra of the TPPS@AuNPs dispersed in aqueous medium under different pH conditions, ranging from pH 4.5 to 9.8.
**Figure S8:** UV–visible absorption spectra of the TPPS@AuNPs in different ionic buffer mediums (~100 mM) under normal physiological conditions (pH ∼ 7.4, 37 °C).
Figure S9: Synthesis of TPPS@AuNPs under optimized condition (i.e. pH ~ 6.8, 1: 0.33 molar ratio of Au(III) to TPPS with 48 h stirring of the reaction mixture) in presence of light (blue trace) and in absence of light (red trace).
Figure S10: Synthesis of TPPS@AuNPs under optimized condition and in presence of different colored visible light. The absorbance of TPPS@AuNPs at 545 nm (SPR band maximum) is plotted as a function of wavelength of visible light, namely blue (450-485 nm), green (500-565 nm), orange (590-652 nm) and red (625-740 nm).
Figure S11: UV-vis spectra of the reaction mixture of 163 μM TPPS and 500 μM Au(III) salt in aqueous medium (pH ~ 6.8) at different time, 0 h (black trace), 2 h (red trace) and 5 h (blue trace).
Figure S12: Normalized UV-vis absorption spectra of TPPS@AuNPs in the absence and presence of α-syn in aqueous medium at 298 K within 520-600 nm. The concentration of gold nanoparticles was kept constant at ~ 0.13 nM in 2 ml and concentration of α-syn was varied from 0 to 5 µM. Before data recording, each of the samples was kept at 4°C for ~15 h.
Figure S13: Double reciprocal plot of $1/\Delta \lambda$ against $1/[\alpha\text{-Syn}]$ using Langmuir equation.
Figure S14: Change in surface plasmon resonance (SPR) peak maxima with increasing α-syn/TPPS@AuNPs ratio.
Figure S15: Detailed interaction plot of TPPS, (A); Au$_{11}$, (B) and Au$_{144}$, (C) at the binding site of $\alpha$-synuclein, obtained through PatchDock, after refinement with FireDock.
Figure S16: Molecular surface representation of α-synuclein depicting the best docking configuration for TPPS, (A); Au$_{11}$, (B); Au$_{102}$, (C) and Au$_{144}$, (D). For clear view of the interaction, α-synuclein configuration is 180° rotated with respect to the Figure 10.
Table S1: Docking results of α-synuclein with TPPS, Au_{11} cluster, Au_{102} cluster and Au_{144} cluster.

<table>
<thead>
<tr>
<th>Ligands</th>
<th>Active Area (Å²)</th>
<th>Binding Energy ΔG (kcal mol⁻¹)</th>
<th>ACE (kcal mol⁻¹)</th>
<th>Interacting Residues Obtained Through PatchDock</th>
</tr>
</thead>
<tbody>
<tr>
<td>TPPS</td>
<td>431.3</td>
<td>-42.25</td>
<td>-14.68</td>
<td>VAL3 (3.15 Å), GLY7 (2.74 Å), LEU8 (2.17 Å), LYS10 (3.66 Å), ALA11 (2.81 Å), GLY14 (2.39 Å), PHE4 (4.3 Å) and LYS80 (5.59 Å)</td>
</tr>
<tr>
<td>Au_{11}</td>
<td>168.0</td>
<td>-5.77</td>
<td>0.0</td>
<td>LYS6 (3.25 Å), LYS10 (4.88 Å), SER9 (2.93 Å) and GLY7 (3.72 Å)</td>
</tr>
<tr>
<td>Au_{102}</td>
<td>444.5</td>
<td>-0.46</td>
<td>0.0</td>
<td>GLY7 (2.37 Å), PHE4 (3.08 Å), LYS10 (3.84 Å) and VAL3 (4.01 Å)</td>
</tr>
<tr>
<td>Au_{144}</td>
<td>484.3</td>
<td>-10.39</td>
<td>0.0</td>
<td>GLY14 (2.34 Å), GLU13 (2.68 Å), ALA17 (2.63 Å), ALA18 (3.10 Å), GLY21 (2.50 Å), VAL66 (3.00 Å), LYS10 (3.88 Å), VAL70 (4.01 Å) and GLN62 (4.00 Å)</td>
</tr>
</tbody>
</table>

Note: ΔG-Lowest binding energy in kcal/mol and ACE – Atomic Contact Energy in kcal/mol.