Development of Nanomedicines Targeting Infection and Inflammation
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Introduction

Star-shaped polypeptides (SPs) are polymers which can be potentially used as a carrier to effectively deliver targeted therapies whilst maintaining safety and uniformity¹. SPs consist of linear polypeptide chains or “arms” and possess advantages over unimolecular nanoparticles due to their chain density whereby within one macromolecule there is high chain density. Several studies have demonstrated their application in therapeutics as a gene delivery vector and degradable hydrogels for drug delivery.

Targeted therapy is an area possessing wide scope for treatment opportunities, with diclofenac being a potential active that can be used as a targeted therapy, particularly in pain management. The aim of this project was to investigate the potential of generation 5-poly(l-lysine) (G5-PLL) as a carrier for diclofenac.

Materials and Methods

- Particles were formed by adding G5-PLL to requisite amount of diclofenac followed by addition of nuclease-free water to a final volume of 1ml. Different mass ratios (diclofenac to G5 PLL) were prepared 1:5, 1:30, 1:50, 1:70 and 1:100.
- Mixtures were left at room temperature for few minutes to allow complexation to occur.
- Z-average of diclofenac-G5-PLL particles were assessed using Dynamic Light Scattering (DLS). Then Polydispersity Index (PDI) for each of the samples was recorded to assess the particle size distribution. Zeta Potentials (ζ) were assessed using a Malvern Zetasizer® Nano ZS using same formulation.
- Nanoparticle Tracking Analysis (NTA) particle sizing was assessed using a Malvern NanoSight 300. The mass ratios used were the same as for DLS particle sizing. Samples were recorded at 60 second intervals with three measurements recorded per sample (each mass ratio) and performed in triplicate.

Results

1. z-average using DLS

![Figure 3: Particle size of diclofenac/G5 PLL complex. The particle size was determined using DLS technique for different diclofenac to G5 PLL mass ratios. Bars represent mean ± SD (n=3). Result: Particle sizes varied depending on drug-polymer ratio. Particle size of < 600 d nm obtained with ratio 1:30 and 1:50.](image)

<table>
<thead>
<tr>
<th>Mass Ratio</th>
<th>PDI (±SD)</th>
<th>Zeta Potential (mV) (±SD)</th>
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<tbody>
<tr>
<td>1:5</td>
<td>0.53 (±0.05)</td>
<td>21.8 (±1.54)</td>
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<tr>
<td>1:30</td>
<td>0.68 (±0.14)</td>
<td>21.9 (±0.73)</td>
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<tr>
<td>1:50</td>
<td>0.70 (±0.13)</td>
<td>29.7 (±2.79)</td>
</tr>
<tr>
<td>1:70</td>
<td>0.56 (±0.05)</td>
<td>12.8 (±0.32)</td>
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<tr>
<td>1:100</td>
<td>0.60 (±0.06)</td>
<td>9.3 (±0.46)</td>
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Table 1: Mean of Pdi (n=3) and Zeta Potential (n=3) to assess surface charge of diclofenac-PLL complex

Result: The Pdi ranged between 0.5-0.7 while Zeta Potential of the diclofenac/G5-PLL complexes ranged between 9 to 30 mV indicating a cationic surface properties

2. Pdl and zeta potential

3. Nanoparticle Tracking Analysis (NTA)

![Figure 4: Mean of NTA particle size (n=3) and D10, D50, D90 of diclofenac: G5 PLL (mass ratio)](image)

Result: NTA particle size shows particle size of < 300 nm for all drug-polymer ratios.

Discussions / Conclusions

These results demonstrate the potential for loading SPs with small molecule therapeutics such as diclofenac. Future experiments will include determining the loading/release profile of diclofenac:G5-PLL, performing stability assays and validating the encapsulation procedure. This, in turn, will increase accuracy of future sampling creating desirable monodisperse sample sizes with high loading efficiency.

References


Acknowledgements

- School of Pharmacy & Biomolecular Sciences, RCSI