**Table S8** Stability study of optimized TFs

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Parameters | Initial results | Long-term stability study  (5°C ± 3°C) | | | Accelerated stability study  (25°C ± 2°C/60% RH ± 5% RH) | | Freeze-thaw (one cycle: -20 °C and 25 °C each for 24 h) and Heating-cooling cycle (one cycle: 40° C and 4° C each for 24 h) | |
| 0 month | 6 months | 9 months | 12 months | 3 months | 6 months | Freeze-thaw cycle | Heating-cooling cycle |
| Color | Milky white | Milky white | | | Milky white | | Milky white | |
| pH | 4.756 ± 0.012 | 4.735 ± 0.038 | 4.894 ± 0.057 | 4.882 ± 0.044 | 4.772 ± 0.021 | 4.898 ± 0.057 | 4.822 ± 0.039 | 4.86 ± 0.015 |
| RI | 1.335 ± 0.0001 | 1.334 ± 0.003 | 1.335 ± 0.002 | 1.334 ± 0.007 | 1.335 ± 0.0001 | 1.334 ± 0.003 | 1.335 ± 0.002 | 1.335 ± 0.004 |
| Structural integrity | Spherical bilayered structure | Spherical bilayered structure | | | Spherical bilayered structure | | Spherical bilayered structure | |
| Sedimentation | No | No | | | No | Slight sedimentation | No | Slight sedimentation after 3nd cycle |
| Precipitation | No | No | | | No | | No | No |
| Phase separation | No | No | | | No | Slight separation | No | Yes (after 3nd cycle) |
| Zavg (nm) | 196.368 ± 1.123 | 204.334 ± 1.368 | 221.56 ± 1.546 | 237.567 ± 2.357 | 228.327 ± 1.159 | 246.354 ± 2.374 | 197.616 ± 1.141 | 219.346 ± 2.352 |
| PDI | 0.185 ± 0.001 | 0.194 ± 0.004 | 0.284 ± 0.002 | 0.467 ± 0.004 | 0.335 ± 0.003 | 0.573 ± 0.004 | 0.187 ± 0.003 | 0.273 ± 0.004 |
| ζ (mV) | - 23.6 ± 1.355 | -22.13 ± 1.275 | -20.461 ± 0.873 | -17.462 2.32 ± 1.225 | -18.772 ± 1.053 | -15.357 ± 1.361 | -23.214 ± 0.996 | -17.354 ± 1.007 |
| EE (%) | 88.545 ± 2.134 | 85.463 ± 1.841 | 78.361 ± 2.134 | 73.253 ± 2.066 | 67.151 ± 2.165 | 53.243 ± 1.273 | 87.165 ± 2.263 | 77.434 ± 3.631 |
| LC (%) | 9.506 ± 0.223 | 9.171 ± 0.537 | 8.408 ± 0.667 | 7.860 ± 0.571 | 7.205 ± 0.356 | 5.712 ± 0.673 | 9.352 ± 0.584 | 8.308 ± 1.546 |
| Flexibility (mL/s ) | 13.719 ± 1.613 | 12.876 ± .0.542 | 10.572 ± 0.879 | 10.135 ± 0.753 | 9.152 ± 2.613 | 7.167 ± 0.786 | 12.435 ± 2.443 | 11.053 ± 0.873 |
| Drug-excipient compatibility | Compatible | Yes | | | Yes | | Yes | |
| Lyophilization stability | | | | | | | | |
|  | Before lyophilization | After lyophilization | | |  | |  | |
| Zavg (nm) | 196.368 ± 1.123 | 198.357 ± 1.004 | | |  | |  | |
| PDI | 0.185 ± 0.001 | 0.193 ± 0.002 | | |  | |  | |
| ζ (mV) | - 23.6 ± 1.355 | -23.14 ± 0.897 | | |  | |  | |
| Entrapment efficiency (EE) | 88.545 ± 2.134 | 86.359 ± 1.364 | | |  | |  | |
| Loading Capacity (LC) | 9.506 ± 0.223 | 9.266 ± 0.643 | | |  | |  | |

Results are presented as Mean ± SD