**Supplementary data file**

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**Figure 1: Structure of AMX (A) and NG (B)**

Diagram, engineering drawing

Description automatically generated

**Figure 2: DSC analysis of pure AMX (A), pure NG (B), lipids (C), physical mixture (D), AMX-NG SLNs (E), AMX-SLNs (F), NG-SLNs (G), blank-SLNs (H)**

Chart, line chart

Description automatically generated

**Figure 3: FT-IR spectra of pure AMX (A), pure NG (B), AMX-SLNs (C), NG-SLNs (D), and blank SLNs (E)**

Chart, line chart

Description automatically generated

**Figure 4: AMX particle size distribution**

Chart, line chart

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**Figure 5: AMX zeta potential**

Chart, line chart

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**Figure 6: NG particle size distribution**

Chart, line chart

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**Figure 7: NG zeta potential**

**Table 1. Summary of the micromeritics parameters like (PS, ZP, PDI) and EE & DL.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Micromeritics (PS, ZP, PDI) and EE & DL** | | | | |  |
| **Drugs** | **Trials** | **Particle size (nm)** | **PDI** | **Zeta potential (mV)** | **Entrapment**  **efficiency**  **(%)** | **Drug loading**  **(%)** |
| **AMX-SLNs** | 1 | 110.1 | 0.366 | -27.6 | 62.1 | 4.14 |
| 2 | 65.93 | 0.259 | -22.9 | 61.6 | 4.07 |
| 3 | 70.82 | 0.296 | -25.3 | 59.8 | 3.9 |
| Average | **82.28** | **0.307** | **-25.26** | **61.16** | **4.07** |
| **NG**  **SLNs** | 1 | 113.4 | 0.458 | -18.1 | 79.1612 | 9.8 |
| 2 | 80.69 | 0.305 | -27.4 | 79.17753 | 9.89 |
| 3 | 84.03 | 0.285 | -31.5 | 79.13404 | 9.89 |
| Average | **92.70** | **0.349** | **-25.66** | **79.15761** | **9.8** |

**Table 2. Colloidal stability studies of AMX-SLNs and NG-SLNs:**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Drugs** | **Time (hours)** | **Batch no.** | **Particle size (nm)** | | **PDI** | | **Zeta potential (mV)** | |
|  | | | **Room temp.** | **4 °C** | **Room temp.** | **4 °C** | **Room temp.** | **4 °C** |
| **AMX-SLNs** | 6 hours | Batch 1 | 65.93 | 94.92 | 0.257 | 0.373 | -22.9 | -23.6 |
| Batch 2 | 48.97 | 47.62 | 0.364 | 0.352 | -22.3 | -21.1 |
| Batch 3 | 61.26 | 61.69 | 0.398 | 0.453 | -17.22 | -18.8 |
| 12 hours | Batch 1 | 64.46 | 94.12 | 0.203 | 0.389 | -20.8 | -19.4 |
| Batch 2 | 69.6 | 66.68 | 0.333 | 0.378 | -8.76 | -17.85 |
| Batch 3 | 41.96 | 61.32 | 0.264 | 0.407 | -21.6 | -22.4 |
| 24 hours | Batch 1 | 64.65 | 70.82 | 0.201 | 0.296 | -13.2 | -25.3 |
| Batch 2 | 103.6 | 88.85 | 0.298 | 0.221 | -5.47 | -15.7 |
| Batch 3 | 53.14 | 64.75 | 0.346 | 0.465 | -12.9 | -27 |
| 48 hours | Batch 1 | 87.7 | 69.24 | 0.277 | 0.269 | -10.8 | -16.27 |
| Batch 2 | 76.92 | 65.14 | 0.300 | 0.365 | -19.5 | -12.6 |
| Batch 3 | 65.57 | 77.77 | 0.372 | 0.378 | -8.76 | -14.3 |
| **NG**  **SLNs** | 6 hours | Batch 1 | 84.03 | 85.04 | 0.285 | 0.315 | -31.5 | -31.4 |
| Batch 2 | 81.9 | 81.66 | 0.327 | 0.328 | -31.1 | -29.9 |
| Batch 3 | 78.99 | 78.34 | 0.266 | 0.281 | -29.8 | -30.1 |
| 12 hours | Batch 1 | 83.4 | 82.19 | 0.274 | 0.283 | -33.2 | -32.4 |
| Batch 2 | 80.87 | 81.46 | 0.303 | 0.314 | -30.2 | -30.2 |
| Batch 3 | 77.05 | 77.05 | 0.278 | 0.277 | -28.2 | -28.2 |
|  | 24 hours | Batch 1 | 82.79 | 84.81 | 0.322 | 0.302 | -16.4 | -9.43 |
|  | Batch 2 | 77.36 | 80.82 | 0.312 | 0.359 | -13.1 | -9.63 |
|  | Batch 3 | 79.34 | 76.95 | 0.276 | 0.314 | -10.2 | -13.3 |
|  | 48 hours | Batch 1 | 82.09 | 95.2 | 0.284 | 0.422 | -7.94 | -8.70 |
|  | Batch 2 | 79.13 | 87.22 | 0.281 | 0.405 | -8.32 | -6.4 |
|  | Batch 3 | 77.46 | 79.22 | 0.255 | 0.316 | -6.47 | -11.7 |

## Table 3. Kinetic modelling on drug release from pure and controlled drug delivery system (AMX-SLNs and NG-SLNs)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Formulation type** | **Parameters** |  | **Release kinetic modelling type** | | |  |
| **Zero order** | **First**  **order** | **Higuchi model** | **Korsmeyer-Peppas model** | **Hixson Crowell model** |
| AMX-SLNs | Slope | 2.595 | 0.0918 | 0.4088 | 0.0399 | 0.0925 |
| Intercept | 18.443 | 2.944 | 0.1172 | 0.3385 | 2.6631 |
| Regression coefficient (R2) | 0.8655 | 0.7723 | 0.9485 | 0.7723 | 0.8062 |
| NG-SLNs | Slope | 5.5544 | 0.3258 | 0.4088 | 0.1415 | 0.2619 |
| Intercept | 2.0739 | 1.1916 | 0.1172 | 1.1416 | 1.4136 |
| Regression coefficient (R2) | 0.9315 | 0.7771 | 0.9485 | 0.7771 | 0.8485 |

**Table 4. Estimated Average Binding Affinities of the top poses of the chosen compounds for CYP3A4 and CYP2D6**

|  |  |  |
| --- | --- | --- |
| **Drugs** | **Binding affinity (kcal/mol)** | |
| **CYP3A4** | **CYP2D6** |
| **5TE8** | **4WNU** |
| AMX  (PubChem CID-2170)  (CHEMBL1113) | -9.162 | -8.373 |
| NG  (PubChem CID 442428)  (CHEMBL451532) | -9.551 | -10.49 |