Supporting Information for "Drug-Dependent Modulation of Micelle Morphology and Encapsulation in Triton X-100 Systems"

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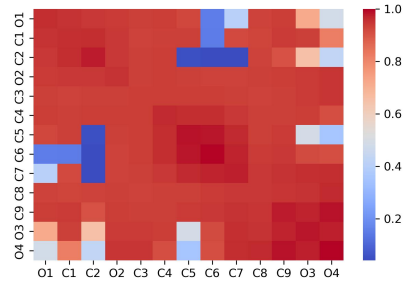
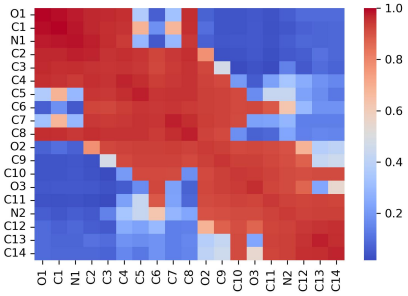
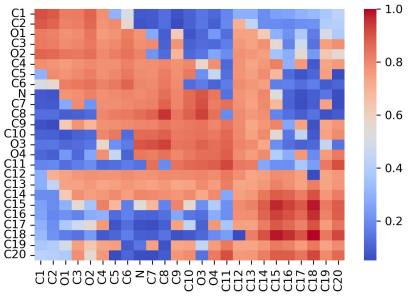
Atomistic description of the interactions between small molecular therapeutics



(a) Aspirin

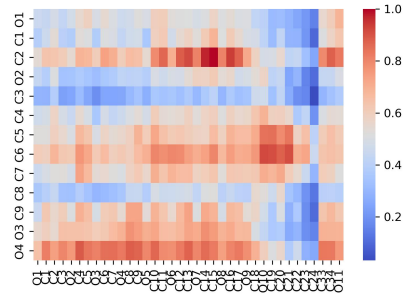


(b) Atenolol

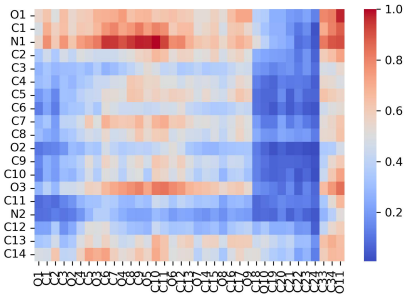


(c) Felodipine

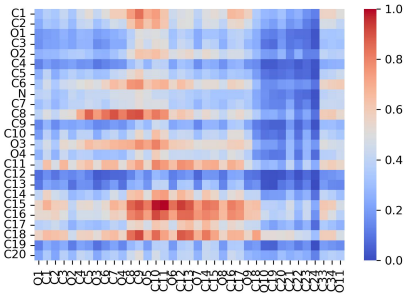
Figure S1: **Interactions between small molecule therapeutics.** Contact maps coloured by the amount of contact between the small molecule therapeutics. A contact event is defined as any pair of non-hydrogen atoms from different molecules separated by a distance of less than 5 Å. The contact frequency for each atom is computed as the fraction of trajectory frames (sampled over the 1 μs production simulation) in which that atom participates in at least one such contact. Red represents a high contact frequency (approaching 1.0), blue represents a low contact frequency (approaching 0.0), and white represents intermediate values. Atom labels follow the CHARMM36 naming convention as assigned by CHARMM-GUI. For aspirin: C1–C7 denote ring and carbonyl carbons, O1–O4 denote the ester and carboxyl oxygens. For atenolol: C1–C11 denote the phenyl and alkyl carbons, O1–O2 denote the ether and hydroxyl oxygens, N1 denotes the amine nitrogen. For felodipine: C1–C14 denote the dihydropyridine and phenyl ring carbons, N1 denotes the ring nitrogen, O1–O4 denote the ester oxygens, Cl1–Cl2 denote the chlorine substituents. Full atom coordinate files and topology files are available from the authors upon request.



(a) Aspirin

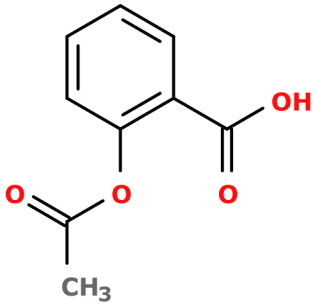


(b) Atenolol

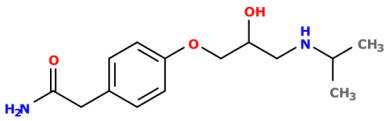


(c) Felodipine

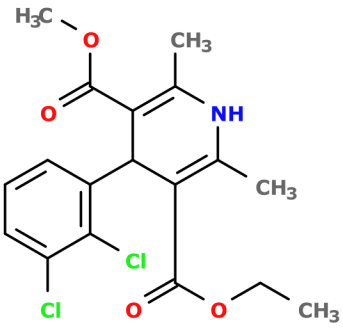
Figure S2: **Interactions between small molecule therapeutics and the Triton X-100 surfactants.** Contact maps coloured by the amount of contact showing the interactions between the Triton X-100 surfactants and the small molecule therapeutics. A contact event is defined as any pair of non-hydrogen atoms from different molecules separated by a distance of less than 5 Å. The contact frequency for each atom is computed as the fraction of trajectory frames (sampled over the 1 μs production simulation) in which that atom participates in at least one such contact. Red represents a high contact frequency (approaching 1.0), blue represents a low contact frequency (approaching 0.0), and white represents intermediate values. Atom labels follow the CHARMM36 naming convention as assigned by CHARMM-GUI. For aspirin: C1–C7 denote ring and carbonyl carbons, O1–O4 denote the ester and carboxyl oxygens. For atenolol: C1–C11 denote the phenyl and alkyl carbons, O1–O2 denote the ether and hydroxyl oxygens, N1 denotes the amine nitrogen. For felodipine: C1–C14 denote the dihydropyridine and phenyl ring carbons, N1 denotes the ring nitrogen, O1–O4 denote the ester oxygens, Cl1–Cl2 denote the chlorine substituents. Full atom coordinate files and topology files are available from the authors upon request.



(a) Aspirin

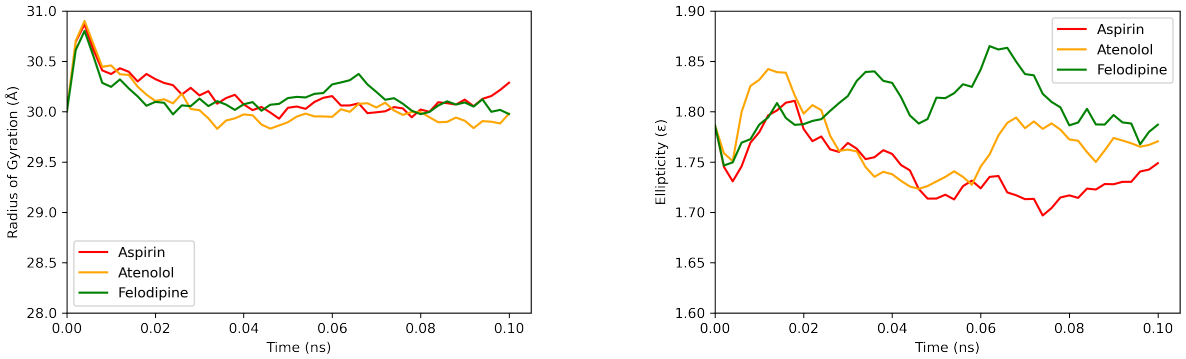


(b) Atenolol



(c) Felodipine

Figure S3: **Two-dimensional chemical structures of the three small-molecule drugs investigated in this study: (a) aspirin, (b) atenolol, and (c) felodipine.** Structures are drawn to explicitly show bond order, aromatic ring systems, and heteroatom connectivity. Atoms are coloured by element: carbon (black), oxygen (red), nitrogen (blue), and chlorine (green). The log P value of each molecule is given beneath its structure. These formal chemical structures complement the three-dimensional molecular representations shown in Figure 1 of the main text, which depict the conformations used in the all-atom molecular dynamics simulations.



(a) (b)

Figure S4: **Equilibration of the drug-loaded TX-100 micellar systems.** (a) Radius of gyration (R_g) of the TX-100 micelle as a function of simulation time for systems containing aspirin (red), atenolol (orange), and felodipine (green). Following an initial relaxation from the insertion of drug molecules, all three systems converge to stable, fluctuating values of R_g, indicating that the micellar core dimensions have equilibrated prior to the production run. (b) Ellipticity of the micelle as a function of simulation time for the same three systems. The ellipticity fluctuates around a stable mean in each case, confirming that the overall micellar shape has equilibrated and that no systematic drift in micelle morphology is present during the production phase.