Electronic Supplementary Information for:

Encapsulation of Dopamine within SU-101: Insights by Computational Chemistry

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Table of contents

S1. Computational details

The encapsulation of dopamine within SU-101 is particular due to the stability of the system. This research is not related to drug design but to drug encapsulation, which is very important when drugs have to be delivered to some parts of the body. The first step in the design of drug vehicles is to determine the interactions that form between the drug and the vehicle. The interaction energy is an important factor, because the drug has to be bound but not strongly bound because it also has to be released at some point. The methodology used in this research makes it possible to determine the bonds and the energies of interaction. Therefore, it is applicable for other drug encapsulation systems and for the design of drug carriers. Computer simulations generate important information that could guide experimental investigations. The challenge is to find carriers that can bind to the drugs of interest. After research like this, which has a computational study and experimental verification, it is necessary to do toxicity tests to see if this system can be proposed for medical tests.

We use a crystallographic data file as a starting point, and add hydrogen atoms to the structure. The electronic density was obtained by applying periodic conditions with the Crystal14 software [1]. Hydrogen atoms and cell parameters were optimized at the theoretical level B3LYP-D*[2] by using the POB-TZPV basis set that was reoptimized to better consider the Basis Set Superposition Error [3]. In the case of bismuth atom, ECP60MFD pseudopotential was used [4, 5].

Two forms of SU-101, hydrated (SU-101-H) and anhydrous (SU-101-A), were studied. In the hydrated form, SU-101 has water molecules within the pores interacting with the metal. In the two forms, different orientations of dopamine within the pores were studied. All dopamine atoms and SU-101 hydrogens were optimized, while all other SU-101 atomic positions and cell parameters were kept fixed. The SU-101-H-dopamine (DA@SU-101-H) and SU-101-A-dopamine (DA@SU-101-A) systems, were studied with the addition of: I) a water molecule and II) a methanol molecule by using the Restricted Isomers Searching by Simulated Annealing (RISSA) program [6]. All the nuclei of the water and methanol molecules were optimized, leaving the rest of the variables fixed.

With the Quantum Theory of Atoms in Molecules (QTAIM) [7] the description of non-covalent interactions was obtained with the Graphics Processing Units for Atoms and Molecules (GPUAM) code [8,9].

The interaction energies were calculated from.

$$E_{int} = E_{SU-101\cdots molecule} - E_{SU-101} - E_{molecule} \quad (1)$$

$E_{SU-101\cdots molecule}$ represents the energy of the total system, E_{SU-101} is the energy of the SU-101-H or SU-101-A, and $E_{molecule}$ is the energy of the corresponding molecule (dopamine, water, methanol).

S2. Experimental details

Chemicals

Bismuth (III) acetate ($(CH_3CO_2)_3Bi$, 99.99 %), Ellagic acid (HPLC ≥ 95 %), Acetic acid glacial (CH_3CO_2H, 99 %), Ethanol (HPLC), High purity deionized water with specific resistance of 18 mΩ cm^{-1}, Oxalic acid (HO_2CCO_2H) (ReagentPlus®, ≥ 99 %), Methanol (CH_3OH) (HPLC 99.9%) and dopamine hydrochloride were supplied by Sigma-Aldrich. All reagents, gases, and solvents were used as received from commercial suppliers without further purification.

Synthesis of SU-101

SU-101 was synthesized following a previously reported procedure [10]. 15 mg of Ellagic acid and 38 mg of Bismuth (III) acetate were dissolved in 30 mL of water and 1 mL of acetic acid. First, the solution was stirred at room temperature for 48 h. Then, the powder was washed with water and ethanol. After that, it was dry overnight at 60 °C.

Analytical instruments

The Powder X-Ray Diffraction Patterns (PXRD) were recorded on a Rigaku Diffractometer, Ultima IV, with Cu-Kα1 radiation (λ = 1.5406 Å) using a nickel filter. The patterns were recorded in the range 2–50° 2θ with a step scan of 0.02° and a scan rate of 0.10° min^{-1}.

Dopamine measurements

"In general, the adsorption experiments were conducted at room temperature, in a batch system, under stirring (200 RPM). The adsorption time was set to 12 h, using 15 mL of dissolvent at a particular concentration. After adsorption, SU-101 was separated by centrifugation (4000 rpm for 8 min), and the aqueous phase was analyzed.

The loading ratio of dopamine was calculated using Equation 1.

$$\%R = \frac{C_i - C_f}{C_i}(100) \qquad (1)$$

Where, % R, C_i, and C_f are the loading ratio, the initial dopamine concentration, and the final dopamine concentration, respectively."

Dopamine analysis was performed in a UPLC Acquity system, which consists of a quaternary pump coupled to an FTN auto-sampler, an isocratic solvent manager, and a 2998 PDA Detector from Waters™. Chromathograms were recorded at λmax = 280 nm with a resolution of 4.8 nm. Samples were separated on an ACQUITY UPLC® CSH™ Phenyl Hexyl 1.7 µm

(2.1 x 75 mm) column at 35°C with an isocratic regime (0.4 mL min^{-1}). The mobile phase composition was (90%) CH_3OH / (10%) 10 mM [HO_2CCO_2H]. With these conditions, the retention time for dopamine was 0.35 min, with a total run time for each sample of 1 min.

S3. Results and Discussions

Computational chemistry encapsulation of dopamine

Table S1: Cell parameters; percentage error is indicated in parentheses. Bond lengths given in angstroms and angles in degrees

Parameter	a	b	c	α	β	γ
SU-101-H	18.37 (1.33%)	18.37 (1.33%)	5.57 (0.46%)	90.00	90.00	90.00
Experimental	18.62	18.62	5.55	90.00	90.00	90.00

Table S2: Interaction energy (E_{int}) and total number of different non-covalent interactions of SU-101-A – dopamine system

SU-101-A – dopamine system	E_{int} (kcal/mol)	Bond-H conventional	Bond-H non-conventional	Bond H-H	Bond dihydrogen	Heteroatoms interactions	Total number
(a) DA@SU-101-A	-47.5	3	8	2	0	5	18
(b) DA@SU-101-A	-41.2	2	9	0	1	6	18
(c) DA@SU-101-A	-37.5	4	6	2	1	4	17

Table S3: Interaction energy (E_{int}) and total number of different non-covalent interactions of SU-101-H – dopamine system

SU-101-H – dopamine system	E_{int} (kcal/mol)	Bond-H conventional	Bond-H non-conventional	Bond H-H	Bond dihydrogen	Heteroatoms interactions	Total number
(d) DA@SU-101-H	-36.4	2	14	2	0	5	23
(e) DA@SU-101-H	-33.9	2	10	1	0	4	17
(f) DA@SU-101-H	-31.4	4	9	2	1	3	19
(g) DA@SU-101-H	-25.2	3	8	1	0	7	19

Table S4: Interaction energy (E_{int}) and total number of different non-covalent interactions of SU-101-A – dopamine – H_2O system

SU-101-A – dopamine – H_2O system	E_{int} (kcal/mol)	Bond-H conventional	Bond-H non-conventional	Heteroatoms interactions	Total number
(h) DA-H_2O@SU-101-A	-28.8	2	1	3	6
(i) DA-H_2O @SU-101-A	-27.9	2	0	3	5
(j) DA-H_2O @SU-101-A	-28.3	3	2	3	8

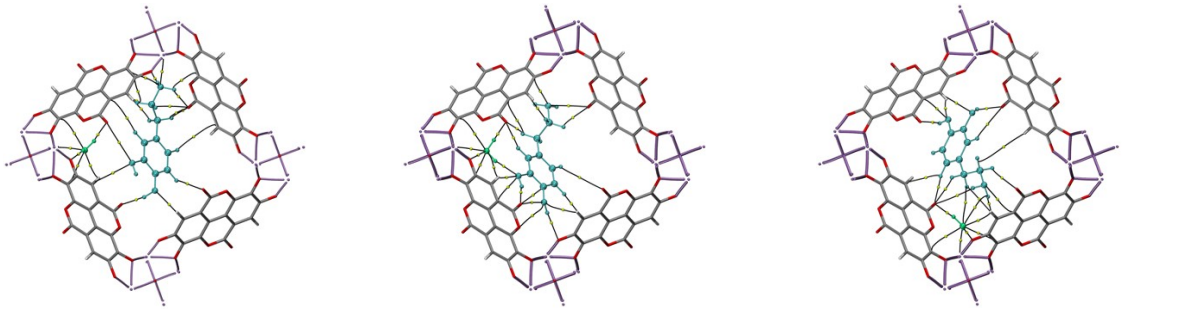
Table S5: Interaction energy (E_{int}) and total number of different non-covalent interactions of SU-101-H – dopamine – H_2O system

SU-101-A – dopamine – H_2O system	E_{int} (kcal/mol)	Bond-H conventional	Bond-H non-conventional	Bond dihydrogen	Heteroatoms interactions	Total number
(k) DA@SU-101-H	-18.0	1	2	0	1	4
(l) DA@SU-101-H	-16.7	2	1	1	2	6

Table S6: Interaction energy (E_{int}) and total number of different non-covalent interactions of SU-101 - A - MeOH system

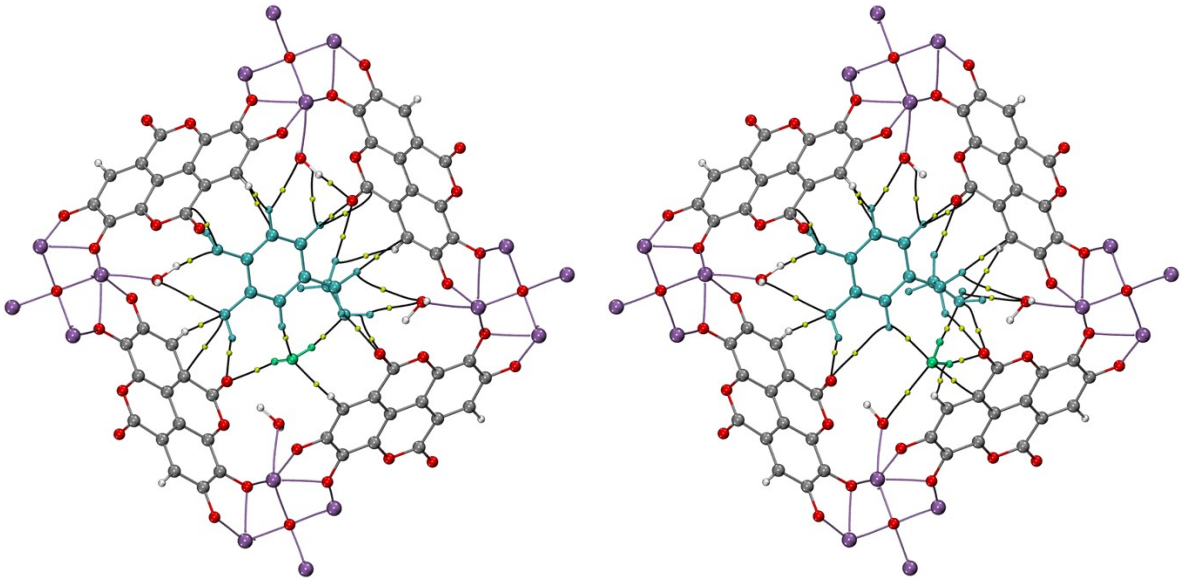
SU-101-A – dopamine – H_2O system	E_{int} (kcal/mol)	Bond-H conventional	Bond-H non-conventional	Bond dihydrogen	Heteroatoms interactions	Total number
SU-101-M	-22.3	1	0	1	5	7
MeOH@SU-101-A	-22.7	1	0	1	5	7

Figures



DA-H_2O@SU-101-A

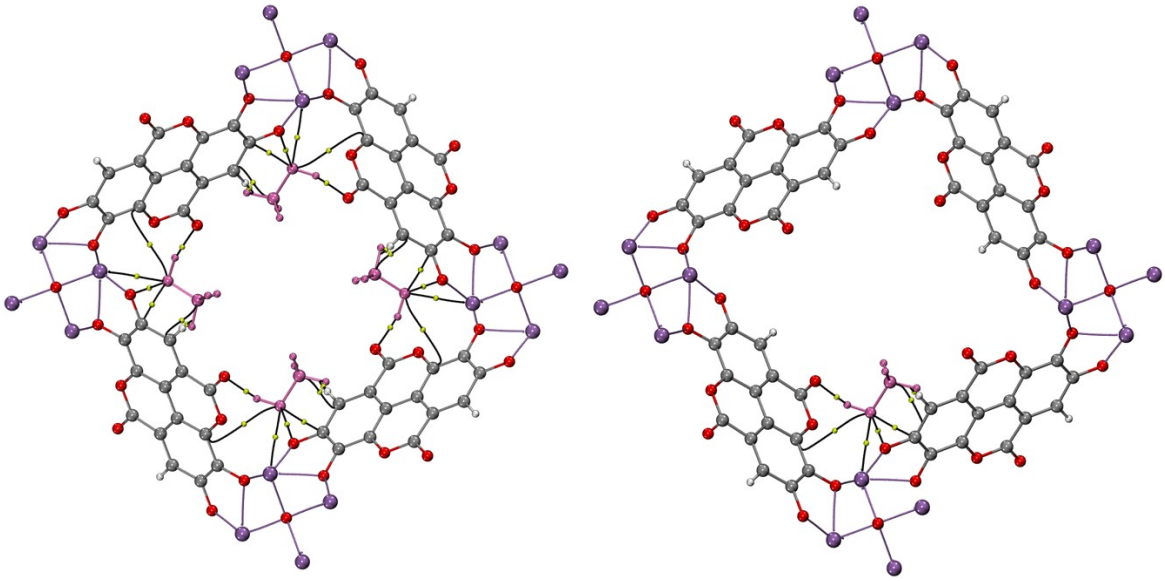
(h) - 28.8 kcal/mol **(i)** - 27.9 kcal/mol **(j)** - 28.3 kcal/mol



DA-H_2O@SU-101-H

(k) - 18.0 kcal/mol **(l)** - 16.7 kcal/mol

Figure S1. Structures and values of interaction energy of H_2O (in green) within DA@SU-101-A [(h) (i) (j)] and DA@SU-101-H [(k) (l)]. Bond paths in black and bond critical points in yellow.



SU-101-M
- 22.3 kcal/mol

MeOH@SU-101-A
- 22.7 kcal/mol

Figure S2: Structures and value of interaction energy between MeOH in pink with SU-101-A. Bond paths in black and bond critical points in yellow.

SU-101 characterization

PXRD

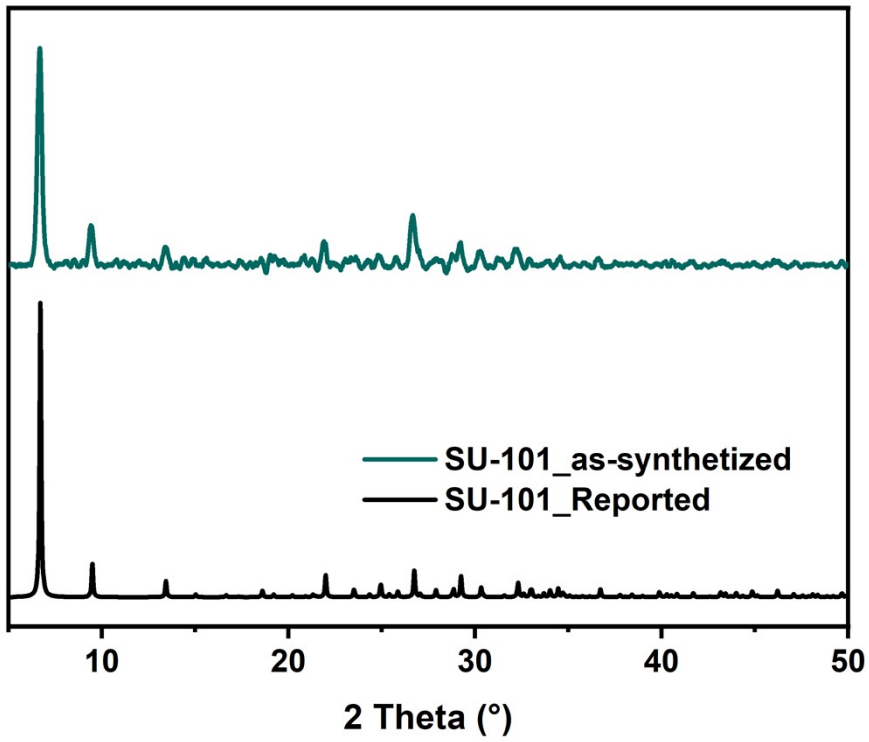


Figure S3. PXRD pattern of SU-101 reported and SU-101 as-synthetized.

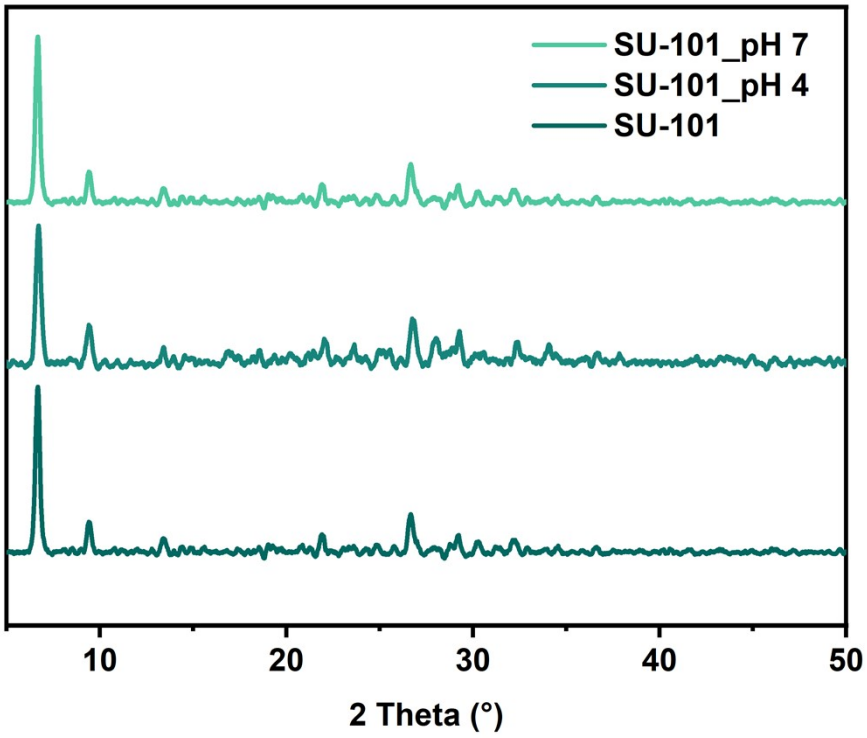


Figure S4. PXRD pattern of SU-101 as-synthetized at pH 4 and pH 7.

Dopamine encapsulation analysis

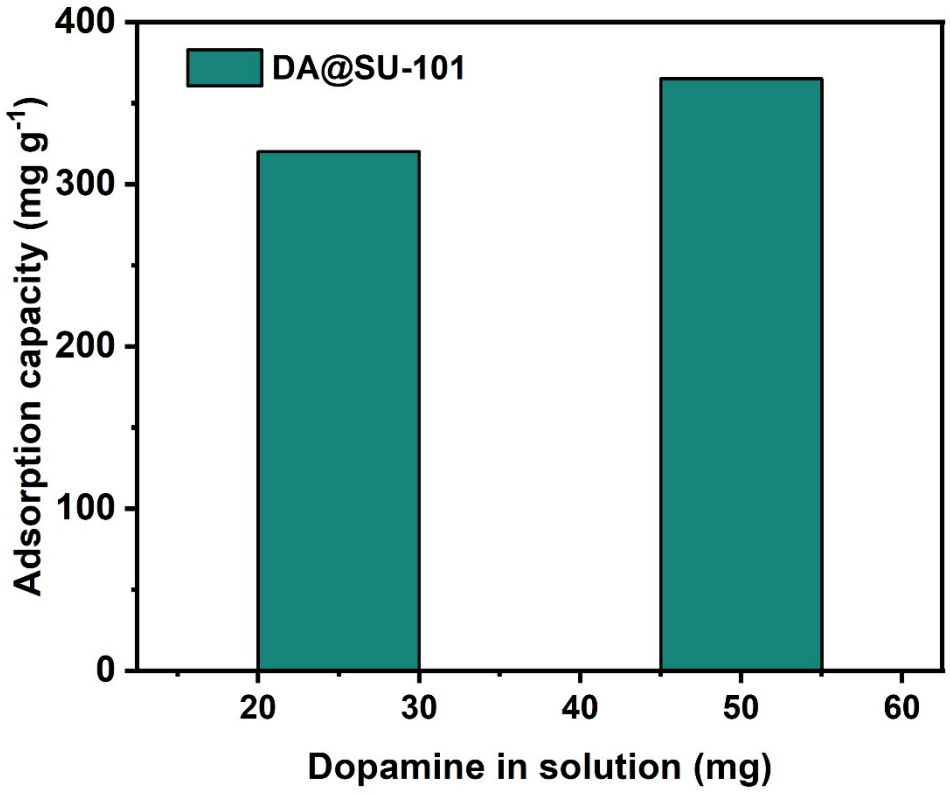


Figure S5. Adsorption capacity of SU-101 using 25 and 50 mg of dopamine.

S4. References

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