ASEC 2024 Conference

The 5th International Electronic Conference on Applied Sciences

04–06 December 2024 | Online

MDPI

Application of computer modeling to the study of nimesulide inclusion complexes with β- and γ-cyclodextrin

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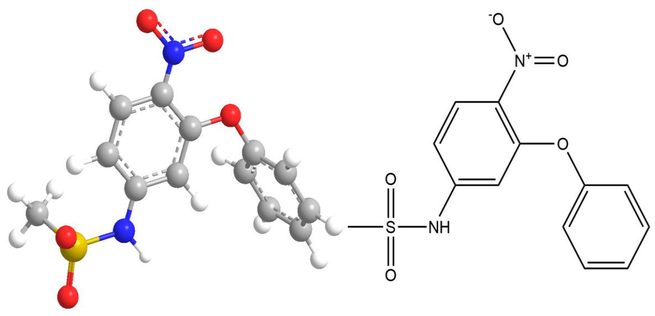
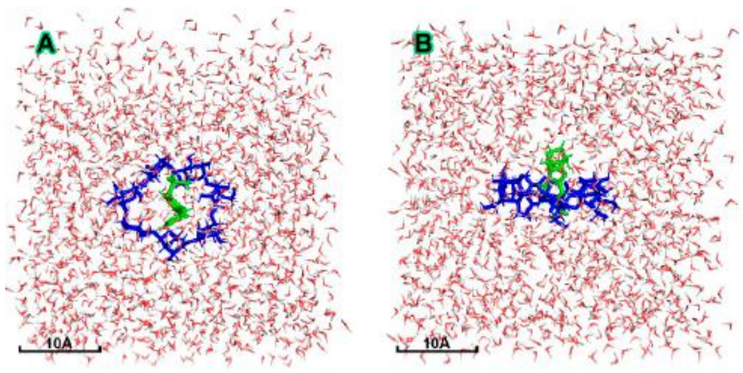
INTRODUCTION & AIM

Incapsulation of low-soluble pharmaceutical agents in the β- and γ-cyclodextrin cavity (β-CD, γ-CD) succesfully solves the current issues, related to bioavailabilty and dose reduction of a variety of anti-inflammatory drugs.



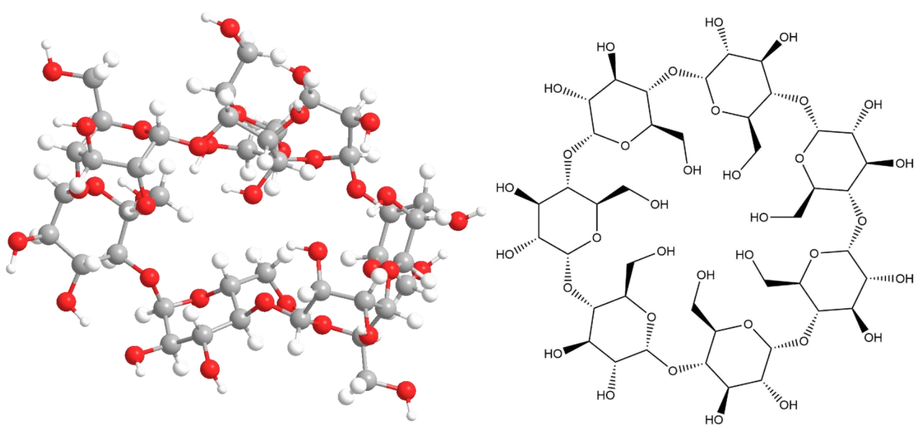
The result of modeling the geometry of the nimesulide molecule



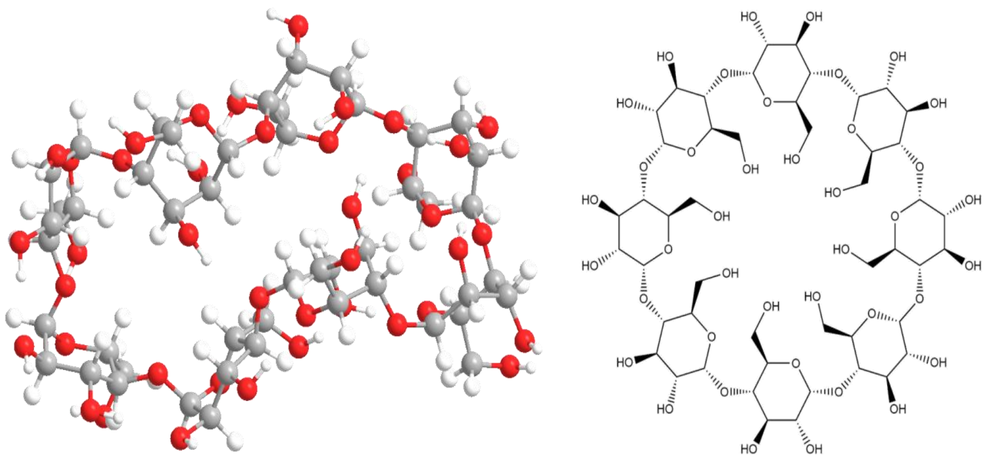
β–cyclodextrin–nimesulide complex in aqueous solution: (A) upper view, (B) side view.

METHOD

The molecular complexation of nim/β-CD and nim/ γ-CD was modelled via the Gaussian 09W computer program using the B3LYP method for DFT calculation. Molecular dynamics simulations of the complexes were performed via the NAMD2 software.



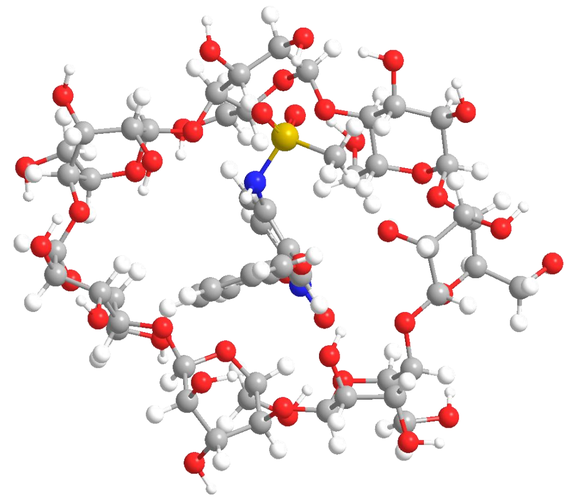
The result of modeling the geometry of β-cyclodextrin



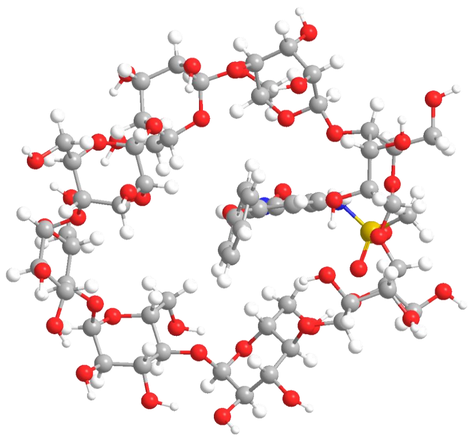
The result of modeling the geometry of γ-cyclodextrin.

RESULTS & DISCUSSION

The results of calculations indicated a low probability of complexation under the standard conditions. Nimesulide molecule exhibits a steric hindrance, leading to instability of nim/β-CD complex with minimal bond distances of 1.92Å. At the same time nim/ γ-CD complex shares a higher stability due to the larger dimensions of the carrier molecule. Conformational analysis indicated a deep minima in the product area of the plot, demonstrating stability of the nim/ γ-CD system.



The result of modeling the structure of the inclusion complex of nimesulide and β-cyclodextrin.



The result of modeling the geometry of the inclusion complex of nimesulide and γ-cyclodextrin.

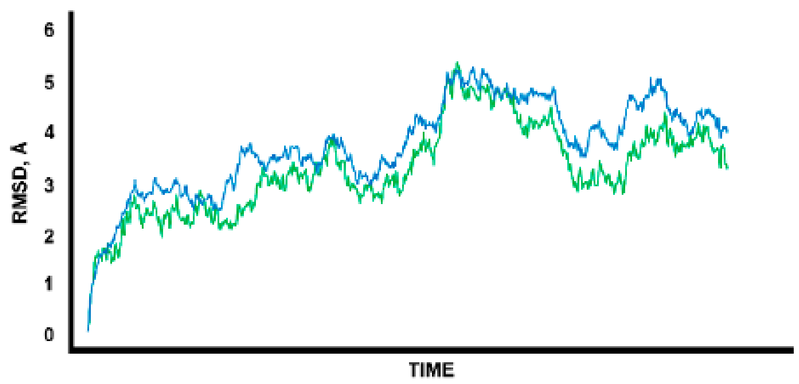


Diagram of RMSD trajectories. Nimesulide is represented blue and β-CD is marked in green.

CONCLUSION

Obtained data supports the idea of complexation and relative stability of complexes. The approaches of computational chemistry in study of supramolecules provide deep insights of complexation and make it possible to evaluate affinity.

FUTURE WORK / REFERENCES

1) Andreev, P.Y.; Barteneva, E.S.; Grekhneva, E.V.; Efanov, K.S.; Breskin, K.A. A New Approach to the Preparation of Inclusion Complexes with Cyclodextrins: Studying Their Stability Using Molecular Dynamics Methods. Eng. Proc. 2023, 56, 245. https://doi.org/10.3390/ ASEC2023-15817

2) Grekhneva, E.V.; Barteneva,mE.S.; Efanov, K.S. Peculiarities of Obtaining and Modeling the Structure of Nimesulide Clathrate Complexes with – and -Cyclodextrins. Chem. Proc. 2022, 12, 53. https://doi.org/10.3390/ ecsoc-26-13707

3) Barteneva Ekaterina*, Grekhneva Elena and Efanov Kirill. Substantiation of the Possibility of Obtaining Complex Including Nimesulide with γ-CD by Computer Modeling Methods. Polymer Sci peer Rev J. 4(5). PSPRJ. 000596. 2023. DOI: 10.31031/PSPRJ.2023.04.000596