High performance computing in the computational study of selected antimalarial and anticancer acylphloroglucinols

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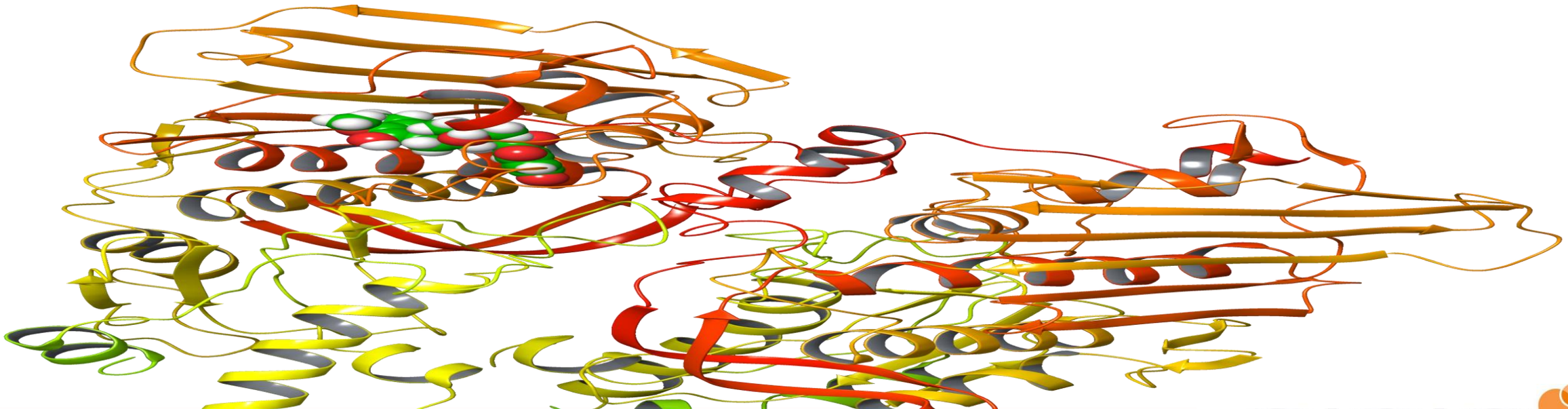

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Motivation

- **What is the purpose of this research?**
  - to use computational methods to determine the properties of acylphloroglucinol molecules having antimalarial and/or anticancer activities.

- **Why are we engaging in this research?**
  - Malaria and cancer are responsible for many deaths worldwide.
  - Resistance to currently-used drug is developing in both cases; therefore, there is need for new drugs with different molecular structures.
  - Acylphloroglucinols have not yet been used clinically. They can be promising.
  - Many drugs that are effective against one of these diseases are effective also against the other. That is why we study them together.

- **What are the expected benefits from this research?**
  - Providing information that will be useful for scientists working on further steps of drug development, to treat malaria and cancer.

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Computational methods

- **How do we determine the properties of molecules?**
  - By using computational approaches implemented in specific software.
  - The more sophisticated the approach, the better the quality of the results.
  - Computations with sophisticated approaches are quite demanding, above all for molecules that are not small-size.
  - A high number of calculations is needed, considering different geometries for each molecule, to obtain results that enable realistic conclusions.
  - Using the CHPC is crucial to obtain results in reasonable time.

- **Our computational approaches**
- Making calculations both for the isolated molecules and for the molecules in solution
- Using three different methods, to have confirmation of identified trends
- After the determination of the molecular properties (using the Gaussian-16 software), we also study the interactions of these molecules with proteins that have crucial roles for malaria or cancer (using the Schrödinger software).

Results

- We have determined the preferred geometries (**conformers**) of the considered molecules. These are the conformers that are responsible for the biological activity (the antimalarial or anticancer activity).

- We have determined the conformers' stabilizing factors and how they influence the energy of the conformers. **Intramolecular hydrogen bonds** are the dominant stabilizing factors.

- We have calculated a number of **molecular properties** (dipole moment, energy gap between the frontier molecular orbitals, vibrational frequencies of the bonds of interest, and others), and studied how they are different for different conformers.

- The study of the **interactions** between the considered molecules and the selected relevant proteins shows that the carbonyl oxygen and the phenolic OH groups of these molecules are involved in the interactions, often via **intermolecular hydrogen bonds.**

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Results (cont.)

- **Significance of the obtained results**

- Many of the calculated molecular properties can be used as **descriptors** in studies aimed at identifying relationships between the molecular structure and the biological activity of these molecules. These studies, in turn, are important for the design of molecules with more powerful pharmacological activity.

- The results about the interactions of the investigated molecules with appropriate proteins are also relevant for the design of molecules with more powerful pharmacological activity.

- Altogether, the obtained results provide an informative picture of the properties of these molecules, which may be useful for researchers working on further steps of drug development.

- We have obtained all these results thanks to the **possibility of using the CHPC.**