Insights from computational studies in drug design and toxicity assessment

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In recent years, computational approaches have emerged as powerful tools to complement and advance the principles of the 3Rs. Among these approaches, molecular dynamics simulations have proven particularly valuable in the field of computational chemistry. Molecular dynamics simulations involve the computational modeling of biomolecular systems, providing insights into their behavior and interactions at the atomic level. The application of molecular dynamics within the 3Rs framework offers numerous advantages, allowing for the reduction in the number of animals required for specific studies. By employing computational models, researchers can decrease the need for a large number of experimental animals by partially replacing animal testing with in-silico modeling. These methods can provide reliable predictions of molecular behavior, drug interactions, and toxicity assessments, offering alternatives to traditional animal experiments.

In this context, the present work aims to highlight the contribution of molecular dynamics simulations to the principles of the 3Rs. Several applications of molecular dynamics will be discussed where in-silico methods complement in-vitro experiments, providing an enhanced understanding of the interactions between proteins and small molecules. Specifically, we will explore the dynamic behavior of protein-ligand complexes, including the HIF-2α:ARNT target for tumor therapy, the loading mechanism of drugs onto functionalized TiO_2 nanoparticles as drug carriers, a structure-based approach to design drugs targeting ALKBH2 for the treatment of glioblastoma and the binding modes of various chemicals to the Ah receptor (AhR) and the Pregnane X Receptor (PXR). These case studies showcase the power of molecular dynamics simulations in elucidating key molecular interactions, offering valuable insights for rational drug design and toxicity assessment.

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Conference presentation: this paper was presented at the Fourth Centro 3R Annual Meeting - The role of 3Rs in the age of One Health: where we are and where we're going - 13-15 September 2023, Università degli Studi Milano-Bicocca.

Biomedical Science and Engineering 2023; 4:228
doi:10.4081/bse.2023.228