Review Article

COMPUTATIONAL CHEMISTRY AND ITS APPLICATIONS IN MEDICINE: A REVIEW

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ABSTRACT

In this paper, the computational chemistry and its importance in diagnosing of compounds, their physical properties, approaches of computational chemistry such as (molecular modeling, molecular docking and quantitative structure-activity relationships) and their applications in medicine and pharmacy were discussed and their importance in the diagnosis of pharmaceuticals and the discovery of drugs in the world of medicine and pharmacy.

Keywords: Computational Medicinal Chemistry, Molecular Modeling, Molecular Docking, QSAR.

INTRODUCTION

Computational Chemistry

Computational chemistry (also called molecular modeling; the two terms mean about the same thing) is a set of techniques for investigating chemical problems on a computer. Questions commonly investigated computationally are: Molecular geometry: the shapes of molecules – bond lengths, angles and dihedrals¹. Energies of molecules and transition states: this tells us which isomer is favored at equilibrium, and (from transition state and reactant energies) how fast a reaction should go. Chemical reactivity: for example, knowing where the electrons are concentrated (nucleophilic sites) and where they want to go (electrophilic sites) enables us to predict where various kinds of reagents will attack a molecule. IR, UV and NMR spectra: these can be calculated, and if the molecule is unknown, someone trying to make it knows what to look for². Computational chemistry is fairly cheap, it is fast compared to experiment, and it is environmentally safe (although the profusion of computers in the last decade has raised concern about the consumption of energy and the disposal of obsolescent machines). It does not replace experiment, which remains the final arbiter of truth about Nature³. There are two different aspects to computational chemistry: Computational studies can be carried out to find a starting point for a laboratory synthesis, or to assist in understanding experimental data, such as the position and source of spectroscopic peaks. Computational studies can be used to predict the possibility of so far entirely unknown molecules or to explore reaction mechanisms that are not readily studied by experimental means⁴.

Computational Chemistry Approaches

Computational approaches become a pivotal step in early drug discovery process. Indeed, it provides time-saving and cost-effective procedures for pharmaceutical companies. The application of these approaches aims to improve the selected lead compounds. Two approaches are mainly used in computer-assisted drug design: i) Structure-based drug design, where the structure of the drug target is used to guide drug discovery. The structural information can be obtained using X-ray

crystallography or nuclear magnetic resonance spectroscopy (NMR). Structure-based drug design includes docking, virtual screening, and molecular dynamics. ii) Ligand-based drug design approach is used in the absence of the three-dimensional structure of the target. It represents a powerful method based on only small-molecule information using a series of known active compounds. This approach includes quantitative structure-affinity relationship (QSAR) and pharmacophore modeling based on ligand properties⁵.

1- Molecular Dynamics (MD) : technique is a powerful theoretical method for the investigation of dynamical processes in biological systems. It provides accurate descriptions of the structure and dynamics of these systems⁶ The Schrodinger equation is the starting point for molecular problems. The symbol $\hat{H}$ is a differential operator called the Hamiltonian operator, which is analogous to the classical Hamiltonian, inasmuch as it is a sum of kinetic and potential energy terms; the symbol E is the total energy for the system. The wave function Ψ depends on the position of all the particles comprising the system⁷.

$$\hat{H} \Psi = E \Psi \quad \dots(1)$$

2- molecular docking: computational docking is an essential component in modern drug discovery. Over the last few decades, it has been routinely and successfully applied in most pharmaceutical and biotech companies for a large number of applications. Molecular docking classifies bio molecules into three categories: small molecules (also called 'ligands'), proteins, and nucleic acids The most important types of docking systems are: protein-ligand, protein-protein and nucleic acid-protein⁸.

Figure 1: Molecular docking of ligand to a protein receptor to produce a complex.

3- Quantitative Structure-Activity Relationships (QSAR), is a method for building computational or mathematical models which attempts to find a statistically significant correlation between structure and function using a chemo metric technique. is used when some property other than the biological activity is concerned. Various QSAR approaches have been developed gradually over a time span of more than a hundred years and served as a valuable predictive tool, particularly in the design of pharmaceuticals and agrochemicals^{9,10}

Applications of Computational Chemistry in Medicine

Computational methods have found a wide application in medicinal chemistry¹¹. Computational techniques have been successfully used in the fields of Pharmacy and Medicine. Specially, identifying drug–target interactions, synergistic drug combinations, and drug repositioning based on heterogeneous biological data and powerful computational models are important topics in the computational biology¹². The investigation of these important problems is critical not only for better understanding of the various interactions and biological processes, but also for the development of novel drugs and improvement of human

medicines¹³. Computational medicinal chemistry is an emerging and exciting interdisciplinary field of research. The significant progress and advances made in the recent years are owed to several factors. First, computer technology has dramatically evolved and matured so that algorithms and computational methods can be applied today that could not be used before, owing to hardware limitations. Second, new algorithms and mathematical concepts have been conceived or adapted for specific purposes in medicinal chemistry. Third, numerous successful applications have created increased awareness of computational approaches in the medicinal chemistry community and have also attracted many young scientists and students to the field. Finally, and this statement represents a more personal opinion, there is simply no excuse for not using computational tools for the design of drug candidates¹⁴. Experimental drug-discovery approaches are ideally supported and complemented by such computer models, which will help us explore new pharmaceutically interesting compounds¹⁵. Computational chemistry within the pharmaceutical industry has grown into a field that proactively contributes to many aspects of drug design, including target selection and lead identification and optimization^{16, 17}.

Figure 2: "Areas of Computer – aided Drug Discovery"

CONCLUSION

In this research we conclude that computational chemistry is of great importance in the diagnosis of large and small molecules. There are several approaches in which to diagnose these compounds. Computational chemistry has an importance in medicine, diagnosis and discovery of drugs and the importance of the docking and QSAR approaches in diagnosing of these pharmaceutical substances.

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