Chapter 3
Advancements in Cancer Therapeutics: Computational Drug Design Methods Used in Cancer Studies

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ABSTRACT

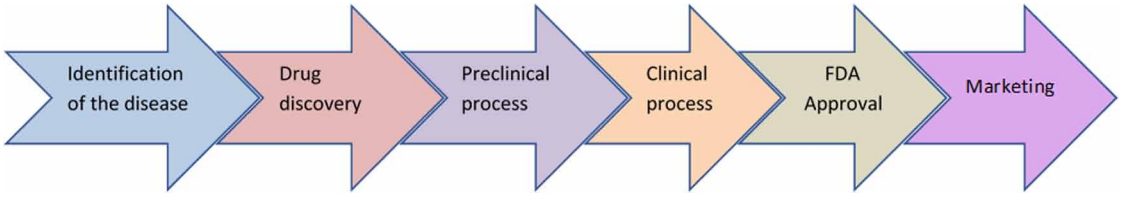
In this chapter, computational approaches for the discovery of new drugs that are useful for diagnosis and treatment of disease will be described in three parts. MD technique uniquely supports protein design attempts by giving information about protein dynamics associated with atomic-level descriptions of the relationship between dynamics and function. The purpose of molecular docking is to provide an estimate of the ligand-receptor complex structure using computational methods. By this estimation, the mechanism of drug binding and action are described by determining the three-dimensional simulation of drug and drug-induced macrostructure. ADME characteristics are physicochemically significant descriptors and pharmacokinetically relevant properties used to design more effective drugs and new analogs. As a result, in-silico calculations can provide robust preliminary information as to drug activity and mechanism in the drug production process, as well as in vitro and in vivo studies.

DOI: 10.4018/978-1-7998-6530-8.ch003

INTRODUCTION

Drugs are a very important factor that affect human life and health. Unfortunately, the discovery of molecules that result in safe and effective drugs involves a process that has high cost at production, development and testing stages; they must go through certain stages as a result of the experiments performed in the laboratory, and then include clinical research. Drug research contains several phases. Phase 1 covers a period of 1 to 1.5 years, in which the pharmacokinetic properties of the drug, its toxicity, and its effect on body functions are determined. Phase 2 is a clinical trial period that lasts 1 to 3 years to determine therapeutic dose limits in order to investigate the clinical efficacy and safety of the product. Phase 3 lasts 3 to 4 years. At this stage, the phase 1 and phase 2 periods are tested. Phase 4 is a process for further clinical investigation of the approval of approved products, indications for administration. These basic studies, which include finding a new molecular structure that can be used as a drug, finding new uses of existing molecular structures, and re-evaluating the adverse effects of a drug, are conducted through clinical tests, thus covering a long and costly process. The drug design, application and development mechanism is shown in Figure 1.

Figure 1. The drug design, application and development mechanism



Designing and developing the most effective drug in a short time and with lower costs attracts the attention of many scientists working in different fields. In the process of designing the most effective drug, in silico (applied in computer environment) methods are preferred because it minimizes time and cost. The appropriate drug structures obtained in accordance with the calculations made with in silico methods allow for more rational drug designs by reducing the processes of organic synthesis with high budget. The aim of molecular modeling methods that define molecular systems at the atomistic level is to show how atoms and molecules can interact with a three-dimensional image and simulation, and to determine the structure of these interaction mechanisms. These models can also be used to interpret existing observations or to predict new chemical behaviors. In the drug design process, in silico methods have become a valuable and necessary tool for the modeling of molecular structures that have been nominated for drugs, for increasing the effectiveness of drugs, and for the design of new drug molecules with unknown molecular structure. With these methods, it is possible to examine the relationship between chemical structure and function from small systems to large biologic molecules and material groups. Molecular biology, protein science, drug design, electronic and photonic materials, and polymer science are among these areas. With the help of in silico methods, information can be obtained from the microscopic details of the system up to the macroscopic properties. In other words, it is possible to understand the biochemical and physicochemical properties of molecules by performing a perfect calculation with these methods under high conditions such as high pressure and temperature. The contribution of modern