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Editorial

Computer Aided Drug Design and Discovery – An Economical Approach to Drug Discovery Industry

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Traditional Approach of Drug Design and Discovery

In the field of therapeutics and medicine a drug discovery is an integrated process by which new drug candidate are discovered. Traditionally, new drug molecules were discovered through identifying the active ingredient from traditional remedies or by serendipitous discovery. This was the case for aspirin, which was derived from the bark of willow tree [1]. As time went and a several number of therapeutically applicable molecules were discovered and a library of molecule with same or different activity. Later chemical libraries with identical or similar parent scaffold of synthetic small molecules, natural products (plants, marine, animals) or extracts were randomly or desirably screened against to specific cells or a whole organism to identify the desirable therapeutic activity/effect known as classical pharmacology. Synthesizing list/derivatives of compound and patenting them is an essential phenomenon to secure the pharmaceutical industry data in preventing the scientific and economical loss. For an individual drug candidate a pharmaceutical industry synthesize >1000 structural derivative and depending on the initial screening results protection of such data is carried out, which significantly increases the cost of drug discovery procedure in its initial phases which is directly proportionate to the number of molecule you design, synthesize and test.

According to PriceWaterhouseCoopers Pharma 2005: An Industrial Revolution in R&D report express that there is increase in pre-clinical testing from 2853 in 1996, 3102 in 1997 to 3278 in 1998 [2]. World's top 20 pharmaceutical companies spent $17.9 billion on R&D in 1993 and streaming 894 projects in preclinical trials [2]. However, given a success rate of 40% for discovery compounds, only 358 drugs could be expected to pass this stage. Only 10% of those – 36 drugs – would ever reach the market [2]. Take into account a typical portfolio turnover rate of four years and the top 20 companies could each expect to produce just 0.45 new chemical entities (NCEs) per year [2]. A study by the consulting firm Bain & Company reported that the cost for discovering, developing and launching a new drug rose over a five-year period to nearly $1.7 billion in 2003 [3]. According to Forbes, development costs between $4 billion to $11 billion per drug [4].

Computer Aided Drug Design and Discovery

In biomedical arena, computer-aided or *in silico* design is being utilized to accelerate and aid hit identification, hit-to-lead selection, optimize the absorption, distribution, metabolism, excretion, toxicity profile and concerned about safety issues. Commonly used computational approaches include ligand-based drug design (pharmacophore, a 3-D spatial arrangement of chemical features essential for biological activity), structure-based drug design (drug-target docking), and quantitative structure-activity and quantitative structure-property relationships. Regulatory agencies as well as pharmaceutical industry are actively involved in development of computational tools that will improve effectiveness and efficiency of drug discovery and development process, decrease use of animals, and increase predictability. It is expected that the power of CADDD will grow as the technology continues to evolve [5].

Molecular modeling techniques such as homology modeling and structure perdition methods are utilizing extensive mathematical expression and helps us to model the 3D structure of target / receptor protein whose 3D-crystallographic structures are not reported. Simulation process is a phenomenon which helps to create a virtual biological environment outside the body and mimics the relative functions. Whereas, active site mapping helps to identify and gather the knowledge of pockets/active site/ binding site region on to the target protein.

Structure Based Drug Design

Structure (target)-based drug design represents molecular docking i.e. ligand binding to its receptor, target protein. Molecular docking is used to identify and optimize drug candidates by computationally examining and modeling molecular interactions between ligands and target macromolecules. Pharmacophore library screening followed by molecular docking represents complimentary screening methods with the combination providing optimum results [6].

Ligand Based Drug Design

Ligand based drug design is an approach used in the absence of the receptor 3D information and it relies on knowledge of molecules that bind to the biological target of interest. 3D quantitative structure activity relationships (3D QSAR) and pharmacophore modeling are the most important and widely used tools in ligand based drug design. They can provide predictive models suitable for lead identification and optimization [7].

A rapid development in this area has been made by development and advancements in dedicated software and hardware, where computational power and optimum designed algorithms have cleverly defined the 3D-spatial arrangements of molecular structure data from X-ray crystallographic, NMR and other structural development technologies. Computer aided drug design and discovery CADDD

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methods is being utilized to identify hit, selection of leads, optimization of lead and screening of ADMET/PK properties. In an alternate way the list of computational techniques helps to minimize time and resource requirements of chemical synthesis and biological testing. Screening to such vital information helps to generate a systematic approach prior to synthesis a particular compound which prevents excess utilization of important resources, failure of lead and overall reduction in time and cost.

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