



"Comprehensive Overview of Drug Design, Discovery, and Process Chemistry"

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ABSTRACT :

Drug design is a process in which we study about how a suitable, maximum pharmacological effect and minimum side effect type of medicine or pharmacological product to be, manufacture. In this term for preparation of good quality of product we perform SAR study of chemical compound and also study about their functional group interchanging by one another to achieving best pharmacological activity. For drug design and development we require to proper support and knowledge of chemistry such as pharmaceutical medicinal and organic chemistry. By proper study of chemistry be also modify existed drug to just changing in their chemical structure with help of SAR study.

Introduction :

Drug design is considered as rational designing or modifying new molecules or functional groups based on the study of biological target. It is an approach by which new ligands or medical product are designed or modifying complementary on the basis of the size and charge of biological target compounds /substance to their target receptor.

For designing and modifying new drug analogue following steps are involve -

- Random screening of natural and artificial polymer
- Arrangement structural analogues.
- To prepare new functional groups or atom based on known structure of biologically active compounds
- Application for biologically purpose.

Drug discovery :

Drug discovery can be referred as the process of identifying chemical compounds having the potential to become a therapeutic agent. Main goal of drug discovery occurred is the recognition of new molecular functional groups that will be beneficial in the treatment of diseases that qualify as presenting actual medical needs. These diseases do not have definitively useful therapies and are actually or potentially life-threatening. Marketed drugs at this point represent a relatively very little number of drug target types. Drug, targeted against Glico – protein coupled receptors, nuclear (hormone) receptor, and ion channels receptor represent of the marketed drugs. By far, drugs directed against enzymes represent the greatest portion of marketed drugs. Expansion into new types of drug targets may be requirement to fill certain pharmacological voids, but the reason of great intellectual challenge is how to choose a target likely effected area of value, especially when venturing into less well- expressed types of drug targets [1].

Drug Design And Discovery :

Drug design and discovery is the process of developing new pharmaceutical drug or medicine / product to treat disease and disorder or improve the effectiveness of previous treatments. It involves identifying potential drug targeted tissue, designing and synthesizing molecules that interact with those targets, and testing their safety and efficacy in preclinical and clinical trials through analysis department. The process ultimately begins with target obtained to identification, which involves discovering the molecular structures or biological pathways include in a disease. This information can be

through a variety of approaches, including genetic studies, bioinformatics, and high-throughput screening. Compounds are analyzed in vivo and in vitro for the assessment of their efficacy and safety. In vitro tests typically involve testing the compounds on cells or tissues in a laboratory level while in vivo tests involve testing them in animals as model for preclinical trial. Once a target has been identified, the next step is to design and synthesize molecules that can interact with it in a specific way. This can involve a range of technical method, including computer modeling, medicinal chemistry, and organic & inorganic chemistry. If the compound promises in preclinical testing, they may then move on to clinical trials in human's community. These trials including to testing the drugs on increasing large groups of patients to ensuring their safety, efficacy, and therapeutic capability at potential level[4].After successfully approval of clinical trial, it can then be approved for use by regulatory agencies like the FDA or EMA, and marketed to healthcare professional and patients[5]. The whole drug design and discovery process can take a long time periods almost many years and involve high investment, but it can ultimately lead to new treatment and medication that improve patient health and protect their life [6].

Target Identification:

Target determination is a critical step in the drug design process chemistry. It presents to identifying the molecular structures or biological pathways that are involved in a disease or disorder and that can be targeted by drugs to various approaches can several therapies that can be used for target identification receptor. Such as -

- Genetics: the transformation and identification of genes that are connected with a disease can provide system to potential drug targets [6]. This can involve sequence wise numbering the genomes of affected particular / individual studying genetic mutations that are correlated to that disease.
- Bioinformatics: This involves using computational methods to enquiring large datasets of genetic and biological information to identify actual and potential drug targets [7].
- High-throughput screening [8]: This involves testing large numbers of molecules or compounds to identify those that have a specific effect on the disease target area.
- Reverse pharmacology: This approach involves identifying drugs that are effective in treating a particular backward and then working backward to identify the molecular targets that they interact with desired affected area.[9].
- Knowledge-based approaches: These are really on existing knowledge of the diseases and its highlighting steps, mechanisms to identify potential drug targets [10].

Once a potential target has been recognized, researchers can use several of techniques to approved it and determine whether it is a legal and actual drug target. This can conclude in vivo and in vitro experiments to understanding the target's role in the particular disease and disorder, as well as tests to determine the target's availability of drug (i.e., because it is applicable to drug binding and inhibition). Overall, target discovery is a crucial step in the drug design and process chemistry term, as it lays the basement for the subsequent points of drug discovery and development in pharmaceutical sciences [6, 7,8,9,10].

Process Chemistry :

Process chemistry is a powerful system / subject used in drug design and process chemistry, in which higher numbers of molecules or functional groups are synthesized simultaneously or in a fast sequence to justify compounds with required biological properties.

Term for managing combinatorial chemistry, including such as:

- Solid-phase synthesis: In this type of, the starting material is attached to a solid support, and various raw material or coloring excipients are added to create a library of molecules.
- After occurring synthesis, the compounds are released from the support and screened for their biological therapeutic response.
- Solution-phase synthesis: In this type of method, the synthesis is carried out in a liquid solution, and various coloring agents / reagents are added to create a group of library of molecules. The finally mixture of compounds is right now, screened for biological activity [10].
- Parallel synthesis: In this method, chain like series of reactions is performed in parallel, each / everyone expressing a different compound. This type of system allows for the fast synthesis of a large number of chemical substance / compound.
- Once a library of compounds has been manufactured, they are typically screened for their SAR (structure activity relationship) using a variety of assays. This can include screening for binding to a special target receptor, inhibition of enzymatic activity, or effects on cell growth or viability.

Overall, process chemistry / combinatorial chemistry is a valuable key in drug discovery, design and development process , as it permits for the rapid creation manufacturing and screening of large group of series of molecules and reactions , which can help to identify and reasearch new drug candidates or optimize existing ones by modifying their chemical structure .

High-Throughput screening(HTS) :

It is a key approach used in drug design to quickly and efficiently screen large numbers of chemical compounds for their biological activity. High – throughput screening typically includes using robotic systems to rapidly test almost millions of compounds in a short duration [11]. The compounds are significantly tested for their capacity to interact with a particular target or to reaching ability till a specific biological pathway.HTS can be used to analysis to lead compounds for drug development, to optimize the quality of existing drugs, or to identify new targets for drug design. The process can be happen by several manners as following Target selection: The first step in HTS is to select a target for testing and screening. This may including to detecting a protein or other molecular structure is involved in a individual or particular disorder / disease or biological process. Compound containing

libraries: Once a target has been finalized, a library of compounds is organized for screening and analyzing. This may involve synthesizing new compounds or selecting from existing libraries of compounds. Assay development: Next, an assay is developed to measure the activity of the compounds on the target. This may involve designing a biochemical or cell-based assay that can be fully automated. Screening: Once the assay has been design and developed, the compounds are screened against the target in a high-throughput manner [12]. This may involve using robotic systems to dispense and test greater numbers of chemical compounds containing various functional groups in their structure. Recorded - data analysis: Finally, the data from the screening is tested and analyzed to clarify compounds that show activity against the target by SAR structure activity relationship technique. These compounds may then be further characterized and optimized for drug design and development by process of chemistry. Overall, HTS is a powerful key in pharmaceutical product design, modifying & discovery that allows researchers to quickly and efficiently screen large numbers of compounds for their biological response [11,12].

QSAR in drug design and modified design :

Quantitative structure-activity relationships (QSAR) have been following for decades in the developing of relationships between the physicochemical properties of chemical materials and their biological action to achieve a reliable standard model for the prediction of the therapeutic response of new chemical species. The fundamental principle, highlighted formalism is that the difference in structural properties is responsible for the changes in the biological activities of the chemical substance / compounds. In the classical standard QSAR studies, loving of ligands to their binding area, inhibition constants, rate constants, and other biological end point of reactions, with atomic, functional group, or molecular properties such as lipid solubility, polarity , electronic and steric properties (Hansch analysis) or with some fixed structural system (Free-Wilson analysis) have been interconnected [13].

A. Hansch analysis

Hansch analysis is the discovery of the quantitative relationship between the biological activity of a series of compounds and their physicochemical substance or global measuring standard representing hydrophobic, electronic, steric, and other effects using multiple regression interconnecting methodology. Hansch equation for dealing with extended hydrophobicity ranges [14].

$$\text{Log } 1/C = -a (\log P)^2 + b. \log P + c. \sigma + k$$

Advantage

Hansch analysis can be applied to explain of the complex biological data, where several different transport processes and equilibrium contribute to the overall structural activity relationships.

In place of harming or spoiling thousands of animals nowadays enzyme inhibition, receptor binding, and cell culture data are used to describe the chemical activity profile [15].

Disadvantage

Only a small number or minimum number of new chemical species can be predicted through a free Wilson analysis. It is limited to linear of adding the SAR (structure-activity relationships)[16].

B. Wilson Analysis

The Wilson Model is free and easy to apply .especially in the starting phase of structure-activity relationship analysis it is a simple method to differentiate substituent contributions and to have a first appearance at their possible dependence on different physicochemical nature of chemical substances [16]

$$BA = a_i x_i + u$$

Drug design on the basis of structure :

SBDD is a more specific, efficient, and rapid process for lead research and optimization because it deals with the 3D structure of a target protein and study about the diseases at the molecular based level. Among the suitable computational technology, structure-based virtual screening (SBVS), molecular docking, and molecular movable system (MMS) simulations are the mostly using technique, used in SBDD. These methods have sufficient applications in the ligand–protein receptor, protein–ligand and–protein interactions, and confirmation analysis of the fixed changes happening during the docking process. In few last years, increasing growth in the software industry has been driven by a massive surge in software packages for effective drug design and research discovery processes. , it is necessary to choose glorious packages for an efficient SBDD process. [17]

Computed aid design :

Drug design and development utilizes chemical biology and computational drug design perspective for the efficient recognizance and optimization of leading chemical atoms. Chemical biology is mostly included in the evaluation of the biological function of a target and the mechanism of action of a chemical differentiator. On the other end, computer-aided drug design makes use of the structural study of either the target (structure-based) or known ligands with biological activity (ligand-based) to facilitate the assurance of promising applicants drugs[18]. The term "design" is to be aware of broadly to surround conceptualization, synthesis, realization, and development of artifacts, procedure, and systems (both natural and organic)[19].

PHARMACOPHORE :

A pharmacophore is a molecular frame like structure that expressed characteristics the vital features responsible for the biological activity of a compound or molecule [19]. Pharmacophore models are originated to increase the sightedness-of protein-ligand-protein interactions. They can be employed in recognizing new molecules that justify the pharmacophore needs and are thus expected to be active [20].

DOCKING :

Essentially, molecular docking aims to give a prediction of the ligand-receptor complex structure using computation methods [20]. Docking can be obtained through two interrelated steps: first by sampling conformations of the ligand in the active site of the protein; then ranking these conformations via a scoring function. Ideally, sampling algorithms should be able to reproduce the experimental binding mode and the scoring function should also marking it highest among all generated response. From these two perspectives, we give a brief discussion of basic docking theory[21].

Conclusion and Discussion :

Drug design and process chemistry is a complex and multiplication process that joins the identification of potential drug targets receptor designing and preparation of molecules that shows interaction with those targets, and testing their safety and pharmacological activity at the time of preclinical and clinical trials.

The process typically begins with target recognition, which include to identifying the molecular structures or biological pathways involved in a disease. This information can be obtained through a variety of approach including genetic studies, bio information, and high-atomic orbital screening. Once a potential drug target has been clarifying, researchers can use a variety of techniques to design and synthesize molecules that can interact with the target in a specific pathway. This can involve a range of techniques, including computer modeling, medicinal chemistry, and combinatorial chemistry. The synthesized chemical substance is tested in vivo and in vitro to assess their efficacy and safety. In vitro tests typically involve testing the compounds on cells or tissues in a laboratory term, while in vivo tests involve testing them in animal models. If the compounds show promise in preclinical testing, they may then move on to clinical trials in humans. These trials involve testing the drugs on increasingly large groups of affected persons to assess their safety, efficacy, and exact amount of dosages. If a drug completes both preclinical & clinical trials, it can then be approved for use by regulatory agencies such as the FDA or EMA, and marketed to healthcare staffs (physician pharmacist and nurses) and patients. Overall, drug design and process chemistry is a time-spending and resources-intensive procedure, but it has the potential to yield new treatments those benefits to health and save their life. The development of new drugs is essential to address unmet medical needs to improve the health related problem and disorder, of patients suffering from diseases.

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