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A Method of Drug Discovery Process.

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ABSTRACT

The drug discovery process supports the entire pharmaceutical industry, which covers the early stages of research from targeted discovery and validation, to the identification of a drug candidate or a leading combination. The first identification of small medical candidates occurs in a variety of ways. Research can lead to a new understanding of disease processes that highlight new ways in which drugs can be developed to intervene. Alternatively, companies develop large-scale diagnostic and error-based programs to identify potential cellular combinations. This is a procedure that is usually performed during the first lead discovery, with a view to taking computer novels beyond pre-clinical testing and treatment.

Keywords: Drug, Pharmaceutical industry, Infectious vector.

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INTRODUCTION

In current year method of drug discovery has come to light science. It has many components that include, among other things, instructions of chemicals, many branches of biology (from molecular to behavioral biology), biophysics, computer science, mathematics and engineering [1].

Distinguishes itself from the biomedical science of education by having its goal and success rate is drug treatment, while the focus is on in the field of education to generate new knowledge. Scientists at the drugstore must, therefore, be able to work on it the various groups, in most cases not their own, have to know pass on their expertise to scientists in other fields [2,3].

They should be equally able to understand the contributions of other professionals in achieving their common goal. Scientists who discovered drugs adapt to their science services on the needs of the project they are providing, and often need to give up one of their ideas in order to contribute to someone else. This is very different from education an environment in which scientists often follow their own and their own ideas interests, which are often generated by the results of their previous or occasional research science 'hot topic'. [1,3].

However, the link between the science of education and the discovery of drugs is important. Health sciences (including chemistry) are absolutely basic availability of drugs because they are needed to improve knowledge of disease processes to empower progress in medical (and biological) medicine. Health science is currently in the descriptive category of knowledge generation, which occurs mainly in the field of education; therefore, drug discovery scientists need a very close and common connection and colleagues [3].

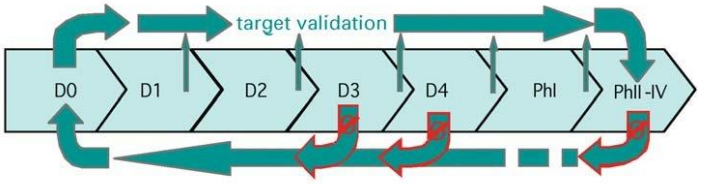
Major advances in biomedical knowledge and technology in the last 10 year have created the need for a complete overhaul of the drug discovery process. Some of the key factors mandating change were;

1. A large increase in a number of therapeutic purpose (intended to treat an accurate molecule the human body interacts with a combination of therapies achieving a biological effect in the context of the disease).
2. Availability of the most complex level of genetic interaction (gene network) and their products, as evidenced by the interaction protein in the process of expression.

By 1996, all available medical agents were working with about 500 targeted drug, but only drug sequences. In the human genome reveals approximately 25000-30000 protein-coding genes. If one considers integration and post-translation conversation, it can be estimated that there should be more than 100000 different operations proteins take up 25000 protein-coding genes, as well as conservative a ratio of five different components of each protein. It is estimated that 57% of the human genome that binds protein indicates other compounds, and that they contain an average of 9exons (8.94), this can lead to about 125000proteins. This number ignores post-translation conversions such as photolytic processing of large proteins into small active cells or RNA sequencing. Some estimates show that there are only 5000-10000 of these proteins may be targeted for drug or (alcohol). However, this was the case based on genetic 'disease' genetic predisposition, and may be high in protein are involved in disease processes rather than the number of 'disease' genes. Anything else the correct number is, it is a sequence of larger sizes than the previous one the number of goals available, which requires a high success strategy to be validated and evaluated [2,3,5].

The Drug Discovery and Development phases

The drug discovery community divides into four main categories of once-discovery four clinical stages.



The phases of drug discovery and development

D0- Basic sciences, target selection
D1- Assay development for high-throughput screening in vitro
D2- High throughput screening of public and proprietary compound libraries, ligand finding
D3- Lead optimization by medicinal chemistry, in vitro and in vivo models, initial pharmacokinetics and safety
D4- Preparation for human studies, bio-markers, extensive pharmacokinetics, safety, metabolism in animals, formulation, chemical up-scaling
Ph1-Proof of concept/mechanism in human, tolerance
Ph2- Dose finding
Ph3- Efficacy, registration studies
Ph4- Post-marketing studies

D0 phase

Before the drug discovery process begins, a selection of treatment strategies areas of interest to the company should be created, as no company will to deal with all areas of medicine [6].

Choice of therapeutic areas and indication [8-10]

Acquisition research departments need to understand the company's priorities, which is usually defined by the internal and external acquisition group scientists, medical and development scientists, and commerce marketing professionals. Essential conditions for selecting study areas include:

- Is expected to have additional medical benefits at the time of delivery compared the available treatment and expected treatment at that time, i.e., medical need
- The existence of an active scientific hypothesis
- Number of patients and expected reimbursement
- Synergy power (i.e., it will work in this area/index also provide in other fields targeted by the company?)
- Company skills and history.

Choice of therapeutic target

Once the treatment sites have been selected, the drug discovery process begins by selecting the appropriate-therapeutic target. A therapeutic target is the cellular structure in the human body where the proposed treatment is available aimed at taking advantage of a disease course or even preventing it. See include:

- Cell membrane receptors and ion channels
- Internal or external enzymes
- Protein for display methods
- Nuclear receptors
- Genetics or genetic control processes

With the exception of the final target phase all the rest are purely protein. Choice the specific goal depends on the level of the scientific knowledge involved its involvement in the disease process to be addressed. Other targets are clinically confirmed, that is, shown to affected patients this target is for therapeutic benefit. However, a very new target they have a very low level of validity, similar to genetic interaction disease, pure guess based on knowledge about this disease procedure, or specific evidence from genetic testing [8, 10].

Transgenic animals that produce mutations in human diseases have become a valuable tool to certify the mediator. Once a protein has been selected as a target, it is important to start the effort determining its three- dimensional structure for a building- based tree chemical experimentation can be initiated as quickly as possible and in line with the above exit test [10].

D1 phase

After targeted selection, targeted protein should be available in sufficient quantities prices and purely to allow for the design of the appropriate high effect test results. Protein is usually produced by the recombinant the pathways can be to bacteria, insects or human line cell. Still included in the appropriate assay for high-impact experiments integrated libraries to allow estimation of its interaction with therapies tool. At this point, the type of treatment tool to be developed is selected based on specific factors. Therapeutic tools in general one of the following [11, 13].

Low molecular weight of compound

Compounds of synthetic low molecular weight (MW) (frequency MW<500) are imitative the natural use of small molecules, such as hormones and neurotransmitters, to adjust biological processes. Their main advantages are:

- Possible access to all parts of the human body
- Low production costs (separately required molecules many and complex practical steps)
- Adapting to a large number of variables for the development of their "drugs", i.e., melting, membrane infiltration, target specification, reduced side effects.

One of the main problems is that, because of its small size, they can be difficult disrupting the major interactions of proteins and proteins [12, 13].

Natural products and low molecular weight of molecules

Such compounds are separated from natural resources, usually as secondary biological metabolites they use in biological activities, e.g., toxins or antibiotics for immune purposes. Their MW ranges from 100 to approx 1000 [14]. Their main benefits are:

- The result of millions if not billions of years of combinatory chemistry and selection, so that the chances are that they will show biodiversity the performance is too high
- They can reach many parts of the human body
- Can be modified to get drugs

This is compared to the main disadvantage, namely the natural compounds in general, they are a very complex structure, including many metals institutions and difficult to integrate with synthetic chemistry methods; generally, they can only be obtained by biological processes such as fermentation [14-16].

Proteins-antibodies and growth factors

Immune therapies can be activated to disrupt certain cell processes and chronic growth factors in order to maintain/correct disease-related lack [16]. Their main advantages are:

- Can be extracted from the human genome
- There are a few effective ways to make the human immune system fully
- The highest specificity and consistency can be achieved; on the other hand:
- They can usually only reach the target of the extracellular/cell surface (mainly immune system)
- Their integration, cleaning and duplication of work can also be costly hard
- Naturally, growth factors are tightly controlled, both locally and internally time and concentration, so that the application of the medical system can they cause unwanted side effects.

Genetic treatment

The most effective way to replace deficient genes it is found in many diseases such as cystic fibrosis, hemophilia, Gaucher's disease, Lack of ADA etc. Genetics, when vet engineer, usually of viral origin, used to transfer an active gene that does not change to defective cells to restore their function [18].

The main advantage of the method is direct modification of the cause of the underlying disease. However, this should be weighed against the disadvantages (today) of:

- often manifestations of inadequate genetic modification to achieve treatment the result
- insufficient control or lack of external genes that cause unwanted results
- control of incomplete genome fusion (retroviral vectors) can lead to oncogenicity
- insufficient tissue specification

Organ transplants, including xeno-transplantation

Repair of defective organ can be achieved by inserting an organ into a corresponding donor. Due to the development of immunosuppressive processes, transplantation to a person today has become a common practice [17, 18].

Its main advantage is that it saves lives. Today, though:

- There is a sufficient number of donors compared to medical need
- Immunosuppressive laws are still incomplete, and some parts endanger lives side effects.

Dealing with donor organs, organ transplant strategy from genetically modified animals to prevent hyper-acute the most common rejection seen in interspecies transplantation has been investigated using pigs as donors (xeno-transplantation). Xeno-transplantation can provide the following benefits:

- 'unlimited' organ donation
- Possible replacement of multiple damaged organs.

Currently, the main disadvantages of this approach are:

- Rejection methods cannot be controlled enough to allow for a sufficient the longevity of the donor organ is in the host
- Incompatible body composition between supplier and recipient is still constrained problem
- Concerns received regarding the recurrence of chronic retroviruses

Treatment of cells: tissue and cells of the old stem and embryonic found

Blood transfusions are an old form of life-saving treatment. Newer versions of cell therapy aims to repair special damaged tissue in the host by taking the benefits of stem cell occur in the body of an infected person the ability to reproduce certain cell types (old stem cells) or all cell types (embryonic stem cells). Cell / stem cell therapy offers key benefits:

- Possible correction of multiple tissues
- No rejection is expected when autologous stem cell transplantation is performed.

Inadequate (today):

- To date, the ability to replicate old stem cells in sufficient quantities without separation have limited success
- Because of their origin there is a moral concern for the use of human embryonic stem cells.

Scientific testing of your strength in both the embryo and the fetus cells in their early stages, especially the ability to repair complex one body parts.

D2 phase

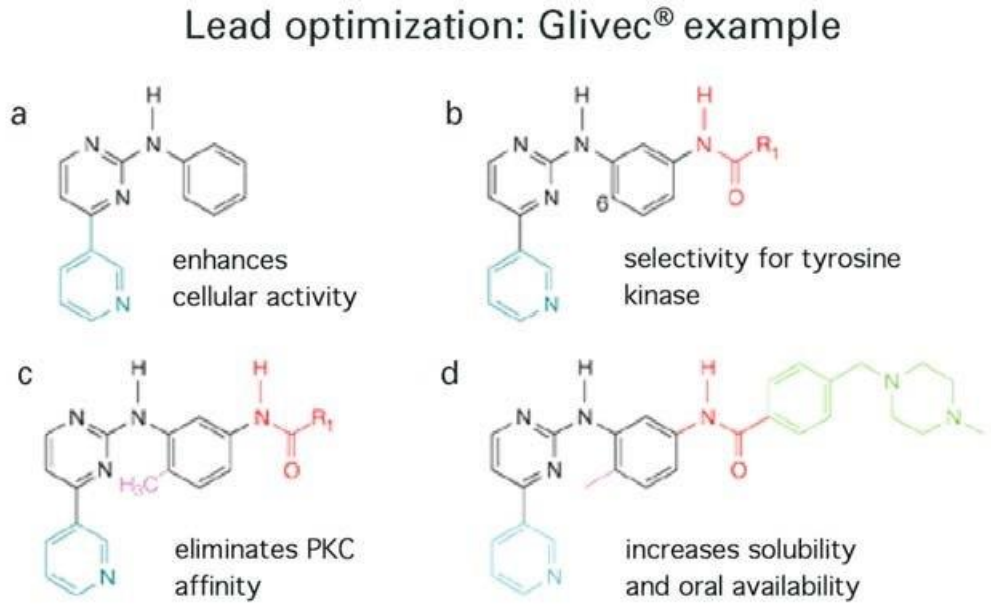
During phase D2, a search of the selected ligands of the target was performed. Ligands are found in many sources:

- Various libraries, usually about 1 million combinations a large pharmaceutical company. Combining management is very automatic to large pharmaceutical company. Combining management is very automatic to allow for effective exploration activities.
- Combined collections are available for sale
- Compatible combinatorial chemistry libraries
- Libraries that are natural compounds from germs or plants that can be pre-selected based on knowledge of traditional medicine
- Proteins and antibodies from genome mines.

Ligands that work with the target are called 'hits' and are often verified by re-testing and recording full volume response curves. These are original hits are also preferred for intoxication (melting, membrane access, in vitro genotoxicity, selectivity,etc.) before proceeding to the next section. The compounds selected are thus called 'lead', in which medical pharmacists and pharmacists do development work [16, 17].

D3 phase

During phase D3, the lower MW tracks found in D2 are repaired and lower to assess the function of a building to improve its melting, strength, selections, metabolic structures, and their effect profile on both sides internally in vitro and complete animal models. The most promising combinations are then tested to at least two suitable ones species to find an indication of specific species of animals target conversion. Long-term studies in imperfect animals were performed to check the result of repeated requests, including the occurrence of potential tachyphyllaxis (decrease in pharmacological effects in the background repeated requests). One of the most important features of this section is obtain data that allows for the evaluation of potential medical benefits patient, compared to existing treatments or treatments that are believed to be available at the time of presentation. This is usually done with extensive comparisons competing courses an treatment agents. The only proper competition benefits are benefits that bring greater medical benefits compared to in previous treatment at the patient`s discretion. A different molecule or the method of doing so is not sufficient unless it will translate explicitly to such medical benefits to the patient. Ownership of a new treatment regimen happened recently section D3. A well-crafted combination moves on to the next stage however traces of various chemical structures are kept for possible backups if possible the first progressive candidate fails. However, backups are better selected when the status of the limited features of the first candidate is evident [18].



Lead improvement: Glivec example. Glivec is a new and flexible machine-focused treatment for chronic amyotrophic leukemia (CML). Addition of original colored areas lead composition has allowed the various desirable properties of the compound to be developed as indicatied.

D4 phase

This phase is the final preparation for a possible clinical trial drug candidate. Includes comprehensive pharmacokinetic, metabolic and safety studies in complete animals at least two species. During D4, chemical uptake It is made, from milligram to kilogram quantities, and appropriate integrated management structure is improved. Health research the strategy is explained, in recent times there has been a strong emphasis on biomarkers, that should already indicate during the first phase of clinical trials whether the concept cientific healing will probably be achieved with the chosen treatment method (conceptual evidence studies) [17, 19].

Throughout the process, methods that provide temporo-spatial information in the possible target distribution of drugs, drug candidate, drug interactions and their effects are very important. Among such strategies, methods such as imaging, which provide non-invasive reading, is very interesting as it often allows for individual interpretation from drug testing to doctors. The rest of the book discusses many aspects of the drug discovery process, where photographic techniques can make a significant contribution [19].

Glivec selection is against panel kinase. The optimized combination has been selected for maximum size selection to Abl kinase (red) but residual alignment in the platlet-based growth factor (PDGF,green) and c-kit receptors (blue) remained, which already provided therapeutic benefits cancer without CML

Kinases	IC_{50} [μM]
v-Abl	0.1-0.3
$p210^{bcr-abl}$	0.25
$p190^{bcr-abl}$	0.25
TEL-Abl	0.35
TEL-Arg	0.5
PDGF receptor	0.1
TEL-PDGF receptor	0.15
c-Kit (stem cell factor receptor)	0.1
Flt-3	>10
c-Fms and v-Fms	>10
KDR	>10
EGF receptor	>100
c-erb B2	>100
Insulin receptor	>100
IGF-l receptor	>100
v-Src	>10
Jak-2	>100

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