METHODS OF GENERAL DRUG DESIGNING PROCESS OF SORS-CoV-2 VIRUS-A RESEARCH REVIEW

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Abstract - *The recent pandemic caused by Covid-19, which lead to the global health crises. There is no effective anti dose of this till now. The virus related to this situation is SARC-COV-2. The development of anti dose is at most priority in the world to get relief from this situation. The research on genome structure provides many target sites for the development of anti dose to this virus. The targets include receptor of virus, replication of virus in the host cell. There has been so much of the work done on the foundation stone of antiviral drug development related to Covid-19. This review summarizes on past and current drug development approach to words SORS-COV-2. The present review lime light on the paths of research, to find the ways to fight against Covid-19.*

Keywords - SORS-COV-2, Antiviral drugs, Drug development, General methods to follow in drug development of antivirals.

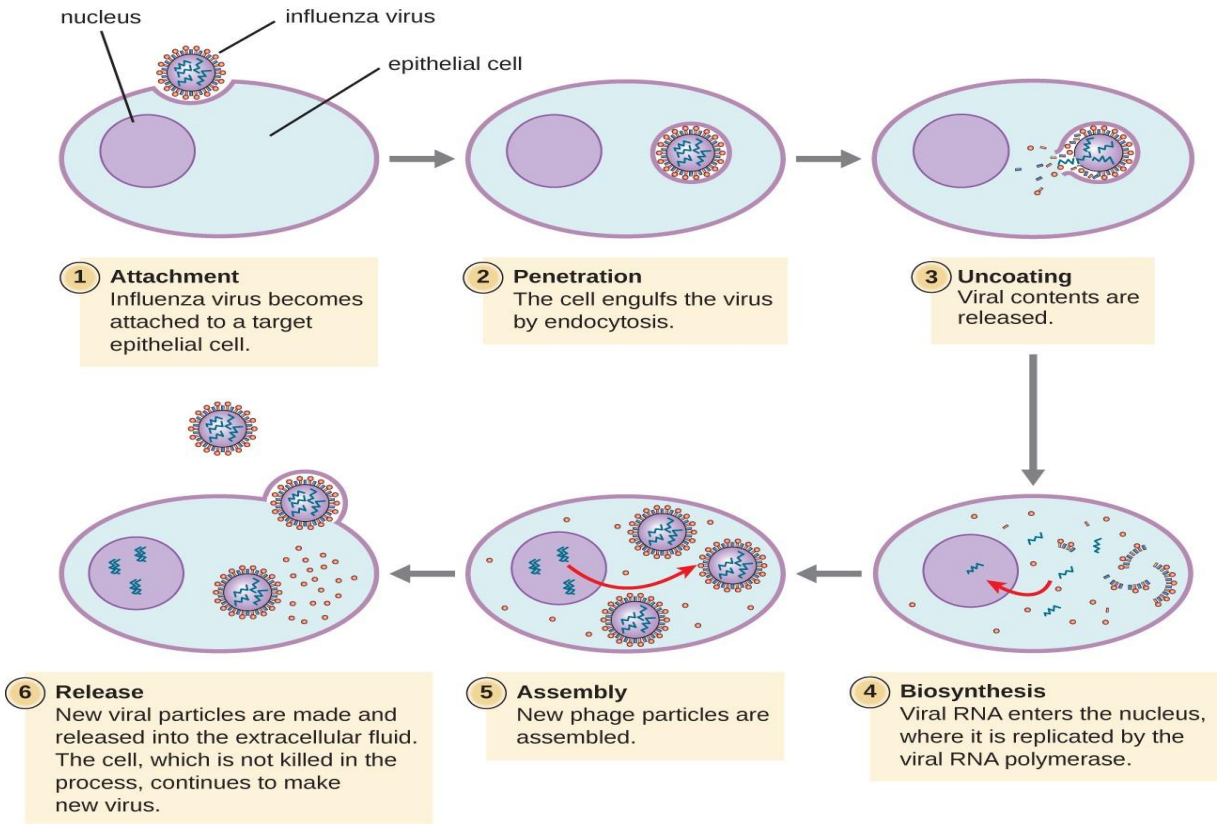
1. Introduction:

Worldwide Viral diseases, caused by morbific virus infections, show high morbidness and mortality rates are one of the principal causes of death in humans. Example present the biggest world problem Corona Virus i.e. Covid-19. A virus is a peculiar pathogen having capability of replicating without a host cell as it spreads by utilizing the host cell environs and cellular components or constituents or genes. This peculiar nature of viruses makes it difficult to design any drug to attack on the virus or to control replication without any adverse effects on the pathogenic cells. Antivirals are a category of drugs used for treating infections caused only by viruses. These antiviral drugs nature is highly specific, although broad-spectrum antiviral medicines are effective against a wide range infections caused by different kinds of viruses. The antiviral drugs don't destruct the target pathogen.

1.1Life cycle of Virus - common features [1]

Depending on the category of the virus, the life cycle of the virus change, but all the categories have a common pattern:

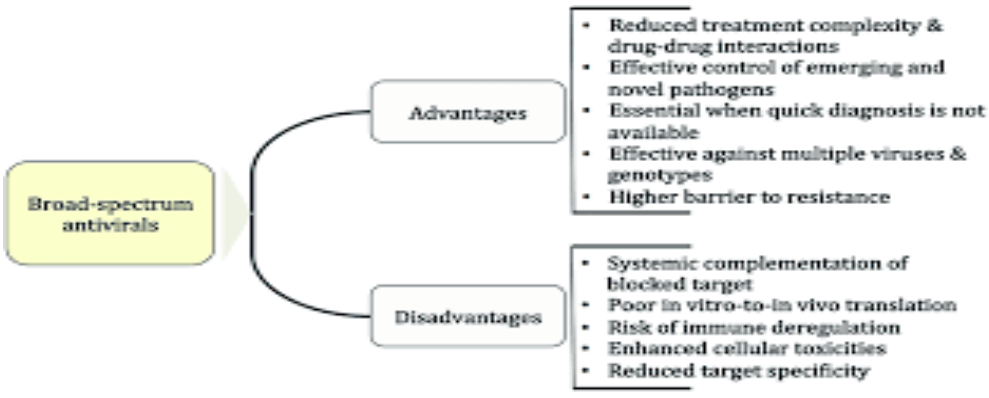
- Adhesion to the host's cell.
- Penetration of the virus, discharge of the viral genes and the enzymes into the host's cell.
- Reproduction of the new viral components by using host cell.
- Replication, transcribtion and translation and Assembly of viral components into complete viral particles.
- Liberation of viral particles to infect new host cells



Life cycle of the Virus diagram1

1.2 COMMON STRATEGIES OF DRUG DESIGNING [2]

- Generally, Antiviral drug designing includes targeting at either viral proteins or cellular proteins.
- The foremost approach is to yield compounds with more specific, high resistance developing, less toxic, narrow spectrum of antiviral activity.
- The second one might be a compound with less chance of resistance developing, but higher toxicity and a broader spectrum antiviral activity.
- In some cases, the drug target includes few transitional stages which are present in the life cycle of the viruses that includes virus cell adsorption, cell fusion, synthesis of viral RNA or DNA and corresponding viral enzymes.
- Ex: Influenza virus neuraminidase host's cellular enzyme (*S*-adenosylhomocysteine hydrolase) and HIV protease host cellular enzyme (inosine 5′-monophosphate dehydrogenase) are targets for certain type of antivirals.



Broad-Spectrum antivirals Advantages & Disadvantages diagram2

Regardless of different genetic materials (DNA or RNA), Viruses share a common stage in their replication cycle, which consists of attachment and entry into the host cell, transcription of viral mRNA, replication of viral DNA, assembly and discharge of virus particles even though the virus have a different offensive strategy, whether it is enveloped with a lipid tissue (enveloped virus) or not.

2. DESIGNING OF NEW DRUG – A BRIEF REVIEW

For the designing of new antiviral drugs the emergence of drug resistant viruses offers a challenge. To solve this problem, it is necessary to design new antiviral medicines, which target the replication cycle of virus by understanding the penetration and replication mechanisms.

ANTI VIRAL TARGETING

The basic principle behind modern antiviral drug designing is to recognize the viral proteins, or some part of protein, that can be deactivated. To reduce the side effects, the 'targets' should differs with the proteins or some parts of proteins that are present in human beings with least feasibility. The targets must be stereotype across various strains of a pathogen, or among different species of corresponding pathogens, so that a single drug will have broad usage or efficiency. Example, a researcher, might target an enzyme which was synthesized by the virus that is common across strains, and the following can be done to restrict it's function. After identifying the target, the drug is selected either from drugs which are familiar with proper effects, or by designing the new drug starting at the molecular level. For testing in the lab, the target proteins are synthesized by introducing the genes that helps in synthesizing target protein in to virus cells. The cells are then cultured and then be subjected to various treatments and evaluated with rapid screening.

VACCINATIONS

Vaccines are preventive primary source of defense against pathogens. Vaccination involves the insertion of a small amount of typically deactivated or reduced antigenic substance to stimulate an individual's immune system through injection. The human immune system responds (to drug) by developing the white blood cells to fight against the introduced anti genic substance, which results in acquiring immunity [2] i.e. finally Vaccination results in increasing immunity with substantial reduction in infection caused by the virus.

The development of new vaccine can be simply classified into two stages.

1) Preclinical stage 2) Clinical development stage

1) Preclinical Stage: In this stage the research is conducted in lab analysis and on animals. It incorporates

A) Recognizing or Identifying appropriate antigens

B) Designing of vaccine according to the requirement

C) Assay of new vaccine effectiveness in the lab on animals.

D) Production of vaccine for practice.

2) Clinical development Stage: In this stage the developed vaccine in the above process is first time tested on human beings. It involves four phases.

Phase 1: These are small-scale (very few individuals) clinical trails to access whether the vaccine is safe or not for human beings and to check the immune response in them.

Phase 2: In this phase a large number of individuals involve out which; some of them are at high risk of getting the disease. These are Randomized, well established and placebo included trails. This phase helps to access for safety, response of individual immune system, scheduling of dosages and immunizations, and mode of vaccination.

Phase 3: this stage involves trails on very large number of individuals consisting of thousands to ten thousands. This trail is double blind, randomized and consists of the placebo. It helps to assay the safety of a vaccine and rare side effects, efficiency of the vaccine.

Phase 4: this involves post marketing of licensed vaccine, which helps to assay the rare and adverse effects and eternal efficiency of vaccine.

Recombinant Vaccines

These are live replicating viruses that consists of genes from different etiological agents are cloned, articulated and tested as vaccines. These extra genes generate proteins against the pathogen i.e. built-up the immunity of the system.

PLASMA THERAPY

Plasma therapy uses blood donated by a recovered patient to transform the antibodies in to the blood of the patients who are under the treatment.

The theory behind this plasma therapy is, when the antibodies of the patient who was recovered are injected into the patient under treatment will begin targeting the pathogen, the immunity of the patient under treatment increases by producing antibodies. In general the plasma taken from one recover the patient can help two people.

ANTIVIRAL AGENTS

Antiviral drugs are used to prevent production of viruses that cause infections. Most antiviral drugs are efficient while the virus is replicating. The antiviral drugs don't destroy the virus but they inhibit the replication process of virus in the host's cell. It is difficult to find drugs that are selective for a particular virus, as most of the viruses comprise of similar metabolic processes of the host cell. Yet, some enzymes or proteins are present in virus only. In such cases the targeted drugs are developed. The modern drug development comprises of identification of compound, which fulfills conditions like the reduction of side effects, metabolic constancy and oral bioavailability, efficiency. The identify such compound, the first step is screen of the compounds which can be converted in to drugs; the chemists will try to improve some of the parameters of the compound like its activity against the target, improvement of absorption, distribution, metabolism and excretion of the compound.

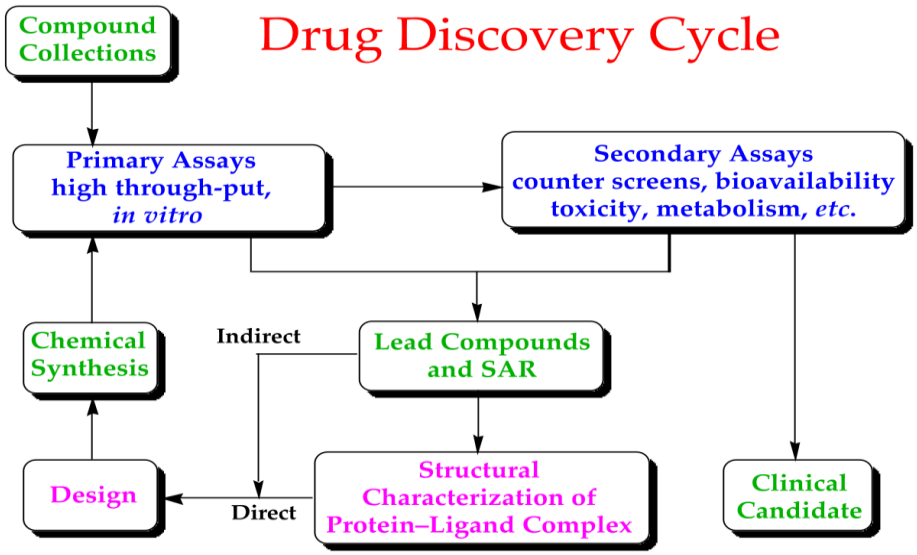
The combinations of anti viral drugs have more than one antiviral medicine in one tablet or dosage. Using a combination of antiviral medicine, results in the reduction of chances of surviving resistant viral strains.

When there is no definite perceptional cure for any infectious disease, when the Internet and social networking websites are flooded with many claims and remedies, instead of getting panic and falling for fraud remedies and claims, it's better to focus on building immunity system to boost one's health. Example –Covid19 as there is no drug right now it's better to improve immune system of the individual.

Now the way to get rid of this problem is using the drugs that are already known which are used to treat other viral diseases are reused to treat Covid-19 may work faster than trying to develop a new drug. There are many researchers took initiation to readout the genes of the Coronavirus also called SARS-CoV-2, come up with the following list. To spread the infection in the lung cells, the Coronavirus must induce its genes, which co-opt with the host genetic material. The cell starts to replicate and synthesizes analogous viral proteins, helps to synthesize new viruses. In the recent study, the scientists have investigated 26 out of 29 SARS-CoV-2's gene, which directs the production of the corresponding viral proteins. Not only that the researchers also found round about 332 human proteins which are targeted by the Covid19.In general some of the viral proteins target one human protein only, while various other viral proteins were capable of targeting nearly dozen cellular proteins of human. The research team identified 24 drugs, which are officially agreed by the FDA to treat distinct diseases such as cancer, Parkinson's disease and hypertension, etc. There are so many Scientists who Scramble to find treatment for Corona Virus.

One of the drugs, which are on the top of the list, is hydroxy chloroquine, which kills the single-celled parasite that causes malaria. Scientists already know that it attaches to a human cellular protein called the sigma-1 receptor. Against the Coronavirus, well-run trials establish whether hydroxy chloroquine is nontoxic and efficient or not.

As Covid-19 characters are not completely disclosed, it is difficult to develop proper vaccine without side effects and exact medicine at present. As clinical trails need some time to come to conclusion, developing immune system of human beings should be concentrated to avoid attack of Covid-19



STRUCTURAL INTERPRETATION OF DEVELOPED DRUG

The basic interpretation of the chemical structure of newly developed drug or chemical must be done to avoid re designing or discovery of the same chemical compound or agent. To know the chemical structure and its activity Chromatography methods and spectroscopic methods like UV spectroscopy, Mass spectroscopy, NMR spectroscopy methods are available.

CONCLUSION

The continuous occurrence and recurrence of viruses during the last few decades and recently new corona virus is a serious public health concern. This may be due to viral dormancy, improper analysis, viral resistance, toxicity and immunosuppressant.

Till date, struggling against the viruses and lack of proof against antiviral therapies, the failure of drugs in human clinical trials, many alternate methods along with past drug discovery strengths and recent advances in biology and Chemistry, gives promise to the therapeutic administration of serious viral diseases.

In future, the rapid development of better antiviral drugs developed by adopting the combinational approach. Hence, the battle among humans and viruses is increasing to a grater magnitude, and both are rapidly refining their strategies to succeed in their way.

The growing knowledge about viruses and the promptly developing tools and techniques are definitely promising for new drug designing and invention of new anti viral drugs, but there is, nevertheless, a long way to go for increasing efficient measures for combating the viral diseases.

Mean while to protect from the virus one should improve immunity by taking food rich vitamins or vitamin supplements specially vitamin c. Hoping for Viral free world with the best antiviral drugs and vaccines to eradicate the virus (SARS-CoV-2).

Conflict of Interest: None

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