In Silico Drug Repositioning Of Hydroxychloroquine (HCQ) For the Treatment of Viral Diseases

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Abstract: - Emerging and re-emerging viral infections are a big human concern and veterinary public health, and the development of antiviral drugs is urgently needed. The high cost of drug development limit the scalability of this antiviral approach. Drug repositioning or drug repurposing or drug profiling is the discovery of new applications for approved or failed drug. Drug repositioning is the development of new approved drug applications. The cost of bringing a medicine to the market is around one million which include clinical and preclinical trials. Repositioning of drugs help in cutting down costs as well as time involve in initial validation and authorization. Recently, there are so many drugs that have been tried and tested for COVID-19 treatment .One of these drugs is an antimalarial drug called as Hydroxychloroquine (HCQ).

Key Words: —*Hydroxychloroquine (HCQ), COVID-19, Antiviral drugs.*

I. INTRODUCTION

Antiviral activities of HCQ made them potential candidate to study against viral diseases. In this study we are going to repurposed hydroxychloroquine(HCQ) for the treatment of viral diseases[1]. The standard method of product production requires vast quantities of time and energy before a compound is labored into the free market. Despite huge investments, a lead molecule often has minimal chances of entering the open market. The research molecule's itinerary remains unpredictable in its entire lifecycle. This situation causes new pharmaceutical companies to discover new drugs on dreams. Drug repositioning is one of the feasible choices for beginners in the area of new drug science. Drug discovery is the process of identification of biologically active small molecules against different disease conditions [4]. Classical drug research starts with the identification of disease targets, the detection of compounds and optimization, ADMET studies and finally to market. Developing a Single molecule may take 10−17 years and the success rate can be as low as 0.01%. The global annual budgets of R&D became $ 130 billion with fewer new drugs. The numbers of new drugs or New Molecular Entities (NME) released in the market are decreased and there is acute pressure on the R&D circle to increase the number of candidate drugs in the late stage pipeline [5].

Considering the large amount of investment that has been put recently in drug development only 23 drugs were approved in the year 2010, which is drastically less when compared to the drugs approved (53 drugs) a decade ago. These NMEs have to go through a number of pharmacokinetic and toxicity studies for their release into market. Molecules with potential drug like activities are evaluated simultaneously for their toxicity effects in cell and animal models. After a strenuous and systematic evaluation of drug activity and other properties, several drug like molecules may have to be dropped because of undesired bio-distribution and toxicity. A new concept called “drug repositioning” is being emerged in the pharmaceutical R&D circle. Drug repositioning is the discovery of new indications for approved drugs. Drug repositioning also known as drug profiling or drug repurposing. The cost of bringing a new medicine to the market is around one million which include clinical and preclinical trials. Drug repositioning procedure is generally performed during the phase of drug development to modify or extend an active molecule's distribution line. The COVD-19 pandemic represents a significant challenge to the world from a health and financial perspective [2].The diseases has a high mortality rate and is very contagious, making it difficult to manage to manage .The complexity of COVID-19 is partially

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evidenced by the disparity of symptoms from extremely mild in childrens and young adults to much more severe in older age group. We propose the urgent repositioning of an old drug hydroxychloroquine (HCQ) as an ideal antiviral prophylactic against COVID-19. This drug is capable of inhibiting the replication of some intracellular microorganism which includes viruses also. HCQ has the ability to block viral infection as it increase endosomal PH and also interfaces with the glycosylation of cellular receptor of SARS-COV .It is an antiviral agents as it is also known to inhibit quinine reductase-2, which is involved in sialic acid biosynthesis .It prevents the attachment of SARS-COV-2 to the target cells by interfacing with ACE 2 receptor glycosylation.

So, the antiviral activities of HCQ made them potential candidate to study against viral diseases. Viruses are major risk for human health and economic well-being. [3] In this study we are going to repurposed hydroxychoroquine for the treatment of other viral diseases such as Ebola, Zika, influenza, chikungunya etc.

II. METHODOLOGY

Protein Selection:

X ray crystallographic structure of all the targets protein was downloaded from PDB.

Ligand Selection:

Structure of HCQ was retrieved from PubChem database (http://pubchem.ncbi.nlm.nih.gov). HCQ was downloaded in SDF format and converted into PDB format file using SMILE.

Molecular Docking:

The 3D structure of targets was used for molecular docking with hydroxychloroquine using Autodock.

III. RESULTS

The results are described in the table and figure belows.

Table.1. Showing binding free energy

PDB ID	DISEASES	DOCKING SCORE
P03120	GENITAL WARTS	-7.71
Q77DJ5	EBOLA	-5.41
OO4350	LASSA FEVER	-7.65
Q786F3	MEASLES	-8.70
QO7817	MARBURG HEMORRHEGIC FEVER	-7.71
015164	VIRAL MENINGILITIS	-5.41
P128823	VIRAL ENCEPHALITIS	-7.65
P06672	RABIES	-11.73
P08563	RUBELLA	-8.70
P0COE6	CHICKENPOX	-6.89
P07612	SMALLPOX	-7.95
P03300	POLIO	-8.38
076463	ROSEOLA	-6.89
P24941	CHICKENGUNYA	-7.95
Q03243	ROTAVIRUS	-11.73

IV. CONCLUSION

Recently, there are so many drugs that have been tried and tested for COVID-19 treatment. One of these drugs is an antimalarial drug called as hydroxychloroquine (HCQ). HCQ has antiflammatory properties and are used for immune disorder treatment such as diabetes, arthritis etc.

Reports suggest that HCQ could be a candidate for COVID treatment .This drug is capable of inhibiting the replication of some intracellular microorganism which includes viruses also. HCQ has the ability to block viral infection as it increase endosomal PH and also interfaces with the glycosylation of

Cellular receptor of SARS-COV .It is an antiviral agents as it is also known to inhibit quinine reductase-2, which is involved in sialic acid biosynthesis .It prevents the attachment of SARS-COV to the target cells by interfacing with ACE 2 receptor glycosylation.

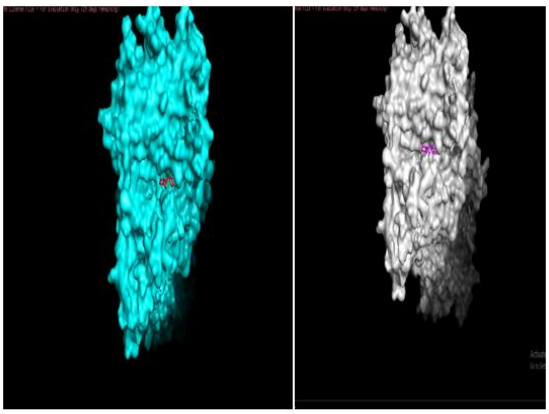

Fig.1. showing docking of Hydroxychloroquine with rabies and rubella respectively

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