

COVID-19: Drug Delivery System, Drug Discovery and Therapy Options

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Abstract

Drug delivery system plays a vital part in destroying the pandemic. Few options on drug delivery is been highly considered. One such delivery is emulsifying system. This system plays important role in reducing water compounds in order for the virus to hunt for an environment to sink in. One of the best options to destroy the virus has few setbacks. They have limitations in precipitation of drugs, formulation design, lack of results in vivo conditions and fatty acids oxidation. Generally polymers containing lipid based formula supercedes the drug after dispersion, in this case they improve environment for virus survival. But there is a solution to tackle this superstition. Usage of triglycerides with medium dose enhances antioxidants of unsaturated fatty acids, thus overcoming the problems. Further steps and usage of this delivery system are discussed along with their limitations.COVID-19 possess challenge for discovery of drugs owing to their ability to cause community and health care associated outbreaks. They destroy respiratory organs causing death. This review will also focus on drug discovery options and virus based and host based therapies.

Keywords

COVID-19; Drug delivery system; Drug discovery; CoV movement.

Introduction

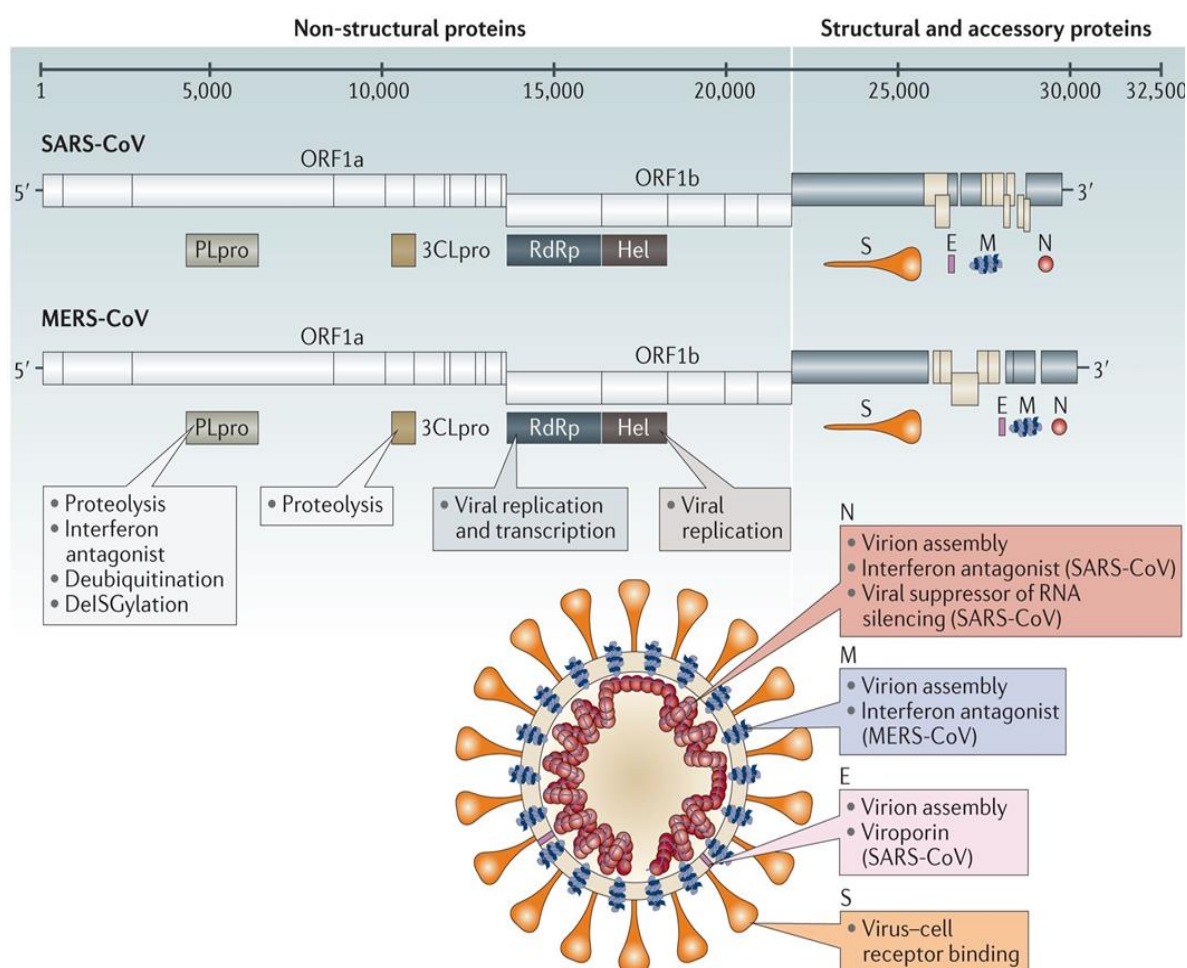
It is essential to understand delivery system formulation techniques. Emulsion, ionization, and lipid formulation. Emulsions are basically transfer of nano meter droplets from one liquid to another [1]. Thermodynamically unstable cloudy and viscous liquid [2]. Transfer can be on any liquid medium. Oil to water, Water to water. Dispersion from oil to water is the most interesting formulation for pharmaceutical applications [3]. Drug based discoveries can be done with this dispersion. The emulsifying agents should be more soluble in aqueous phase and stabilised by surfactants in oil phase [4]. More promising approach towards drug

discovery is emulsifying drug delivery system. With the above concept in mind, nano emulsification concepts are approached [1]. Their diameter are in nano range, hence they take help from external factors. The energy for thrust should be either mechanical or chemical concepts. Since it is defined in nano meters they are kinetically stable and thermodynamically unstable in equilibrium and are very slow. As the result, nano emulsion droplets through drug delivery remain stable during temperature changes when diluted [5]. The process is little complicated to obtain stability. Surfactants are mixed with water and then they are allowed to enter the oil phase to obtain emulsion. A technique called dynamic light scattering is used to estimate size distribution of sample through delivery system [6]. They do not have any problem or disturbances on influence of droplets size and shape. One of the most suitable requirements is solubilisation of drug from intestinal tract [8].

Understanding anti-COVID-19 therapeutics

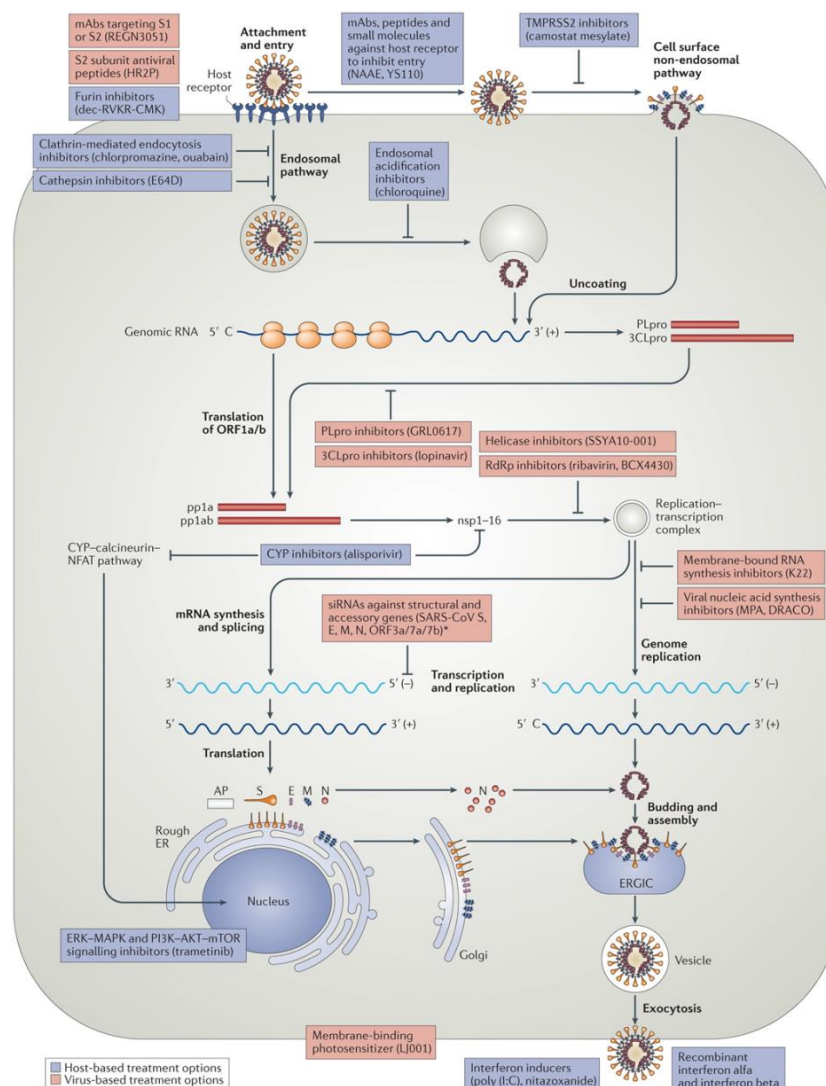
For the start, understanding COVID-19 strain is very important.

Figure 1: The strain [1].



A single stranded RNA genome which is not segmented, kb range of 25-30, with methylated caps 3' and 5' polyadenylate tail arranged from 5' segments genes, replicating genes, genomes structural proteins, membrane and nucleocapsid protein with tail and then 3'. It has partially overlapping open terminal frame (ORF 1a/b). Major part of the genome is polyprotein. Polyprotein are cysteine based or serine based which help in producing nonstructural protein, RNA polymerase [8]. With the knowledge of genome structure, COVID-19 offers design potential for therapeutic targets. Corona Virus (CoV) uses low pH entry point of cell surface endoderm pathway. Since they are dependent on protease to integrate into S1 and S2. CoVs enter, disintegrate and then disassemble nucleocapsid and RNA into the cytoplasm and replicate the genome. Replication is by polymerase and helicase found in it. When they enter the cytoplasm, translation and replication starts. The helicase formed interacts with proteins and then the RNA is released in the endoderm. The positive strand forms a full length negative strand which intern laps protein producing mRNAs [6-8].

Figure 2: Shows the CoV movement into the body [6].



Emulsifying drug delivery pathway components

Basic components of delivery system include surfactant, liquid like oil or water, co surfactant and a drug [5]. Liquids are firstly considered to be in transportation mode. Medium triglycerides with oxidation effects and solvent capacity greater for transportation is often the first choice. The surfactants are the film layer which eases lower tension surface that helps in movement [9]. Emulsifying factor should be high, in order to attain that, rapid spreading of formulation should be attained. The lipid bilayer should be greater than 12 for the above process to take place. Next are the co-surfactants. They help in reduction of tension between the film to almost negative. In order to adapt that surface tension low chain alcohol is required [10]. Finally is the drug, typically low dose drug is always considered a good factor. Smooth metabolism is the negative criteria. Solubility level should be high. There should be a desired need for liquid, surfactants, and co surfactants.

Vaccination pathway for drug

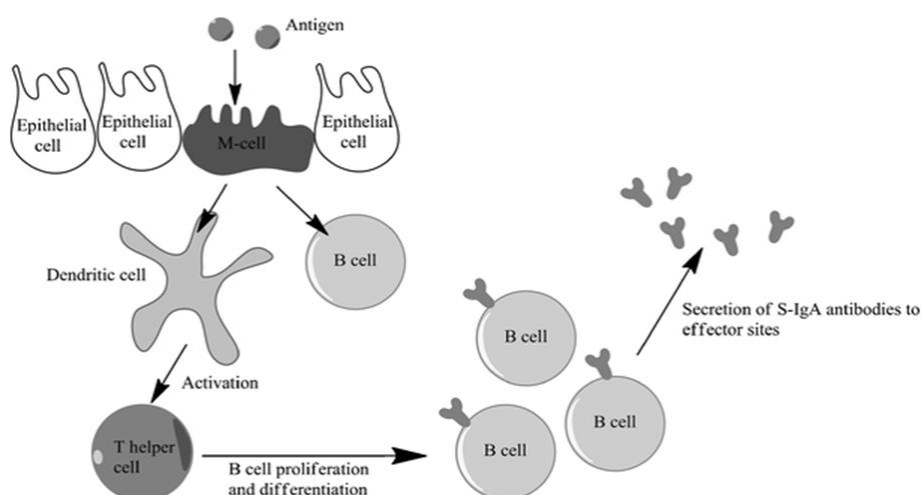
Vaccination ends the spread of pathogen. Pathogens accumulate at the mucous layer [8]. Vaccination generally has the antigens which is promising in approach to kill the pathogens. Many diseases have been prevented by invention of vaccinations. Futuristic invention of vaccination is at the mucous level; hence this route of antigen travel will be novel method to eradicate CoV [11]. Nasal method of injection is the best method for administration of drug. Mucous surface is defended by immunoglobulin antibodies which further shields pathogen. However biological feature is different from one organism to another. In order to design a vaccine, in vitro conditions should be set up [9].

Figure 3: The nasal mode [1].



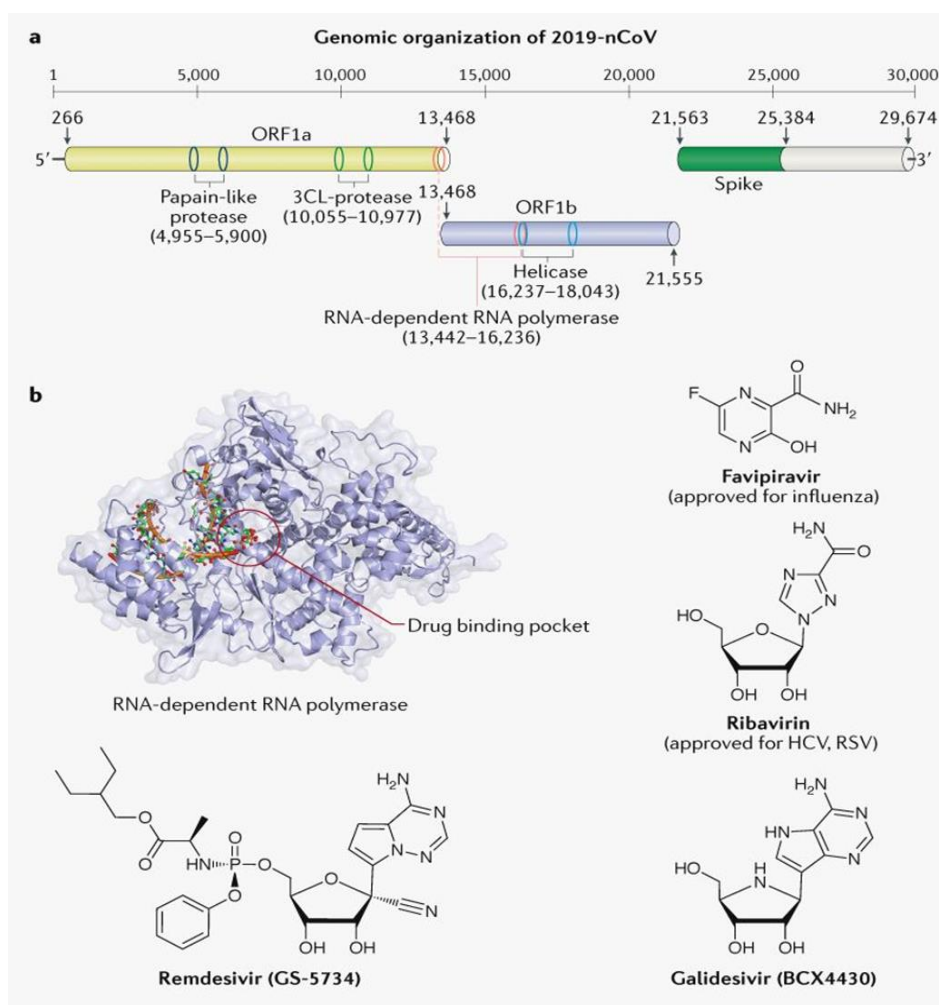
Taking the physiological factors of different organism and their cell types, vaccine efficacy should be analysed.

Figure 4: Immunological pathway of CoV behavior [3].



Information of CoV is pretty familiar. Single strand, RNA beta, envelope layer, genome encoded by proteins (no structures), helicase. Below is the genomic organisation of CoV [2].

Figure 5: Genomic organization of 2019-nCoV [6].



General analysis observed from sequences, non-structural protein plays a key role. There is also a slight increase in glycoprotein for viral interaction. Hence total of five proteins represent targets for development of vaccine [8]. The protein point out drug bonding loops for optimisation of pathogen that destroys vaccines [12].

Drug discovery methods

Standard assays are generally used for measuring the drug effects. There are few methods in discovering drug for anti-CoV. First method, drug should possess inhibitors, which should plaque the live CoV. However some inhibitors have their side effects. Rectifying the side effects, will attain full glory in drug discovery [5]. Second method, assembling all possible compounds or rather databases of chemicals to restructure transcription in cell lines. There are many factors to be considered [3]. Most important of them is physiological; neurotransmitter receptor, lipid metabolism, oestrogen factor, kinase and finally DNA repair. Third and final method of drug discovery will involve development of genetic agents targeting inhibitors responsible for replication. Overall host based, individual biology factors play a major role in producing a drug [10]. CoV uses different receptors to enter. Their activity is a narrow spectrum of target; hence drug delivery system should be analysed in vivo. Furthermore the damage caused to biological and immunological functions have to be carefully evaluated during drug discovery. The whole new pharm kinetics approach is to be discovered [3].

Challenges in development of a drug

Most unpredictable challenges in drug discovery are patient linked or target based inhibitors. CoVs are rapidly replicating groups hence target based apparatus with individual biology should be an area of concentration [3-5]. Therefore; any anti-CoV drugs should be effective at that target stage. The most sophisticated application is viral enzyme inhibitors. Another important aspect is testing. Since there are limited animal models to test, it should pose a challenge [1].

Solution to animal models

Drug delivery system should be tested in animals. The most commonly employed mode is intestinal duct model. The most commonly used animal is rat, but pigs and sheep have common characteristics of human. Rat model is being used at various levels such as pre and post-operative procedures, drug injection, fistula ion, and rehydration [12]. The best method to inject drug is through veins. Intravenous injection model helps in calculating plasma exposure of blood as the drug is absorbed through portal vein. Many animal models use annulation, a common procedure. However nano particles have been employed to improve MRI imaging of intestinal system. Iron oxide nano particles are the agents used in annulation. This method largely improves drug discovery [9].

Conclusion

The methodology of novel drugs provides immunity. Mucous administered drugs shows

relevant strategy to fight pathogens. The invention of needle free, invasive nasal route drug is advantageous as it also improves delivery system. Formulation for soft gelatine drugs has its own disadvantages. Delivery system is unreliable and also cost of manufacture is high. Hence delivery system should be formulated in such a way that could lower handling issues and keep the cost affordable. Furthermore they should also overcome stability problem in liquid product. Physical environment should sync in with delivery system and poor soluble drugs. All these factors should be taken into consideration when formulating a drug for CoV. Any attempt made in discovery should be in complete exploration of drug delivery system and the above factors. Going forward, clinical trials should include combination of therapies targeting CoV. Animal models should expand beyond mouse; long term development of novel, broad spectrum anti CoV drugs may present penultimate solution to CoV infection.

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