



## FOCUSED THERAPEUTIC AND PREVENTIVE CANDIDATE AGAINST COVID-19: A BRIEF REVIEW.

### Medicine

**Mehedee Hasan\***

Executive, Healthcare Pharmaceutical Limited, Dhaka ,Bangladesh \*Corresponding Author

**Dr. Moonmoon Aktar**

Institute of Health & Wellbeing ,University of Glasgow,UK

### ABSTRACT

World Health Organization (WHO) on 30<sup>th</sup> of January announced the COVID-19 outbreak as a global emergency for public health observing the situation in China and subsequently, on 11<sup>th</sup> of March, COVID-19 is declared as a pandemic.<sup>1</sup>

As per the statement of WHO, there is no available vaccine or drugs right now to defend novel corona virus.<sup>2</sup> Bright side is that, researchers from all over the world are working harder and faster to find out a substantial therapeutic management (Vaccine, Antiviral drugs, monoclonal antibody, nanomedicine etc.) This review is intended to sum up the all available and concurrent therapeutic measure to fight against the virus.

### KEYWORDS

COVID-19, Corona, Antiviral, Vaccine, Nanomedicine, Autophagy, Monoclonal Antibody.

### INTRODUCTION

The whole world faced various pathogenic viral aggression like Nipah, Zika, Dengue, Chikungunya, Ebola, Middle East Respiratory Syndrome Coronavirus (MERS-CoV), Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) throughout the last decade and latterly in 2019-2020, novel Coronavirus disease also known as COVID-19.<sup>3</sup>

Genotypically and serologically Corona virus is classified into four subfamilies ( $\alpha, \beta, \gamma, \delta$ ). Only  $\alpha$  and  $\beta$  Corona virus is responsible for human infection.<sup>4,5</sup> After sequencing, it was initially confirmed that CoV-2 belongs to  $\beta$  Corona virus.<sup>6,7</sup> Phylogenetic observation depicts that this virus shares 79.5 % sequence identity of SARS-CoV and 50% of MERS-CoV.<sup>6,7,8</sup> SARS Cov-2 genome size was found 29.9 kb and possess a diameter of 60 to 100 nm as oval or round shape. This virus can be inactivated by heating at 56°C below than water evaporation/boiling point or by UV and exerts sensitivity to diethyl ether, chlorine, 75% ethanol, chloroform and 75% ethanol.<sup>9</sup> It has been suggested from structural and biophysical study that Cov-2 S protein binds to human ACE2 receptor and the binding affinity is 10 to 20 fold higher than SARS-CoV.<sup>10</sup> Major transmission of Covid-19 is respiratory droplets and direct contact with infected along with risk of fecal to oral transmission.<sup>11</sup> The viral incubation period was observed 14 days ranging from 3 to 7 days.<sup>12</sup> Fever, dry cough and fatigue are the most common sign and symptoms of COVID-19 infection along with or without sore throat, headache, nasal congestion arthralgia and myalgia.<sup>13-15</sup>

Due to the lack of vaccine, anti-viral medications and others interventional equipment whole world is facing an unexpected and sudden disaster. In this review, almost all available therapeutic options are discussed for having an insight on near successful intervention and for mapping potential candidate to treat Covid-19.

### Method:

PUBMED search engine was used to trace all updates. Key words for search was "Corona Virus", "COVID19", "Treatment", "Medications", "Drugs", "antiviral drugs". Advanced search and BULIAN operation were performed for more precise filtering. Exclusion criteria was having no therapeutic drugs or strategy.

### Chloroquine:

*In vitro* trials show that Chloroquine or Hydroxychloroquine an FDA approved drug was highly effective to control Covid-19 infection.<sup>16</sup> Recommended dosage and course of treatment with Chloroquine is longer than administered in malarial disease. That is why, awareness regarding acute poisoning and even death caused by poisoning of this drug must be reinforced.<sup>17</sup>

### Remdesivir:

Remdesivir is a broad spectrum anti-viral drug and one of the highly discussed drug candidate against Covid-19 infection. Various clinical trial on human of Remdesivir is being conducted all over the world and

some positive insight also found during treatment of first patient of United States who was treated with intravenous Remdesivir from the 7<sup>th</sup> day of infection and his condition was reported improving on the 8<sup>th</sup> day without any adverse event of Remdesivir before the discharge of patient. In addition, 17 patients of diamond princess cruise ship were treated with intravenous Remdesivir for consecutive 10 days. Physicians involved in this intervention (Affiliated with US National Institute of Health) observed that patients were less prone to ventilation after Remdesivir administration.<sup>18</sup>

However, any conclusion on Remdesivir can not be drawn now before proper clinical trial on human against Covid-19

### Ribavirin:

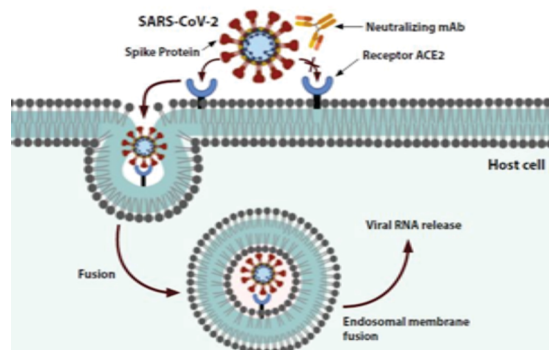
The government of China initially recommended the administration of Ribavirin for Covid-19 treatment on the basis of previous clinical experience in case of SARS and MERS. Since Covid-19 is a novel virus, vigorous clinical trials are necessary to establish the safety, efficacy and tolerability of Ribavirin.<sup>19</sup>

### Immune suppressive and stimulating drugs:

R Beth et al reported that, Prednisolone in low dose and Tacrolimus may have beneficial outcomes to treat SARS-Covid-19. anti-TNF $\alpha$ , JAK kinase inhibitors, NSAIDS, cytotoxic drugs, low dose methotrexate are contraindicated. Blocking of IL-6 pathways is logical and expected to be practiced during pandemic progression based on their review.<sup>20</sup>

### Monoclonal antibody:

Shanmugaraj B et al suggested that monoclonal antibody can be potential therapeutic candidate for Covid-19. They also proposed a hypothetical neutralizing pathways of this virus by monoclonal antibody as below:



**Fig 1: Schematic representation of Covid-19 neutralizing mechanism**

Spike protein of virus and cellular receptor play the vital role for entrance of virus into targeted cell. Targeting the spike protein of virus

by monoclonal antibody could be a potential neutralizing pathways.<sup>21</sup>

### Nanomedicine:

Nguyen V et al noted previously in 2017 that nanomedicine can be a potential therapeutic candidate against Corona family based on Nanoparticle-absorbed proteins, usage of active proteins for editing nanoparticles to gain reduction of toxicity, enhancement of circulation time including targeting effect. Predictive model on the basis of the protein corona was first established utilizing gold Nanoparticles with various size and alterations of surface. A well accepted precise model prediction could not be possible because physicochemical properties including size, zeta potential, absorbance spectra failed to provide adequate information. However, a model on the basis of fingerprint of protein corona and physicochemical properties of Nanoparticles provides a more precise assumption of Gold Nanoparticles cell associations with  $R^2=0.86$ .<sup>22</sup>

This drug design process needs more and more understanding and proper knowledge for future innovation.

### Vaccine:

Remarkable global investment and efforts to develop vaccine for novel Covid-19 is on process. United States collaborated with Moderna to prepare RNA vaccine and a safe clinical trial with 45 volunteers is going on. China is working with Cansino Biologics Inc. and conducting a phase I safety trial for a recombinant adenovirus vaccine candidate deploying 108 volunteers in Wuhan from March, 2020.<sup>23</sup>

### Autophagy:

Last two decades, researchers have gained proper understanding on the significance of endocytic pathway along with autophagy process of viral entry and its replication. Therefore, endocytic pathway has become substantial targets for establishing therapeutic strategies to fight against disease caused by novel Corona.<sup>24</sup>

### Melatonin:

Rui Zhang et al. reported based on substantial data that Melatonin slows virus-induced disease and may also be beneficial in COVID-19 intervention though further experiments and clinical trials are mandatory to support the claim. Melatonin used as an adjuvant in COVID-19 has been repeatedly exerts anti-inflammation, immune response regulations, anti-oxidation effects in respiratory complications models caused by infection and it has considerably high safety profile.<sup>25</sup>

### DISCUSSION:

Although researchers from all over the world are searching for an optimum medicine to fight Covid-19, still there are no promising drugs found with clear mechanism of action. Physicians are applying drugs based on thumbs rule. Some medicine like Remdesivir is slightly ahead in the line. Scientists are also talking about Favipiravir, but no vivid light is seen. So, we need to search for more and more antiviral candidates. Since, the virus seize ACE2 receptor, this pathway will open new window to design a promising drugs so far we can predict.

### CONCLUSION:

In summary, whole world is waiting eagerly for a convenient, cost-effective, safe antiviral to fight the global pandemic of Covid-19 as well as an effective vaccine. We expect very soon a good news will come and nil the death toll as well as number of affected. Till that time, personal hygiene, social distancing and other preventive measurements may lessen the impact of pandemic.

### ACKNOWLEDGEMENT:

We pay our heartiest salute to all front line warriors including health care professionals, policy makers, media-activists and all known, unknown fighters in this perimeter of disaster.

### Limitations of the study:

Each and every day, newer findings are coming out but we could not incorporate all the newer and newest findings in our study. Besides, traditional medicine and ethno-medicine were skipped in this review.

### Authors Contribution:

Corresponding author extracted all the relevant papers and second author contributed to inclusion and exclusion of articles as well as proofchecking.

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