EGYPTIAN ACADEMIC JOURNAL OF

BIOLOGICAL SCIENCES

PHYSIOLOGY & MOLECULARBIOLOGY

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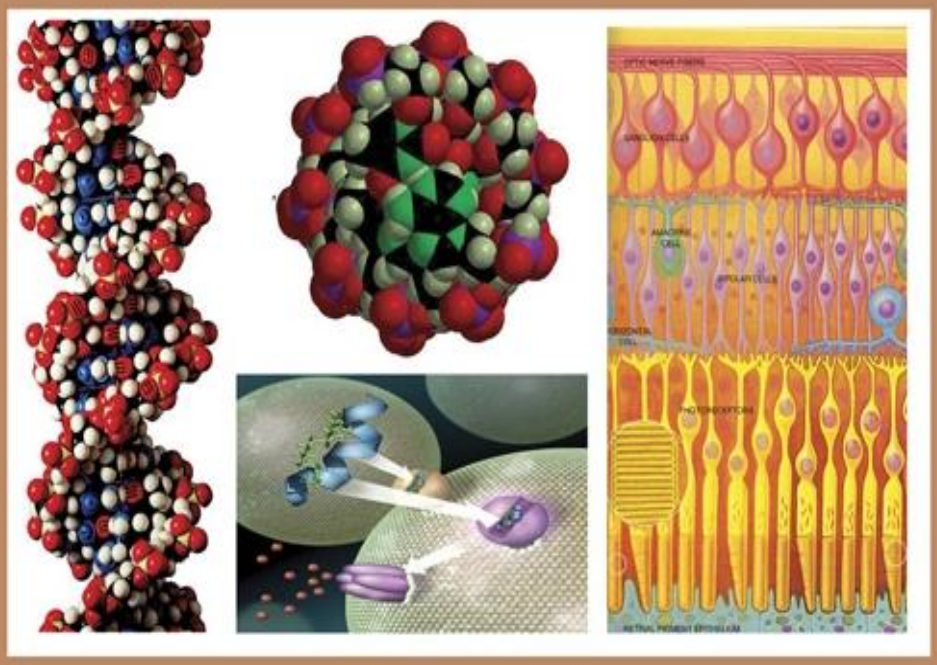

ISSN
2090-0767

WWW.EAJBS.EG.NET

Vol. 15 No. 1 (2023)

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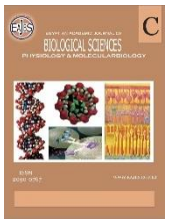
Citation: *Egypt.Acad.J.Biolog.Sci. (C.Physiology and Molecular biology) Vol. 15(1) pp403-407 (2023)*
DOI: 10.21608/EAJBSC.2023.298541

Egypt. Acad. J. Biolog. Sci., 15(1):403-407 (2023)

Egyptian Academic Journal of Biological Sciences
C. Physiology & Molecular Biology
ISSN 2090-0767
www.eajbsc.journals.ekb.eg



Role of the Drug Favipiravir in the Destruction of Spike Protein in Patients with Covid-19

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ARTICLE INFO
Article History
Received:10/4/2023
Accepted:11/5/2023
Available:17/5/2023

Keywords:
Favipiravira, Spike protein.

ABSTRACT

The Spike protein is one of the virulence factors of viruses, which is responsible for the attachment of the virus to the host cell. This study included the study of the effect of Favipiravir on S protein at different concentrations, as it showed the highest effect at a concentration of 0.5 and an amount of 9.66 ± followed by the concentration. .025 by 7.06 ± to have a gradual effect of (5.23 ± ,, 3.63 ± 2.53 ±, 1.60 ±, 0.06 ±, 0.00) at a concentration of (0.015, 0.03, 0.06, 0.125, 0.07, 0.02), respectively, as once the virus interacts with the cell The host causes a structural rearrangement of the S protein, which allows the virus to fuse with the host cell membrane. Because of the seriousness of the Covid-19 virus and its components, it has become necessary to find a drug that controls the spread of the pandemic.

INTRODUCTION

Coronavirus is considered one of the viruses that most threaten human life. This virus causes a number of serious diseases in humans, the most important of which is the severe acute respiratory syndrome that emerged at the end of 2002 in southern China, and it is a disease caused by a virus called SARS (SARS-CoV) that causes Acute respiratory failure characterized by damage to lung tissue, the SARS epidemic spread to 37 countries, and as a result, 8273 cases of infection were discovered, of which 775 were fatal, with a death rate of 17%. The World Health Organization announced the end of the epidemic in July 2003, and the Coronavirus in 2012 also caused Kingdom of Saudi Arabia with the emergence of Middle East Respiratory Syndrome, as the structural structure of the virus includes four structural proteins, which are proteins that fill the surface of the virus and determine the way to attack the host, and they include the spike protein (S)) and the protein envelope (E)) and the protein Glycose (Membrane (M)), Nucleocapsid (N)) In addition to the protein (Hemagglutinin Esterase (HE)) (Astuti, 2020; Thomas, 2020), as shown in Figure (1).

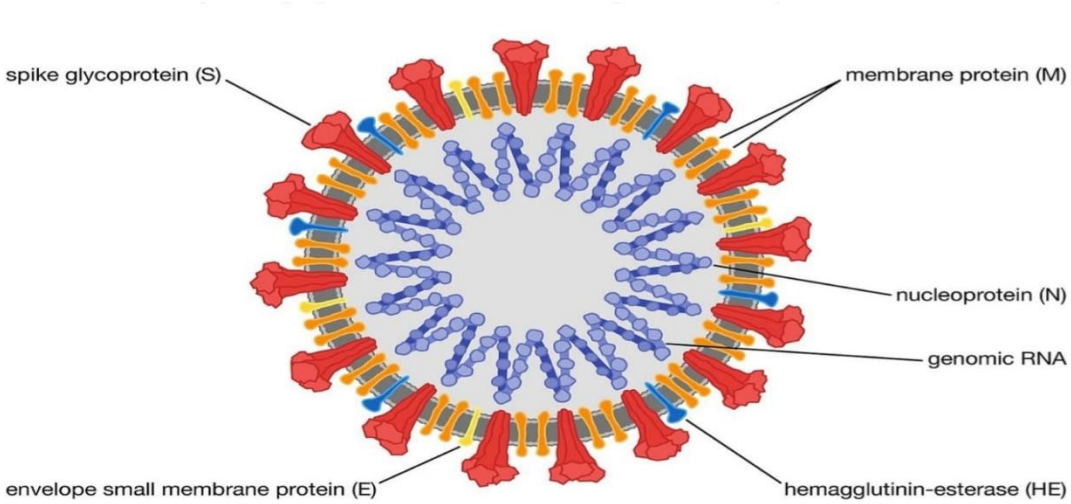

Fig. 1: The structure of the emerging coronavirus and its outer surface proteins (Shaikh *et al*., 2020).

The spike proteins are homologous and prominent to the outer surface of the virus through the transmembrane protein, where the spike protein is the primary determinant of attachment to the host cells because it is the main target for neutralizing antibodies and therefore it is of great importance in terms of the immune response(Watanabe *et al*, 2020, Xia *et al*,.2020). The spike protein consists of two functional subunits, the (S1) subunit) which is responsible for binding to the host cell receptor and the subunit (S2) and is responsible for the fusion of viral membranes with cell membranes (Astuti, 2020; Lotfi *et al*., 2020). n the case of the new Coronavirus, the spike protein is cleaved by type 2 transmembrane serine protease, as it facilitates the process of fusion of the viral and cellular membranes, as a result, the viral genome enters the cytoplasm, and in the next stage, the RNA genome of the virus is translated. This leads to the formation of a new structure of the virus and non-structural proteins, these proteins are responsible for the replication of the viral genome, followed by the stage of "maturation" ((Khedkar & Patzak, 2020)) Therefore, therapeutic strategies based on the understanding that potent antiviral drugs against SARS-CoV-2 are necessary to reduce the impact of subsequent local waves of COVID 19 (Torneri *et al*., 2020). Drugs combined with quarantine showed a significant reduction in the final size of the outbreak. And the peak of its occurrence is the role of an effective antiviral to change the spread of COVID-19 by affecting the viral load, the discovery of favipiravir by examining the chemical substance that possesses antiviral activity against the influenza virus, which is a prodrug (T-705) with a molecular weight of less than 157.1 g / Mol. approved for medical use in Japan, in 2014, for the treatment of novel or recurrent pandemic influenza virus (Shiraki and Daikoku, 2020; Hayden & Shindou, 2019). In February 2020, favipiravir was also approved for the treatment of novel influenza in China (it is an analogue of a purine base that is converted to and is being studied further in a Chinese population for experimental treatment of young adults. Favipiravir underwent metabolic activation through ribosylation and phosphorylation to form the non-activated metabolite Favipiravir-RTP. Effective against deoxyribonucleic acid (DNA), but has high activity against viruses with ribonucleotide (RNA) (Wiess *et al*., 2020).

MATERIALS AND METHODS

Sample Collection:

The study included patients who had a confirmed diagnosis of the virus through the

positive result of the reverse transcription polymerase chain reaction (RT-PCR) test through a swab taken from the nasopharynx of the upper respiratory tract and who were suffering from symptoms of infection with the virus, blood samples were collected From Samarra General Hospital and external laboratories in the district from Covid patients.

Working Principle:

The test is based on the principle of the enzyme immunoassay of enzyme-linked immunosorbents based on the technique of binding antibodies to the antigen to examine the effect of the drug Favipiravir on the Coronavirus. It depends on the interaction between the immune antibodies that cover the pits prepared in the test kit and the antigens of the Coronavirus present in the swab taken from the nasopharynx.

RESULTS AND DISCUSSION

The results of the current study showed high sensitivity towards Favipiravir according to the concentration, as it recorded the highest level of sensitivity at a concentration of 0.5 by 9.66pg/ml, and there was no antigen effect at a concentration of 0.02, as shown in Table 1.

T**able 1 :** represents the activity of favipiravir on the spike protein of SARS-CoV-2

Aggregates	0.5	0.25	0.125	0.06	0.03	0.015	0.07	0.02
Favipravira	9.66 ± 1.68Ac	7.06 ± 1.22Be	5.23 ± 0.814ce	3.63 ± 0.65Dd	2.53 ± 0.05Ee	1.60 ± 0.43Fc	0.06 ± 0.05Ge	0.00 CD

The results of the current study are similar to the findings of (Li *et al*. 2020), which demonstrated the effectiveness of the antibody through its effect on many influenza viruses, including swine flu virus (H1N1) and avian influenza virus (H7N9). In addition, it may stop the replication of many influenza viruses. Other RNA viruses including arenaviruses, adenoviruses and coronavirus (COVID-19) as antivirals can shorten the course of the disease by targeting the host cell receptors and thus shorten the clinical course of the disease by reducing viral shedding (Sabre-Ayad *et al*., 2020).

It is also considered a potent inhibitor of error-prone viral nucleic acid (RdRps) that leads to chain termination or leads to the accumulation of deleterious mutations. Favibravera, a broad-spectrum inhibitor, is also considered a potent antiviral drug against SARS-CoV. 2- Necessary to reduce the impact of subsequent local waves of COVID (Torneri et al.,2020). The effect of the local antiviral intervention was shown to reduce the spread of the disease as Favipiravir was discovered by screening a chemical important for antiviral activity against influenza virus by chemical modification of pyrazine which is an analogue of the 6-fluoro-3-hydroxy pyrazine carboxamide derivative 2-pyrazinecarboxamide. These findings support the role of favipiravir in reducing viral load (Furuta *et al.*, 2017).

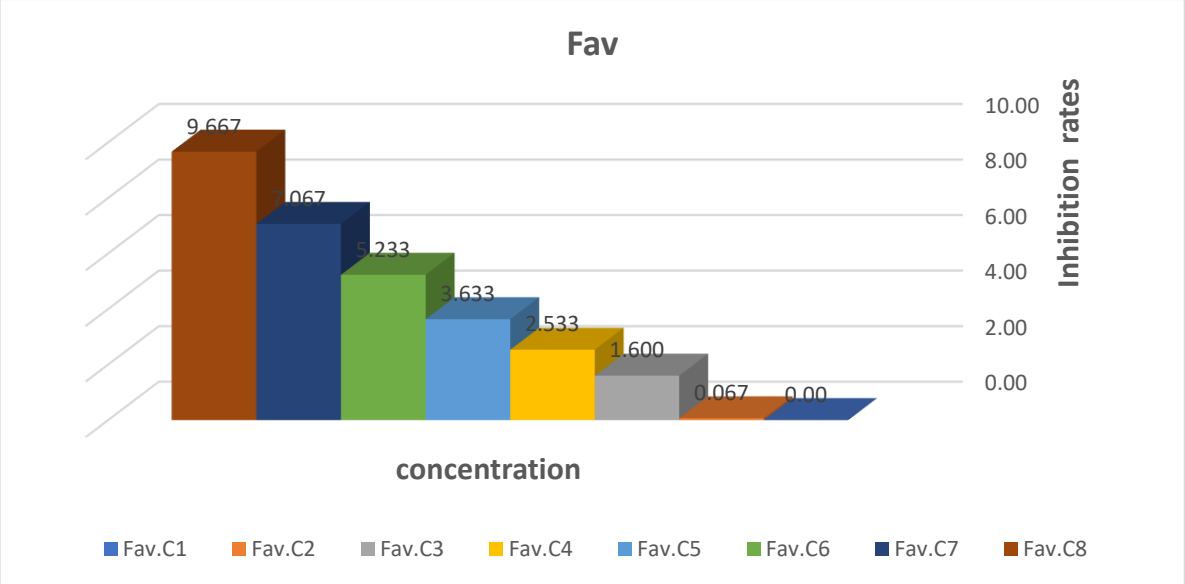

Fig. 2: Shows the effect of different concentrations of Favipiravir ugn on the SARS-CoV-2

Where Figure (2) shows that there is a significant difference between the concentrations, as the concentration of 0.5 had a high effect on the Coronavirus, followed by the concentration of 0.25 in the effect, and then followed by the concentrations (0.125, 0.06, 0. 0. 03, 0.015, 0.07, and 0.02), respectively.

Conclusions

The effect of different concentrations of Favipravera on Coronavirus by affecting the spike protein of the virus, which is considered one of the factors of virus virulence and urging the use of Favipravera to reduce the viral load

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