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A biochemical approach towards sealing viral replication pathway and also simultaneous approach to dampen immune response

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ABSTRACT

All Apart from all three domains of life [namely: archea, bacteria and eukaryotes], we might have come across a suspected molecular organization, whose existence as a living organism is still in question. This is a living as well as could be said to be non-living is still a dilemma. It was really a fascinating thing for student having interest in searching for scientific causes and loves to study about organism there behavior and the way they interact environment, during our days of high school when we had just a glimpse of introduction about an organism that could be considered as living [i.e.; the reproduction is observed] only when it's inside a living cell or so called host. It was in a last century when viruses became a big concerned matter of research for scientists and a matter of fascination of entire humanity to have knowledge about the virus and its mechanism of survival, it was by an outgrowth of HIV [Human Immunodeficiency Virus] that cause AIDS[Acquired Immuno Deficiency Syndrome] was reported that it started from ape and being transferred to humans and was capable of killing humans via its mere invasion inside the human body because the HIV totally hijacks the immune system by making T-Cells work for it, that consequently make the immune system of the HIV infected person so weak that their body give up the surviving capacity even by being infected from common bacterial, fungal or protozoal infection. It is really next to impossible for a person [here; HIV infected person] to be totally isolated from the cosmopolitan infecting agents that is present everywhere and can potentially infect the person, but the immune system of patient with HIV becomes so weak that it can no more fight with any infectious agent and person dies. Apart from the dangerous perspectives of HIV infection its positive aspect is that, as it was reported, HIV spreads only through blood transfusion, so it can be prevented. Unfortunately this is not the case with the world wide rife popularly known as "corona virus pandemic", scientifically called as SARS CoV- 2[Severe Acute Respiratory Sydrome Cororavirus 2] a causative agent for COVID 19 [Coronavirus disease of 2019], it is named coronavirus due to the viral coat present over it, having appearance like a crown. The researchers and scientists all over the world are trying to make out the vaccine for the virus but it might not be wrong to say that it could take months even years for the clinical trial of the vaccine so that it could help human to get rid of the occult catastrophic, devastating and drastic danger of this new form of coronavirus. It is even dangerous to produce any form of vaccine of this virus because we are still unknown that it might become virulent and can revert back as infectious monster. At point of time to save lives we could try to make an approach towards a probiotic and an preventive measures which can at least save the life and humanity.

Keywords— *Viral Replication, Dampen Immune Response, Biochemical*

1. Introduction

This abstract is an approach to save lives of people by some of the suggestions which could be proved useful, here let me first describe some basic mechanism of viruses, in common, when they infect the living cell, where we will also see the basic mechanism of viral replication and how could we stop it. It starts with infection when virus enters the cell through attachment to cell membrane and then it gets inside the living system by its spikes attached to cell receptor which let it get inside the cell membrane, this is the penetration.

The receptors on the surface of cell get the virus inside the cellular system then occur the upcoating, where the viral coat is released out and the viral genome gets inside the nucleus it is incorporated to gene of the host cell and hijacks its replication, transcription and translation machinery for its own use. This is not the case with corona virus, rather it does hijacks the ribosomal machinery for making its viral capsid and spikes. It does not enter the nucleus of host cell. Then comes the phase of replication, where the viral genome replicates. Then is the **lysis** of cell and a huge outburst of virus. This is the basic mechanism of viral entry.

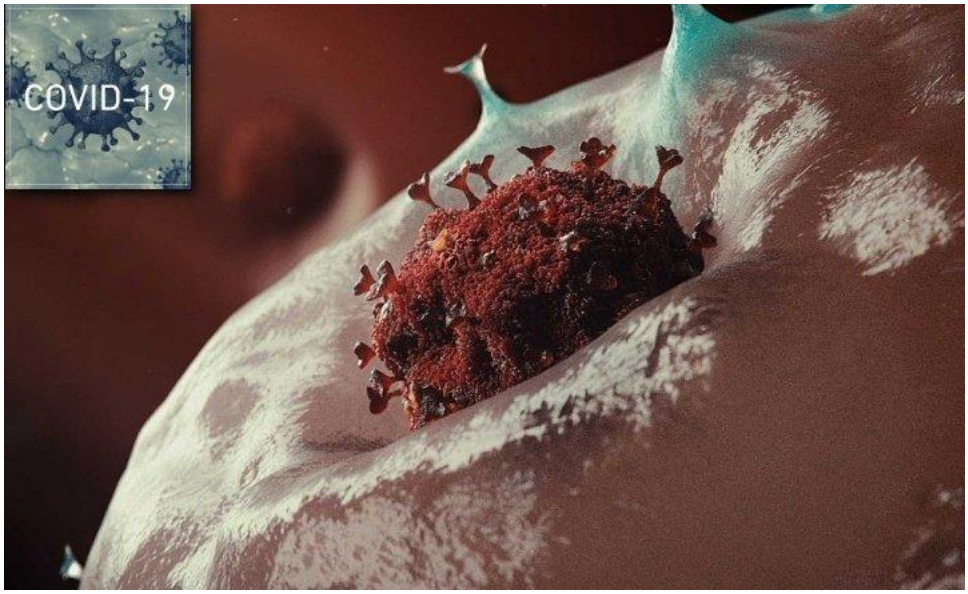


Fig. 1: Covid 19 penetration inside cell.
Source: Google images

1.1 Sub-headings

What if we generate a non- responsive cellular system in which the host cell will not response towards the virus, means the cell of our body rejects to perform the hospitality of Covid 19 virus. This is not a fantasy, in fact it could be done through gene regulation by which we could inactivate the protein which make the receptor active after coming in contact with viral spike and gets incorporated with the host cell by some sort of chemical dialogue [that is, ligand and receptor chemical talk], as a result of which virus enters the cell.

Likewise, the other protein-protein interaction which results in activation of the activities of biochemical pathways where messages are delivered in the form of receptor- ligand system this is what the cell signaling is, here also same thing occurs. The corona virus makes out a chemical signal which is recognized by the host cell and it gets entry inside the host cellular system. This will not be the case when the spikes of upper coat of this virus would not bind to the cell receptor or the cell do not accept the binding of virus. This would occur either by gene regulation as mentioned above or any sort of enzyme which could make the receptor insensitive or non-responsive towards the viral ligand.

This article is mostly going to focus about the possible therapeutic solution that could serve the humanity at this time, we cannot think for vaccine as a quick server of the disease because it would take months or years to make vaccine and provide it as a solution for disease. The vaccine needs to be tested among a huge population then could be preferred for the clinical trial. The approach of the article is going to deal with numerous perspectives of therapeutics for the treatment as well as some of the probiotic approaches to prevent the disease.

Let's see each perspective in detail and the paces of treatment, which could be made, as the corona virus entering the human system. The very first approach deals to block the receptor. It is a well-known fact to us that ACE II [Angiotensin converting enzyme II] receptor is serving as the receptor of this virus if we block this receptor by some of the common medicines usually taken by high blood pressure patient. They are simply telmisartan or it could be valsartan or losartan. If these medicine of 0.25 mg is taken as daily dose, I don't think it is not going to harm if taken with a balance diet and some extra calories.

Let me first give a brief explanation of the physiological function of ACE II receptor [angiotensin II converting enzyme receptor]. For this a short introduction towards RAAS [rennin angiotensin aldesteron system] where we would come to known how kidney-lungs-adrinal gland- heart as well as brain functions in collaboration. Start of this classic endocrine pathway occurs by release of Angiotensinogen into circulation by liver, this is the response for low blood pressure and the adverse changes in the Na^+ concentration now comes the rennin from liver which cleaves the Angiotensinogen to a decapeptide commonly known as Angiotensin I.

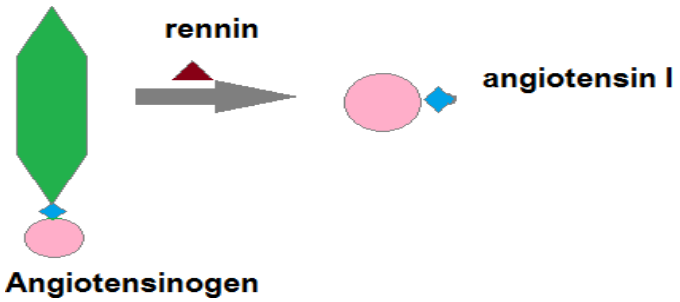


Fig. 2: Illustrating Angiotensinogen converted to Angiotensin I by rennin

Now, this Angiotensin I is converted to Angiotensin II by an enzyme that works in further physiological functioning in increasing blood pressure. We will not be looking for the further details of these physiological functioning here. After all our area of concern

is rapid approach for medicine of this virus that is infecting the world. Experimentally it has been proved that person having less ACE 2[Angiotensin Converting Enzymes 2] were less susceptible to this disease, if in future the condition will be up to the mark then it will be proved with further research work in this area of therapeutics for the disease. At least this approach will save the lives, though with a temporary increase in blood pressure, which could be treated by some sort of heamodialator or blood pressure increasing medicines.

One more effect it causes is the blocking bradykinin pathway, this leads to alteration in ADH [Anti-diuretic Hormone] action, mechanism and furthermore it's not an issue we could manage it by bradykinin proper administration or managed doses. Bradykinin itself works as indicator or a chemical messenger.

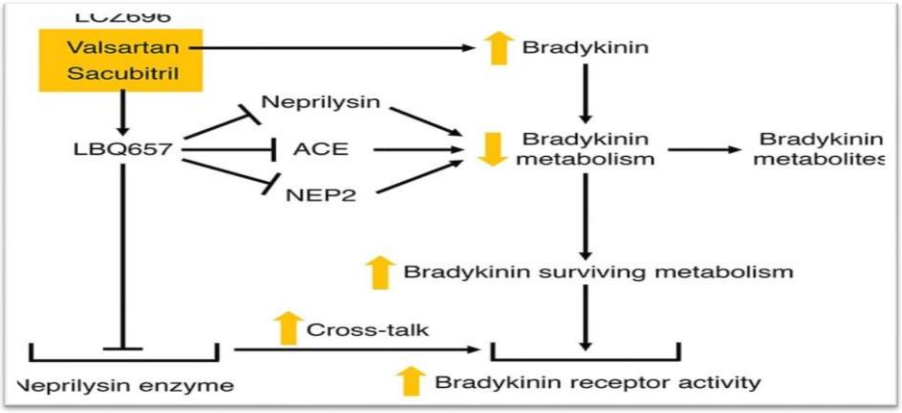


Fig. 3: Showing bradykinin functioning as well as its relation with ACE

Apart from this approach we can have another classical approach in which we will try to enhance the JAK/STAT pathway of cell signaling systematic. Here we will see the interferons which are produced by the virally infected cell could serve as the chemical to kill the viral infection. As we heard of the recent treatment, that is convalescent plasma therapy, which include injection of the blood plasma, of the cured patient to the sufferer of disease, this tries to provide readymade antibodies against the virus but what if own body produces antibody against the virus. There could be a thought of therapy that can induce, inside the bodily system, enhancing JAK/STAT pathway. Let us check it out how it could be done, it starts with the recognition of PAMP [Pathogen Associated Molecular pattern] molecule of pathogen by PPR [Pattern Recognition Receptor] of cells of host body in common.

This causes secretion of Interferons e.i; INF alfa and INF beta, that in turn does a variety of biochemical functioning which could lead to secretion of autocrine biocatalysts that further blocks the viral replication mechanism. This could be seen by the illustration bellow, the physiological as well as the biochemical pathway is seen in this manner, the PRR recognizes the foreign body and expresses INFs[Interferons] these INFs which is always seen as one pathway that proves it as an activator of the real cell eating monster that could activate the CD^{8+} [cytotoxic] T-cells that could kill the cells in response to INFs, it is a simple well known mechanism in which the INFs from viral infected cell induced dsRNA – dependent kinase this leads to protein synthesis thus causing blockage of viral replication.

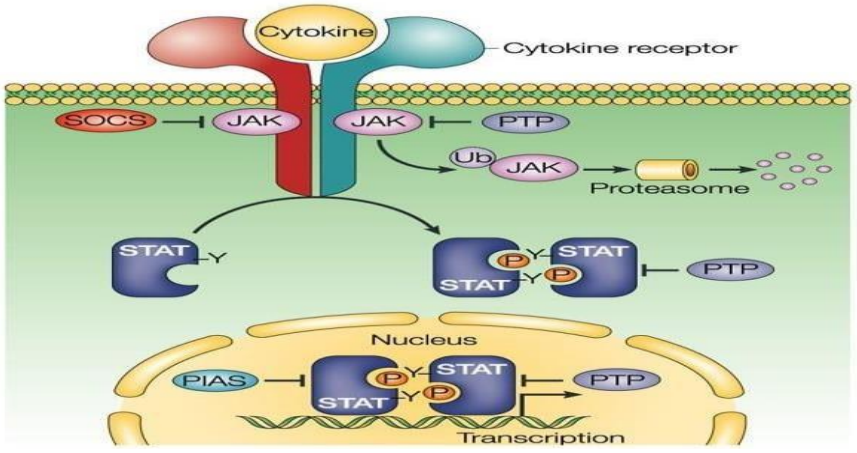


Fig. 4: JAK/STAT Pathway
Source: Nature reviews

Binding of interferon to NK cells [natural killer cells] would lead to the inception or initiation of lytic activity which causes the killing of the viral infected cell. This is only the case with the corona virus, where immunogenic tolerance is often misguided and creates hustle and bustle to immune system response leading to exaggerated immune response and an army of CD^{8+} or cytotoxic t-cell is recruited at the place of invasion or infection. This is the point where inflammation at its high rate occurs and the consequence is the pneumonia in which alveoli is filled with cellular secreation added to the cell debris created via in response to CD^{8+} cells action of killing the cells.

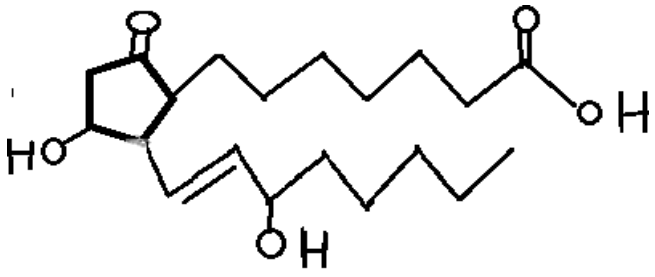
This could be monitored properly by damping the immune response by anti- inflammatory drugs and also some of the immunosuppressant drugs, proves useful so that we can suppress the immune respose, which could be various treatment, there can

be a hope for using drugs which treats various autoimmune diseases'. Not so much confirmed about the clinical trial but this could be seen as a hope that these medications can be helpful for treatment of this worldwide disease at least we can save lives. There can be some more approaches readily made regarding the treatment in near future or it can be manipulated for saving lives:

(a) An approach can be made for treatment with the prostaglandins, aspirin and other anti- inflammatory agents, this could be other ecosinoids too.
(b) Treatment by Apigenin

Let us examine both of these treatments one by one with the hope that it would be used to save lives.

The first one is the treatment using the compound discovered by Ulf Von Euler, got Nobel prize for it in 1970. It was discovered as a secretion from prostate gland hence named" Prostaglandin", although it is found in every cell. It is a compound as a result of Archeodonic acid metabolic pathway and the consequence is the Ecosanoid that is the prostaglandin.



prostaglandin

Prostaglandin and other ecosanoids can be a possible treatment because it have the capacity to reduce inflammation, they are very unstable compound with the half-life of about 30 second ($t_{1/2}$ =30 seconds), so are needed to be synthesized when there is need. At cellular level it is produced by phospholipids A2 and prostaglandin H synthase synthesizes it from Arachiodonic acid. The prostaglandin can be an activator of the transcript and it can also act as a blood vessel constrictor, which could be used as increasing blood pressure of patient when ACE 2 blockers are administered as mentioned above.
The following fig will illustrate these statements:

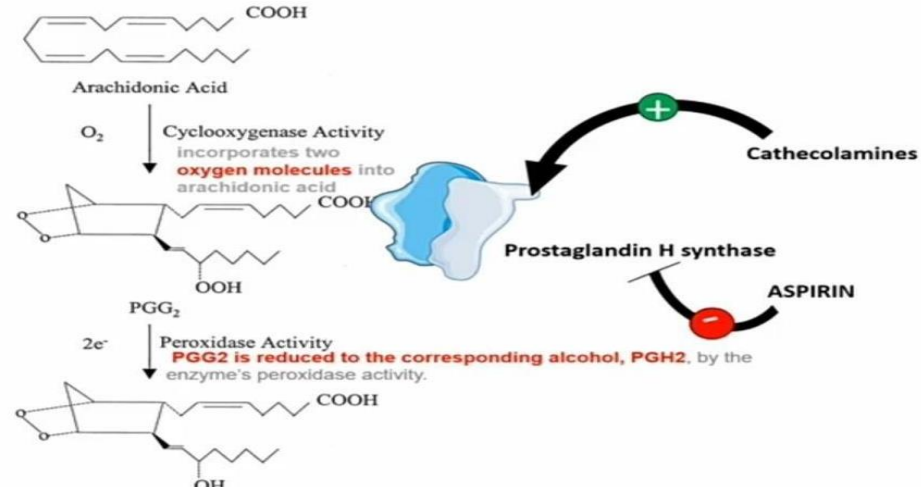


Fig. 5: Pathway of prostaglandin formation

Here it can be clearly visualized that Arachiodonic acid forming prostaglandin, through cyclogenase activity incorporated with O_2 molecule and prostaglandin H synthase also acting in this series of reaction to form the final product and there is certain activity of peroxidase, thus the reaction proceeds to form suitable and the desired product.

Lets now see the enzyme prostaglandin H synthase having two catalytic sites of activity ;one is having cyclogenase activity and the other is having the peroxidase activity and thus by this way it helps in conversion of archiodonic acid to prostaglandin

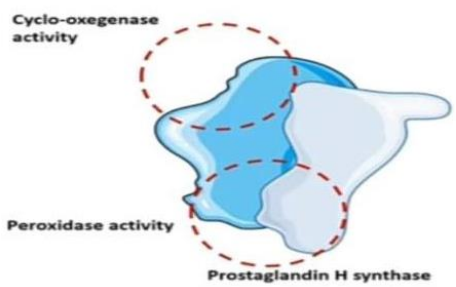


Fig. 6: Enzyme prostaglandin H

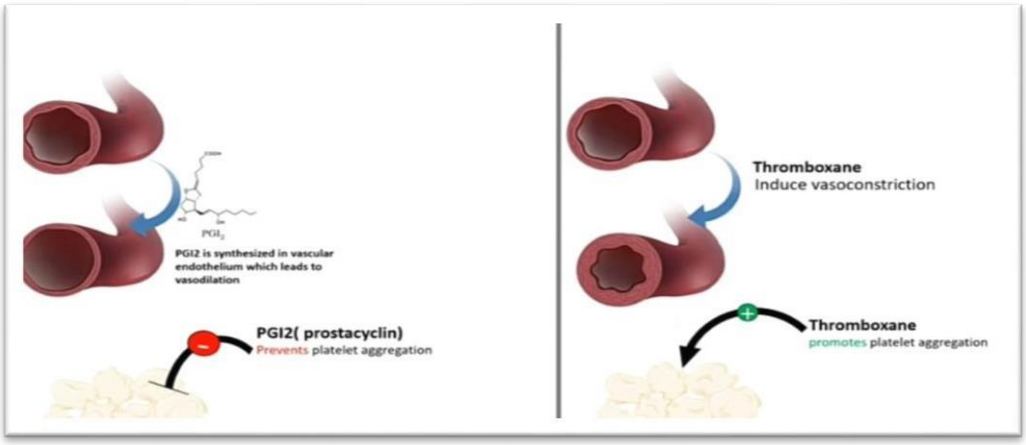


Fig. 7: Showing both the function of prostaglandin that could act as a vassodialator and can increase the blood pressure or the patient under treatment of telmisartan or lobsarton as mention in the very first approach.

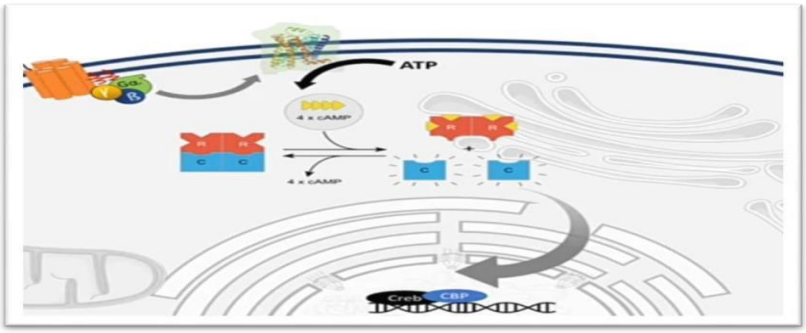
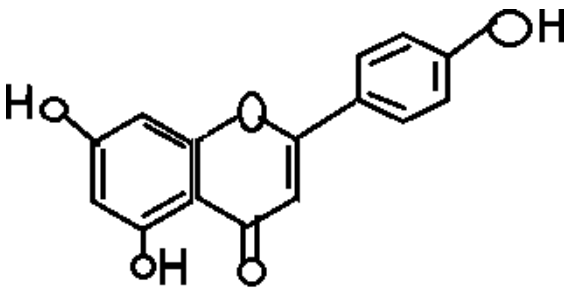


Fig. 8: This illustration is showing how the enzyme is acting upon the cell signaling mechanism to effect the transcription

2. CONCLUSIONS

Asprin can also be a potent drug to control the inflammation as well as the ibuprofen can serve in saving lives not as a full claim but these al can be potent drug for an action to save lives. Let us see the final series of the abstract in which I do mentioned for the Apigenin which is a classified form of plant derived natural compound [glycosides] that could serve as anti-bacterial, anti-fungal and a potent anti-viral drug.



Apigenin

There is lot to be researched in this scenario it's a challenge, though it would take a big length of time to be assured about vaccines of the catastrophe which is a worldwide spread disease. Abstract should be ended here by messege that it is still just an approach with yhe hope that by any of the mechanism which could be the potent treatment of the disease and we do hope that ongoing research would bring some of the robust treatment strategies. I myself is searching for any potent organism which could serve as inhibitor of viral replication. The problem lie within is the mutation of the gene segments of the corona virus SARS CoV 2 that could be used to inhibit the replication of virus.

There could be solution for this, that lies within the recognition of those segments of the viral genome which do not mutate much or are a bit mutated if we could be able to recognize those segments then the medicine is in our hand and further we could eradicate the viral pandemic.

With this hope of good in future and a potent medicine could come in to cure the disease we should try to include some of hygiene associated procedure and other guidelines so that at least we could be able to prevent it.

