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NOVEL APPROACH TO ENHANCE THE ANTI VIRAL ACTIVITY OF EXISTING DRUG/DEVELOPING VACCINE AGAINST PANEDMIC COVID-19

N.Jaya Chitra
Professor and Head
Department of Chemical Engineering
Dr.M.G.R Educational and Research Institute
Maduravoyal, Chennai-95, TN, India

A.U. Santhos Kumar
Assistant Professor
Department of Chemical Engineering
Dr.M.G.R Educational and Research Institute
Maduravoyal, Chennai-95, TN, India

***Abstract*— Due to the outbreak of the novel coronavirus disease COVID-19, caused by the SARS-CoV-2 virus, this disease has spread rapidly around the globe. Considering the potential threat of a pandemic, scientists and physicians have been racing to understand this new virus and to find effective drug and vaccine to treat against this pandemic disease. To support the current research and development, a novel approach had been of invitro/invivo saponification in alignment with the current drug had been suggested.**

Keywords: ***COVID-19; SARS-CoV-2; Pneumonia; Hydroxychloroquine***

I. INTRODUCTION

According to the World Health Organization (WHO), the Centers for Disease Control and Prevention (CDC), and the U.S. Food and Drug Administration (FDA), there are currently no medications or vaccines proven to be effective for the treatment or prevention of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and for the existing crisis of pandemic Covid-19.
We like to provide our suggestions and idea of simple invivo/invitro saponification process with edible substances in alignment with existing medicine to develop vaccine that may cure the patients at the earliest. Further we hope the information provided in the report will be an intellectual support of ongoing research and development for discovery and development to enhanced drug activity (or) vaccines.

II. REVIEW OF LITERATURE

At present for direct antiviral treatment of SARS-CoV-2, China International Exchange and Promotive Association for Medical and Health Care CPAM recommends use of lopinavir; ritonavir [2 capsule (dose undefined) by mouth twice daily] in combination with nebulized alfa-interferon (5 million units in Sterile Water for Injection inhaled twice daily). This recommendations of CPAM has based on historically controlled studies, case reports, and case series that suggest clinical benefit of lopinavir; ritonavir in the treatment of other coronavirus infection [i.e., 2002 SARS-CoV and 2012 Middle East respiratory syndrome coronavirus (MERS-CoV)]. Chu CM et al
Based on Korean physicians with experience in treating SARS-CoV-2 infected patients have different recommendations for the treatment of COVID-19. According to them antiviral medications are not recommended for use in young healthy patients with mild symptoms and no underlying comorbid conditions due to the side effect risk. However, treatment with lopinavir 400 mg; ritonavir 100 mg (2 tablets by mouth twice daily) or chloroquine (500 mg by mouth twice daily) should be considered for use in older patients or patients with underlying conditions and serious symptoms. If chloroquine is unavailable, they recommend considering use of hydroxychloroquine (400 mg by mouth once daily). Gao J et al and Tim Smith et al

Further some options for potential future treatment had been suggested by Tim Smith et al which include

1. Remdesivir (GS-5734), an investigational nucleoside analogue: Remdesivir has been administered to several hundred patients with confirmed severe SARS-CoV-2 infections in the United States, Europe, and Japan through Expanded Access or Compassionate Use programs. (9)
2. A clinical trial evaluating the efficacy of remdesivir in patients infected with SARS-CoV-2 is currently being conducted in China. Data from this trial are expected by April 2020. (9)
3. In preclinical trials, remdesivir has demonstrated significant activity against coronavirus and a high genetic barrier to resistance. Remdesivir has shown prophylactic and therapeutic efficacy against 2002 SARS-CoV in a mouse model. (10) (14)

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4. Data from a molecular docking experiment using the SARS-CoV-2 RNA dependent RNA polymerase (RdRp) model identified tight binding of sofosbuvir and ribavirin to the coronavirus RdRp, thereby suggesting possible efficacy of sofosbuvir and ribavirin in treating the COVID-19 infection. (11)
5. Lopinavir; ritonavir in conjunction with ribavirin and corticosteroids(4): Open-label trial involving newly diagnosed 2002 SARS-CoV patients who had not developed acute respiratory distress syndrome (ARDS)
6. Based in cell research (16) also reveal that their findings on remdesivir and chloroquine are highly effective in the control of 2019-nCoV infection in vitro. Since these compounds have been used in human patients with a safety track record and shown to be effective against various ailments, we suggest that they should be assessed in human patients suffering from the novel corona virus disease.
7. Based on abg intellectual property (17) three biotech companies have announced their intention to **develop a vaccine** against Wuhan coronavirus Novavax, Inovio Pharmaceuticals and Moderna Therapeutics.
8. We have recently known that the European Medicines Agency (EMA) has launched a plan to speed up development and approval of vaccines and antivirals for the prevention and treatment of SARS-CoV-2 coronavirus infection.

III. CURRENT TRENTS ON VACCINE INVENSION

According to Bickerton et al (10) Patent No: US 10,130,701 B2 (45). The vaccine may by a live attenuated form of the coronavirus, the genome of the coronavirus strain may lack the part of the present invention and may further comprise a pharma the replicase protein corresponding to the part provided by ceutically acceptable carrier.

It had been defined that a modified protein is formed through 40 ceutically acceptable carriers suitable for use in the insertion of the nucleotide sequence provided by the plastion are well known to those of skill in the art. Accordingly the carriers used can include ethanol, polyols, and sequences for the vaccinia virus genome, suitable mixtures thereof, vegetable oils, and injectable. The above method it had been suggested the use of organic esters, Buffers and pH adjusting agents may also be recovery of recombinant coronavirus comprising the employed. The positive recombinants may then be verified to contain the 65 preparation of these pharmaceutically acceptable composi modified replicase gene.

From the last week of 2019 through March 1, 2020, more than 500 journal articles related to the virus were published electronically or in print, with numbers steadily increasing week-by-week. Topics included clinical manifestations, treatment regimens, viral structure and mechanisms, antiviral agents, and diagnostics. To date, more than 500 patents have been issued for vaccines and for therapeutic agents, such as antibodies, cytokines and nucleic acids, that could help prevent or treat coronavirus infections. Because SARS-CoV-2 is similar to other corona viruses, such as SARS-CoV-1 and MERS-CoV, the researchers Cynthia Liu et al highlighted therapies previously explored for these other viruses that could also be applicable to SARS-CoV-2. (19)

IV. CLEANING PRODUCTS CAN KILL THE COVID-19 VIRUS

COVID-19 has only been around for a few months, so at this point scientists don't know that much about it. But more is being learned every day.

It's easy for an infected person to spread the virus particles through coughing, touching other people or leaving the virus on surfaces. Undoubtedly, hand-washing after being in public spaces is key to reduce the spread of COVID-19. The researchers looked at a number of different viruses including SARS-CoV-2 – the coronavirus that has caused COVID-19. And it found that the survival times varied according to the type of surface. (19)

Generally Soap and water, sodium hypochlorite, Ethanol, and benzalkonium chloride are used for cleaning purposes

Soap and water are your first line of defence to remove the virus from surfaces. The detergent in soap will interfere with the fats in the virus shell and lift the virus from surfaces and this is then rinsed off by water. The active ingredient in bleach – sodium hypochlorite – are effective at killing the virus. The bleach works by destroying the protein and what's known as the ribonucleic acid (RNA) of the virus – this is the substance that gives the blueprint for making more virus particles in an infected person. Ethanol has been shown to kill coronaviruses in as little as 30 seconds like bleach, the alcohol destroys the protein and RNA that the virus is made up of.

V. DIRT REMOVING MECHANISM OF SOAP

Soap are formed when alkaline solution like NaoH or KoH reacts with triglycerides, leading to the formation of chain of fatty acids with base, also called as alkaline hydrolysis.

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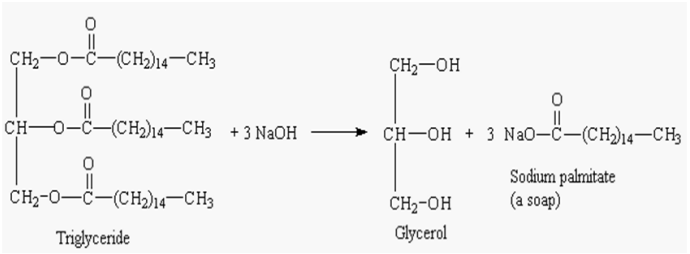


Fig 1: Sapanification Reaction

To understand the mechanism, when soap bar immersed into water, there will be reaction between water and soap leading to micelle formation. There are a few stages in which the soap removes grease stains. (Stearate ion is from sodium stearate, which is a constituent of soap).

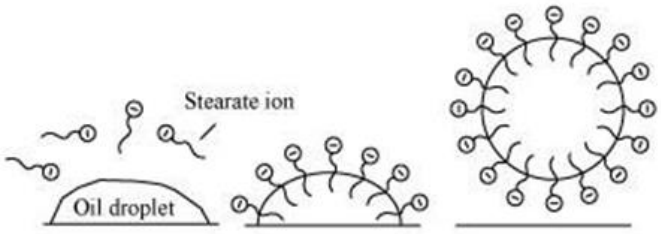
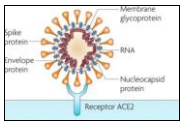


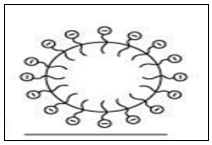
Fig 2: Schematic representation for dirt removal mechanism

The final micelles (above) have negatively charged "heads" of soap molecules which will link with positive end of dipole of water through ion-dipole attractive force. Thus bound to water the micelle with grease at its centre will be carried away by water, leaving behind grease-free surface. When soap is dissolved in water, its hydrophobic ends attach themselves to the dirt and remove it from the hands. Then, the molecules of soap arrange themselves in micelle formation and trap the dirt at the centre of the cluster. These micelles remain suspended in water like particles in a colloidal solution.

VI. SCOPE OF THE ARTICLE

- As detergent in soap has the capacity to interfere with the fats in the virus shell and lift the virus from surfaces that can be rinsed off by water as per the similar mechanism of dirt or oil removing mechanism of soap.
- Given below are the suggestions for the formulation of new vaccine or enhancing the curative nature of current drugs are given
- Edible soap can be made using higher fatty acid with weak base invitro
- Higher fatty acid that can be used for preparing edible soap are as follows with their respective medicinal properties (Source: A very foodly dairy)
  - ✓ cacao butter (it is high in Vitamin E and antioxidants)
  - ✓ coconut oil (known antifungal and antibacterial agent)
  - ✓ macadamia oil (an emollient that helps to soften skin)
  - ✓ avocado oil | rich in essential oils and sterolins)
  - ✓ olive oil (contains omega3 and omega6 fatty acid, reduces inflammation)
- Weak base
  - ✓ sodium citrate (IUPACName: trisodium;2-hydroxypropane-1,2,3-tricarboxylate)- This chemical is commonly found as trisodium citrate which is used as an emulsifier, acidity regulator, calcium sequestrant, and preservative.
- Substances similar to the composition of soap can be admixed with prescribed components of vaccine or drugs (19)- In vivo soap formation.
- Edible oils in required quantities can be mixed with prescribed drugs (19) and consumed along with sodium citrate - in vitro soap formation.
- Both the above methods can be performed at higher temperature of around 60-70°C to enhance saponification action and dissolve lipid content virus.
- The above methodology will form soap either in vitro or in vivo and will remove the oil in the virus shell thereby deactivating it.
- The schematic picture is as described below





Noval Anti Viral Agent

Structure of Carona Virus Edible soap from essential oil Effective drug or vaccine

VII. CONCLUSION

The information provided in this report provides a strong intellectual support of ongoing research and development for discovery and development of enhanced drug activity and vaccines for treatment of COVID-19 and coronavirus-related diseases. Because of the existing worst situation, this report devotes minimal attention to current efforts involved in advancing more efficient and accurate COVID-19 diagnosis methods.
We had given simple process of saponification invivo/invitro that has to be involved with current clinical drug development. Ofcouse due to current uncertain situation I am able to provide only theoretical concept that has to be executed practically

with aid of bio laboratories. Hope with help of government support we can effectively manage the current uncertainity due to COVID 19, as the world prepared to manage former major out breaks of coronavirus SARS and MERS respiratory illness. Further in near future the mechanism of reaction between drug and virus via sopanification can be explored.

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