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Pocket K

COVID-19 Treatment Efforts Using Plant Technologies

GLOBAL KNOWLEDGE CENTER ON CROP BIOTECHNOLOGY

In December 2019, Wuhan City in China became the epicenter of a respiratory disease outbreak with mysterious origins, that spread to many countries immediately. To investigate on the matter and control the disease roll out, suspected and infected patients were placed in isolation, contact tracings were conducted, and detailed clinical and epidemiologic data were gathered. These efforts led the Chinese experts to finding the cause of the disease – a novel coronavirus strain from patient groups in Wuhan. The outbreak is believed to originate from a local market in the City that sells wild animals as food.[1]

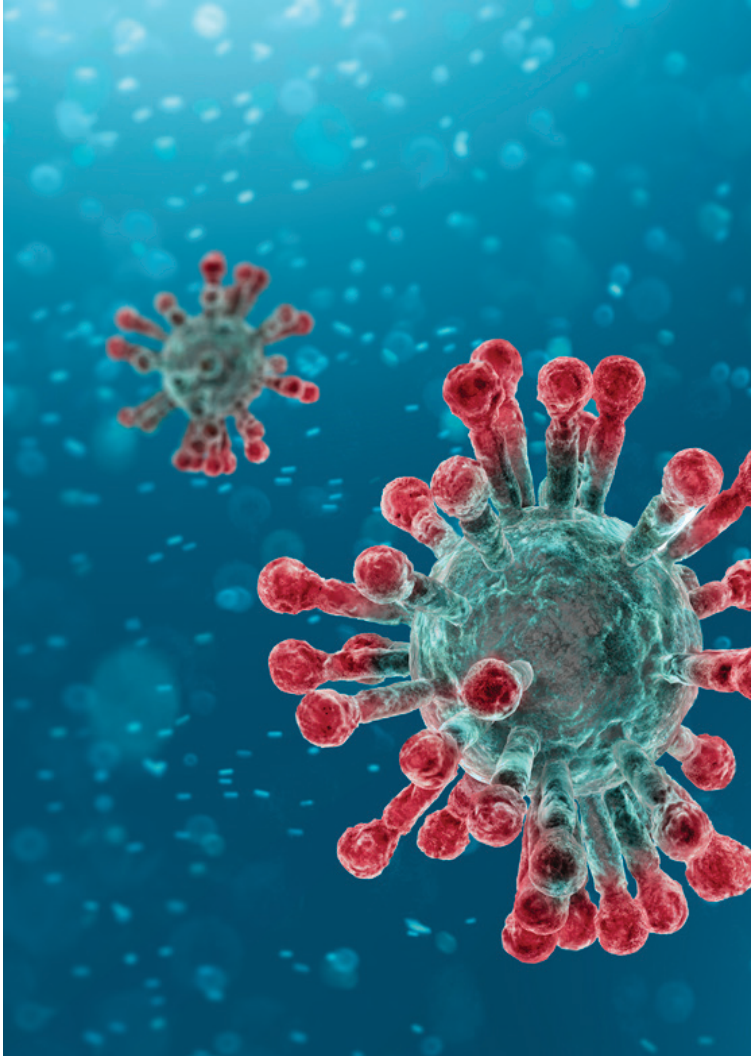
Coronaviruses is a large family of viruses. Some of the viruses cause diseases among humans, while others among animals such as camels, cattle, cats, and bats. A few animal coronaviruses evolve to infect humans, such as those that caused SARS, MERS, and COVID-19 outbreaks.[1]

On March 11, 2020, the World Health Organization (WHO) characterized COVID-19 as a pandemic.[2]

In May 2020, the number of reported cases globally reached close to 4 million, with about 300,000 deaths.[3]

Questions about the origin of the COVID-19 virus (SARS-CoV-2) were raised, and some even speculated that the virus is a product of genetic engineering. In a Nature Medicine article, scientists from the US, UK, and Australia reported that the genome sequence of the COVID-19 virus evolved naturally erasing the popular myth.[4]

Similar to other viruses, the COVID-19 virus spreads through droplets of saliva or nasal discharge. Infected individuals experience mild to moderate respiratory illness and can recover without medications. However, older patients with underlying medical concerns such as heart disease, diabetes, cancer, hypertension, and chronic respiratory disease are more likely to develop serious illness. Thus, scientists from various fields all over the world are working hard to come up with effective treatments to curb the pandemic.



Diagnostics: Test Kits Using CRISPR and Algae

COVID-19 testing is conducted through various means in different countries. Some methods detect the presence of the virus itself through RT-PCR and isothermal nucleic acid amplification, while other tests detect antibodies produced as a reaction to the infection.[5]

Polymerase chain reaction (PCR) method is considered as the gold standard for disease diagnostics, however, it requires expensive equipment and knowledgeable manpower. Thus, researchers at the University of Connecticut's Department of Biomedical Engineering developed the "All-In-One-Dual CRISPR-Cas12a" (AIOD-CRISPR), a low-cost, CRISPR-based diagnostic platform to detect infectious diseases, including

the COVID-19 virus. The CRISPR technology is used in almost all organisms but it's early applications were in plants.

The AIOD-CRISPR test kit is intended for use at home or in small clinics, reducing disease transmission risk. Compared to PCR, AIOD-CRISPR system has better sensitivity and specificity. The test kit successfully detected the DNA and RNA of SARS-CoV-2 and HIV.[6]

Western University and Suncor are developing serological test kits for COVID-19 using algae as a production factory for making the vital proteins for antibody identification. Algae are plant-like protists that inhabit aquatic environments. Current tests rely on proteins developed in insect or mammalian cells, which are expensive and difficult to scale. Algae is a better biofactory alternative because they are easy to grow and can be easily modified to produce the viral proteins.[7]

Therapeutics: Potential Plant-based Treatments

Studies have shown that the genome sequence of SARS-CoV-2 is highly similar to the genome of SARS-CoV, which wreaked havoc in 26 countries in 2003. Thus, Guangxi University and Huazhong Agricultural University researchers used a 3D homology model of the sequence and used it to screen against a medicinal plant library with 32,297 potential antiviral phytochemicals and traditional Chinese medicinal compounds. This led them to 9 specific plant molecules that may be used to develop drugs against COVID-19 (Table 1).[8]

Table 1. Potential phytochemicals for antiviral drug development

Phytochemical name	Plant source
5,7,3′,4′-Tetrahydroxy-2′-(3,3-dimethylallyl) isoflavone	Mojave indigo bush (*Psorothamnus arborescens*)
Myricitrin	Wax myrtle (*Myrica cerifera*)
Methyl rosmarinate	Marubio oscuro (*Hyptis atrorubens*)
3,5,7,3′,4′,5′-hexahydroxy flavanone-3-O-beta-D-glucopyranoside	Common bean (*Phaseolus vulgaris*)
(2S)-Eriodictyol 7-O-(6″-O-galloyl)-beta-D-glucopyranoside	Indian gooseberry (*Phyllanthus emblica*)
Calceolarioside B	Chinese flowering ash (*Fraxinus sieboldiana*)
Myricetin 3-O-beta-D-glucopyranoside	Tea tree (*Camellia sinensis)*
Licoleafol	Chinese liquorice (*Glycyrrhiza uralensis*)
Amaranthin	Edible amaranth (*Amaranthus tricolor*)

In another study, researchers from Indonesia used molecular docking to search for potential inhibitors of COVID-19 main protease (M^{pro}), which is a potential drug target. They searched for bioactive compounds from medicinal plants. They found that nelfinavir and lopinavir may represent potential treatment options, while luteolin-7-glucoside, demethoxycurcumin, apigenin-7-glucoside, oleuropein, curcumin, catechin, and epicatechin-gallate have the best potential to act as COVID-19 M^{pro} inhibitors. Further studies are needed to confirm their potential medicinal use.[9]

Another molecular docking study in the University of Maragheh led to nine low risk and neutral drugs that have inhibitory activities against novel COVID-19 protease. These are thymoquinone, salvinorin A, bilobalide, citral, menthol, noscapine, forscolin, beta selinene, and ginkgolide A, which has a strongest bond and high affinity with protease among others.[10]

Vaccines: Using Plants as Biofactories

Vaccines are known to be the most cost-effective and efficacious method to lessen the disease burden of infectious diseases. Thus, experts are striving towards developing an effective vaccine to combat the spread of COVID-19. This includes plant-derived vaccines, which can be produced with less cost in high amounts, carrier plants are readily accepted by patients and antigens derived from them are stable and can be stored for a long time.[11]

A team of researchers from the Queensland University of Technology led the genome sequencing of a native tobacco plant (*Nicotiana benthamiana*) years before the COVID-19 pandemic broke. They used the genome sequence of the plant in the development of a vaccine for COVID-19. The plant is a good candidate as biofactory because of its potential to make large quantities of high-quality

vaccine and antibodies considering it has 60,000 genes, which is double the number of genes of an ordinary plant.[12]

Medicago, a biopharmaceutical company based in Canada, have successfully developed a Virus-Like Particle (VLP) of the coronavirus 20 days after obtaining the SARS-CoV-2 genetic sequence using proprietary plant-based technology. Obtaining the VLP is the initial step towards developing a vaccine for COVID-19, which will be followed by preclinical testing for safety and efficacy. Instead of using egg-based methods to develop vaccine, their technology inserts a genetic sequence into *Agrobacterium,* a common soil bacterium that is taken up by plants. Then the plant produces the protein that can serve as a vaccine.[13]

British American Tobacco, through its biotech subsidiary in the US, Kentucky BioProcessing (KBP), is developing a potential vaccine for COVID-19 and is currently in pre-clinical testing. Experts at KBP

cloned a part of the genetic sequence of SARS-CoV-2 which they used to develop a potential antigen. Then the antigen was inserted into tobacco plants for reproduction. Compared to conventional methods, the use of tobacco as biofactory is considered safer because the plants cannot host pathogens that can cause human diseases and allergies. The production time is also faster because the elements of the vaccine accumulate in tobacco plants much quicker – six weeks in particular, compared to several months using conventional methods. The vaccine formulation can be stored at room temperature, unlike conventional vaccines which must be stored in low temperature. Moreover, it can possibly deliver effective immune response in just one dose.[14]

Nanoengineers at the University of California San Diego are exploring on using a plant virus in developing a COVID-19 vaccine that can be shipped anywhere around the globe without the need for refrigeration. The team is using a plant virus that infects legumes, thus non-infectious to humans.

They engineer the virus to look like the COVID-19 virus then molecular signatures specific to SARS-CoV-2 will be placed on the surface of the virus to stimulate immune response.[15]

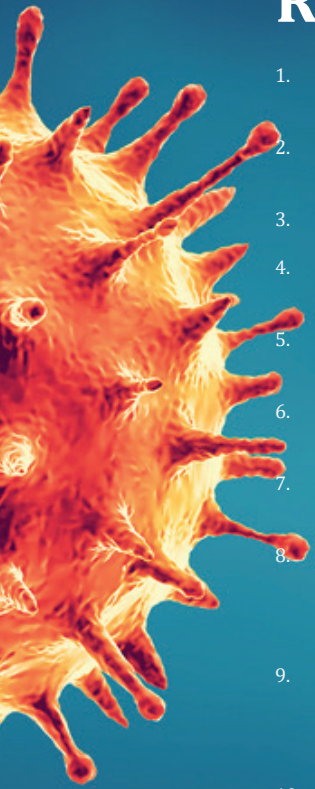
Global Efforts to Combat the COVID-19 Crisis

To accelerate the development, production, and equitable global access to new COVID-19 essential health technologies, WHO launched a global collaboration among health actors, private sector partners and other involved institutions around the world on May 4, 2020. They called on the global community and political leaders to support their mission and asked for the necessary resources to hasten the achievement of their objectives. The global health actors, including WHO, Bill and Melinda Gates Foundation, Coalition for Epidemic Preparedness Innovations, Global Alliance for Vaccines and Immunisation, Global Fund, Unitaid, and Wellcome

Trust, and partners declared their commitment to be accountable to the world, to communities and to one another to pursue their shared aim.[16]

There are about 800 million people suffering from chronic hunger prior to the COVID-19 crisis and this number is expected to go up dramatically. Thus, it is necessary to make deliberate actions towards ensuring that the COVID-19 pandemic would be prevented to become a global food and humanitarian crisis. This led major businesses, farmer groups, industry, academy, and non-governmental organizations to call on world leaders to create response measures to minimize the risks of the pandemic on food supplies. Their key actions include keeping the global market open for trade, improve support to those prone to malnutrition, invest in sustainable and resilient food systems.[17,18] In line with this, the International Seed Federation also called on the governments to facilitate the international movement of seed during the crisis to avoid disrupting the agriculture supply chain.[19]

As of this writing, pathogens such as coronaviruses continue to evolve through time, scientists are forced to double their efforts to combat diseases, particularly COVID-19, with the aid of every instrument in our global health technology toolbox. It is imperative that the best vaccine and best medical therapy be available and accessible immediately to control the disease and prevent more damage to the population and the economy.



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