

# The 2020 Coronavirus (COVID-19) Global Pandemic, a Call to Arms to Pharmacognosy Researchers – Plant-Based Antiviral Approaches

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## ABSTRACT

**Background:** The unprecedented modern pandemic that is COVID-19 has awakened a global fear of viral disease and an activation of viral targeted drug discovery not seen before in modern times. Whilst the vaccines about to enter the market, are an important component of the strategy to combat COVID-19, vaccination should be considered a part of a wider strategy to address this and future zoonotic viral outbreaks. Plant-based approaches may provide valuable avenues for viral disease management. **Methods:** This commentary combines an appraisal of the existing literature with the authors thoughts on key challenges that pharmacognosy may be able to assist with, in the management of zoonotic viral disease. **Results:** There are many avenues for plant-based antiviral research in the context of the present COVID-19 pandemic. This narrative review discusses the use of plant-based approaches; as viral drug leads, as agents for managing the cytokine storm associated with acute respiratory distress syndrome, as agents for elimination of viral reservoirs and as agents in hand sanitisation. **Conclusion:** Whilst the arrival of vaccines is an important step in the

response to the current COVID-19 pandemic. Pharmacognosy still has a role to play in the management of this and future viral pandemics. The support of researchers in this domain is needed to combat viral pandemics via arming clinicians with a broader range of options for prevention and treatment of viral illness on a global scale.

**Key words:** COVID-19, Severe acute respiratory syndrome, Coronavirus, COVID-19 vaccine, Drug discovery, Anti-viral agents.

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## INTRODUCTION

The unprecedented modern pandemic that is COVID-19 has awakened a global fear of viral disease and an activation of viral targeted drug discovery not seen before in modern times.<sup>1</sup> The global response placed on research initiatives to combat this virus should involve pharmacognosy in its approach to manage the current pandemic and prepare for future viral challenges to human survival.

### Zoonotic Coronavirus Disease

COVID-19 is a zoonotic encapsulated ribonucleic acid (RNA) virus from the wider coronavirus family.<sup>1,2</sup> Coronaviruses primarily cause infection in mammalian and avian species but in recent times outbreaks from the coronavirus family have increasingly demonstrated zoonotic properties resulting in human disease.<sup>1</sup> Previous outbreaks of coronavirus such as the severe acute respiratory syndrome (SARS CoV-1) in 2002 and Middle East respiratory syndrome (MERS) in 2012 were warning signs for the impending coronavirus pandemic of 2019-2020.<sup>1,3</sup> In fact, it was only a matter of time before a new coronavirus outbreak was destined to occur. High levels of genetic variability amongst coronavirus species coupled with the numerous animal reservoirs harboring these viruses was an evolutionary melting pot of advancing genetic evolution leading towards COVID-19.<sup>4,5</sup> Indeed, this zoonotic reservoir has long been identified as a source of future diseases,<sup>6,7</sup> and is a harbinger of novel coronaviruses for years to come.<sup>4,8</sup> Regression modelling predicts ongoing risks of zoonotic emerging infectious disease outbreaks to continue in the areas linked to COVID-19, linking forested tropical regions experiencing land use changes with mammalian wildlife diversity in these areas as predications of future zoonotic outbreaks.<sup>9,10</sup>

Persons to person transmission of coronaviruses such as SARS, MERS and now COVID-19 can present in some patients as mild influenza like disease but its progression to acute respiratory distress syndrome

(ARDS) is associated with significant morbidity, mortality and burden on healthcare systems.<sup>11-14</sup> The ARDS syndrome is characterised by a cytokine storm that results in severe inflammatory respiratory collapse and multiorgan failure.<sup>14-17</sup>

Previous outbreaks of coronavirus zoonotic disease have been likely limited by public health response, with isolation and hygiene being the primary focus of disease control. However, the current COVID-19 pandemic has substantially exceeded previous coronavirus infections on the global scale.<sup>8</sup> Hygiene responses currently focus on social distancing, isolation and the utilization of alcohol based hand sanitizers to limit contact spread.<sup>18,19</sup> There is concern that the relative success of these strategies during the first wave of the pandemic may in fact paradoxically leave the global population at greater risk of a worsening pandemic due to subsequent waves of infection.<sup>20</sup> The present focus of the pharmaceutical response sits largely in two camps: those with research focus on development of a vaccine, and those with focus on developing or repurposing antiviral or other existing drug treatments.<sup>20-22</sup>

### Vaccine Development

Whilst we have many vaccines about to enter the market, a vaccine based approach is useful in patients prior to exposure and thus offers limited relief to those already infected.<sup>20</sup> The unique nature of COVID-19 transmission offers unique challenges. Asymptomatic individuals are thought to have significantly longer periods of potential disease transmission and lower levels of antibody mediated immunity,<sup>20</sup> and this may in fact be counterintuitive to traditional approaches to vaccination of higher risk individuals when vaccine supplies are limited. Vaccination of lower risk individuals on a global scale may thus be an important aspect of the vaccine approach to managing COVID-19. Therefore, vaccination programs in the developing world are a concern

in an environment where developed nations are buying up potential vaccine candidates to vaccinate their populace, limiting access to the developed world to a finite supply chain.<sup>18</sup> Vaccine uptake may also be limited in the developed world via anti-vaccination ideologies within some communities,<sup>23-25</sup> resulting in potential reservoirs of ongoing viral carriage. Distribution and economic barriers are significant in the developing world and thus human reservoirs of ongoing COVID-19 clones are increasingly likely due to the global nature of travel, and thus the global impact of this pandemic. Whilst some cross-reactivity of existing human coronavirus immunity is thought to mitigate the risk of severe infection in SARS-CoV-2 infection,<sup>25</sup> a rapidly waning antibody response to these coronavirus may require ongoing boosters and/or novel vaccine developments to contain seasonal virus control. Whilst less likely than antimicrobial resistance, vaccine resistance is possible.<sup>26</sup> Thus a vaccine approach may be limited by the evolving nature of the virus resulting in a lack of absolute coverage of viral clones that may emerge. Similar to the vaccine program for influenza, a system of 'educated guessing' of potential clones may be required.<sup>8,26,27</sup> Although there are multiple mechanisms at play that minimise the chance of vaccine resistance, to negligible levels.<sup>26</sup> It remains a potential concern, given the high proportion of COVID-19 vaccine candidates that target the spike protein of the virus or its receptor binding domain.<sup>28</sup> A mutation in this vaccine target would potentially induce resistance to a large proportion of agents. Should this occur, vaccine platforms that generate a broader immune response (similar to naturally acquired immunity) may be necessary. This may be the need to use attenuated live vaccines which generally result in greater chances of adverse reaction.<sup>28</sup> Cold chain requirements of the vaccines (particularly encapsulated mRNA vaccines that require frozen storage) will likely be a significant impediment to a global vaccination program.<sup>28</sup> Among the new vaccine platforms DNA vaccines are the platform with most potential to avoid cold chain restraints, thus enabling mass vaccination.<sup>29,30</sup> Other vaccinations including traditional vaccination platforms can be stabilized via lyophilisation and targeted excipients, however the process can lead to loss of efficacy and increased lead times. The urgency of vaccine rollout makes it likely that we will not establish long term stability data until after the point of utilization.<sup>30</sup> Additionally the ongoing potential of new novel zoonotic coronavirus transfer poses an ongoing challenge in developing new vaccines ahead of emerging disease. The tendency of suppressed innate immunity resulting in the delayed mass inflammatory response seen in ARDS patients is also of concern.<sup>15-17,20,31</sup> Vaccines with a higher reactivity such as live attenuated vaccines may be required due to the lowered immune response seen in older individuals,<sup>28</sup> the very people who require the greatest need for immunoprotection due to enhanced ARDS risk.<sup>17</sup> Rapid establishment of a comprehensive immune response to COVID-19 infection in the lung mucosa may be critical.<sup>30</sup> Thus, the efficacy of a vaccination program targeting individuals at risk of severe disease, particularly those at risk of ARDS, as part of an opportunistic or preventative vaccination program may be limited without a high reactivity lung mucosal delivered vaccination.<sup>20,28</sup>

## Vaccine Concerns

With a significant number of vaccines in various stages of development, the global dependence on vaccination as an approach to management is heavily invested in. In addition to significant government funds being delivered to vaccine producers via projects such as the U.S. governments Project Warp Speed,<sup>32</sup> lead products are also being bought on mass by well-resourced nations prior to final approval in an effort to secure the health and thus financial security of their populations.<sup>20</sup> This poses a unique risk for the management of COVID-19, as well as future zoonotic viral diseases. At the time of writing, concerns have been raised with some of these lead candidates. The US government backed

Pfizer-BioNTech product that is currently being rolled out on mass to healthcare workers in the UK and US, is currently under increased scrutiny in the media due to exaggerated immune responses to the vaccination from susceptible patients with existing histories of allergic responses to vaccines.<sup>33</sup> A lead vaccine candidate from the University of Queensland and biotech company CSL in Australia has also concurrently been pulled from trials due to false positive HIV results, with the study investigators and the Australian government citing loss of public confidence in the vaccine being an impediment to its ongoing success.<sup>34</sup> Notably, these false HIV positive results are not expected to impact the efficacy of the vaccine. However, a decrease in patient confidence due to these effects would impact the uptake of the vaccine and therefore its value. It is also noteworthy that the University of Queensland vaccine had only begun phase 1 clinical trials (which evaluate safety) and had yet to begin phase 2 trials (which test efficacy). Therefore, it is not certain at this point whether that vaccine would have proved effective. Whilst these issues are common during the development of pharmaceuticals and potentially have little serious impact on health outcomes, these back to back concerns are likely to feed ongoing concerns from the public in regards to vaccine safety,<sup>23</sup> thus potentially limiting the uptake of a global vaccination strategy. Hence the safety of any potential vaccine candidates is of paramount concern to a vaccine success.<sup>20</sup> Vaccine success in eliminating disease is dependent on both the efficacy of the vaccine and the uptake of the populace to achieve herd immunity. We are yet to assess the efficacy of these vaccines in the wider populace, nor the potential uptake of global vaccination.<sup>27</sup> Even with a vaccine that is 100% efficacious and gives lifelong immunity, it is estimated that 60-72% of the population needs to be vaccinated. If efficacy is less than 80% then it is likely that the entire population will need to be vaccinated.<sup>27</sup> Therefore, whilst an important component is our strategy to combat COVID-19, vaccination programs should be considered a part of a wider strategy.

## Antiviral Drug Discovery

The drug treatment approach focuses on the development of both new novel agents and the repurposing of existing pharmaceutical treatments for coronavirus infection. The latter case may initially have more direct benefits in the management of the existing pandemic due to shorter lead times to utilization and the ability to be used in human clinical trials prospectively during the pandemic.<sup>35</sup> The treatment based drug research approach currently focuses on targeting RNA replication via RNA polymerase or false analogues of viral RNA components.<sup>13,21</sup> Other targets are the protease inhibitor drugs responsible for cleaving RNA produced proteins into viral components.<sup>13,21</sup> Cinaserin is one such example that has shown the ability to cause significant targeted coronavirus replication inhibition.<sup>1,36</sup> Immunomodulators such as those currently utilised for autoimmune disorders and novel immunomodulatory agents are the current drugs of interest in managing the cytokine storm of severe respiratory and end stage disease.<sup>13,14,21</sup> Dual antiviral, anti-inflammatory or antibacterial agents such as chloroquine and azithromycin have also been investigated.<sup>1,14,21</sup>

## Elimination of viral reservoirs

Outside of vaccines there is limited development of drugs for prophylaxis or eradication of viral reservoirs in human and animal hosts, nor are there plans for ecological and environmental prevention of newly emerging zoonotic disease.<sup>10,37</sup> Whilst the use of existing agents is likely to assist in managing the disease due to the shortened lead time, the lack of specificity is unlikely to remove the potential for future outbreaks. Targeting the eradication of zoonotic reservoirs is likely to be culturally and ethically difficult to achieve.<sup>10</sup> Previous responses to pandemics such as avian flu have focused on the culling of animal hosts rather than eradication of host disease.<sup>38</sup> Additionally eradication

of zoonotic reservoirs via eradication of host disease is unlikely to be economically feasible in the developing world as demonstrated by ongoing programs targeting vector borne illness such as malaria and zika virus.<sup>10</sup>

## Pharmacognosy and the pandemic

Like the impending antibiotic apocalypse that looms as a result of evolutionary genetics of bacteria in response to antibiotic selection of increasingly resistant clones,<sup>39</sup> The zoonotic viral apocalypse currently being lived out in the form of the novel COVID-19 coronavirus pandemic calls for a global response from all sectors to evolve the human arsenal of treatment against viral disease. Pharmacognosy has a part to play in building and broadening the potential agents in this domain.<sup>40,41</sup>

Pharmacognosy adds to, and in many places extends the ability to fight this evolving threat to human well-being and prosperity. With the wider world currently utilizing plant based medicine for treating disease,<sup>42,43</sup> phytochemicals offer a unique scope within the global healthcare response as well as the research domain. Pharmacognosy offers a wide range of parent molecules for development of new target agents, with existing agents demonstrating antiviral properties in different contexts.<sup>2,21,40,44-56</sup> The faster time to market of these agents may provide a valuable asset in this race to novel drug discovery.<sup>57</sup>

Key challenges that pharmacognosy may be able to assist in:

1. The development of novel agents for drug development towards a broad range of viruses including coronaviruses.
2. Development of agents that combat the cytokine response to novel viral infections.
3. Potential development of plant-based sources of treatment to coronavirus human and animal reservoirs to combat future zoonotic transfer and assist in elimination of infections in the developed world.
4. Development of topical agents that may be used in hygiene practices to eliminate person to person transfer of disease.

## Plants as sources of novel agents in viral disease

Plants have been a continued source of pharmaceutical drug leads for further optimisation and development, with a strong focus on antimicrobial properties, particularly as antibacterial agents. Whilst not as prolific as antibiotic drug discovery, antiviral plant leads are actively being investigated. Traditional medicine systems such as those identified in South African tribal medicine indicated strong associations between medicinal plants and viral respiratory disease. The lack of lead discovery conducted on this and other traditional medicine systems indicates an untapped repository of ethnobotanical data that may be crucial in the rapid discovery of new drugs.<sup>46,58-60</sup>

During previous coronavirus outbreaks, plant-based agents were identified with *in vitro* activity against coronavirus species. However the transient short lived nature of these events limited the progression of these compounds to *in vivo* trials.<sup>40</sup>

## Antiviral secondary metabolites

Plant secondary metabolites such as polyphenols, alkaloids, saponins, terpenoids and carbohydrates offer a diverse array of compounds shown to exert activity against viral pathogens.<sup>40,45</sup> Flavonoids including the flavones, flavanols and flavans have a long history of known biological and antiviral activity.<sup>56</sup> Plant based polyphenols such as lignans have been identified as examples of plant based antivirals with wide ranging mechanisms. Podophyllotoxin and bicyclol are examples of plant based ligands used for antiviral purposes.<sup>61</sup> Triterpenoids have been investigated as plant based viral fusion inhibitors in Ebola, HIV and

Influenza A viruses,<sup>62</sup> which are all enveloped RNA viruses similar to SARS-CoV-2. Flavonoids have been demonstrated to be *in vitro* antiviral agents, although, like many other phytochemicals, the limiting factor in their utilisation has been the need to increase bioavailability of these agents whilst retaining antiviral activity *in vivo*.<sup>56</sup>

## Plants derivatives with activity against coronavirus species

More specifically plant-based extracts have demonstrated activity against members of the *Coronaviridae* family such as avian infectious bronchitis virus (IBV).<sup>63</sup> Phytocompounds such as terpenoids and lignoids have demonstrated activity against the closely related Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-1).<sup>64</sup> Glycyrrhizic acid derivatives have also been utilised as agents for lead development of agents against SARS-CoV-1.<sup>1,40</sup> Lycorine, an extract from *Lycoris radiate* was found to have anti SARS-CoV-2 activity, as well as anti-herpes simplex virus type 1 activity.<sup>40</sup>

## Novel plant based approaches

Other examples of antiviral plant approaches include the identification of plants that possess properties that contain RNA silencing properties that are activated in response to plant viral infection.<sup>49</sup> These plant generated small interfering RNAs (siRNAs) may be useful in the generation of prophylactic preparations to treat RNA-based pathogens, with their use supported by similar approaches being explored for the development of vaccines and new drugs for genetic disease.<sup>25</sup>

The myriad of potential plant based antiviral properties currently present a wide ranging potential for antiviral development. The diversity of their mechanisms may be the key to more universal preparations for future novel zoonotic viral disease as standalone agents or potential synergistic agents in combination with synthetic drugs phytochemicals and phytobiologicals must be part of the ongoing research landscape.<sup>60</sup> Drug optimisation and progress towards advanced *in vivo* clinical trials must be a priority in managing this and future zoonotic viral disease threats.<sup>40</sup>

## Plants in immunological management of cytokine release

Traditionally the approach to the immune effects of plant based phytochemical agents in infectious disease such as the use of *Echinanacea pupurea*,<sup>65</sup> has been to search for agents that enhance, rather than inhibit the immune system.<sup>60</sup> The cytokine storm responsible for many of the deleterious effects of COVID-19 and other related infections seen in those patients with severe responses to infection<sup>15</sup> is a unique target for phytochemical research. A recent study which backs up previous evidence of plant flavonoids as antiviral agents,<sup>56</sup> identified the potential for flavonoids of citrus fruit as potential lead agents for combating the cytokine storm generated in severe COVID-19 disease.<sup>66</sup> The specificity for the angiotensin converting enzyme 2 (ACE2) is significant as this is an identified target for ARDS treatment that is downregulated by coronavirus and is actively being explored by the conventional medicine streams.<sup>4,13,17</sup> The enhanced specificity of COVID-19 for ACE2 as the entry receptor for the virus on cell membranes when compared to SARS-CoV-1, provides even more promise than previous coronavirus outbreaks.<sup>45</sup> Previous work on Chinese medicinal herbs from the family *Polygonaceae* identified emodin, an anthraquinone compound, as being active in preventing the coupling of previous coronavirus infections (SARS-CoV-1) to ACE2.<sup>21,67</sup> The ACE2 receptor is also linked with viral entry to the respiratory epithelial cells, providing a dual purpose strategy in reducing disease from COVID-19 exposure.<sup>8,16,21</sup>

## Plants as delivery mechanisms for antiviral therapy

In addition to existing antiviral plant extracts and whole plants as antiviral sources, plant-based antiviral therapy offers a unique approach to the elimination of viral load in developing nations.<sup>68-70</sup> Delivery of therapeutic agents with plant-based foodstuffs and the novel delivery of plant-produced vaccines are two such avenues. Nutraceuticals have been proposed as potential strategies for enhanced nutrition and delivery of potential bioactives, particularly in the developing world. However, to date the limited study of plant constituents has not transferred to nutraceutical food crop studies.<sup>71</sup>

## Benefits of a plant-based approach

Plant based therapy offers cost advantages in the developing world; the inexpensive mode of production, less refined purification, storage and the shelf life of plant based agents endears itself to delivery in a low resourced world prohibitive to cold chain restrictions and development costs associated with traditional temperature sensitive vaccines and biological agents.<sup>68,69,72,73</sup> The major advantage of this approach may be the ability to harness the very people likely to benefit from this treatment approach.<sup>70</sup> Enhanced support for plant based medicine production holds a unique ability for the citizens of the developing world to benefit, not only in health outcomes, but also in economic outcomes from production.<sup>74,75</sup> This is in sharp contrast with “BigPharma” approaches to healthcare that in most instances exclude the majority from economic benefits.

## Plant based vaccines

Plant based vaccines via food stuff have been investigated for the delivery of viral antigens for vaccinations with the delivery of Hepatitis B antigens on transgenic potatoes being the first proof of concept in the delivery of immune response via food.<sup>76</sup> Plant-based lectins have been investigated as potential agents to inhibit HIV in its initial establishment of infection and other viral disease.<sup>60,68</sup> Additional studies have shown the production of antiviral lectins and proteins as vaccines in tobacco and lettuce crops as a cost effective measure for the mass production of plant based vaccines that is extendable to the wider developing world.<sup>68,69</sup>

Although the current framework for genetically modified drug delivery does not support the ethical delivery of these agents on mass in food crops, processing of such crops into lyophilised powders or tablet forms delivered as pharmaceuticals may be an ethical alternative.<sup>69,75</sup> Cold chain free chloroplast polio vaccines are touted as potential agents to replace the viral based polio vaccine.<sup>72</sup> Plant-based vaccines have been proposed as an effective method of delivering mass vaccination in a cost effective fashion due to the elimination of the need for purification.<sup>73,75</sup>

A novel approach to future viral threat management may involve the distribution of transgenic food crops to developing nations to animal food sources utilised by zoonotic disease populations.<sup>60,75</sup> Development of transgenic plant products for the delivery of vaccines in plants with known existing antiviral properties may provide a broad spectrum response to viral reservoirs particularly in the developing world.<sup>68</sup> Incorporation of vaccination, plant-based antivirals and nutritional approaches into a single food crop may provide a triumvirate approach to infectious disease control that relies heavily on pharmacognosy in its approach.

## Plants utilised in topical application for elimination of viral carriage

Current strategies to eliminate the person to person transfer of coronavirus include hand sanitation to remove viral contaminants from person to person contact and environmental transfers.<sup>18</sup> Soap and water washes are ideally utilised, however inconvenience, access to clean water

and time constraints limit the compliance levels in most instances.<sup>77</sup> Alcohol based hand sanitizer solutions are highly effective in eliminating coronavirus from the skin surface,<sup>78</sup> but again their utility is limited by compliance with application and convenience of use.<sup>19</sup> Despite their rapid action, the rapid evaporation of alcohol based sanitisers eliminates their retention on the hands and activity against recontamination between uses.<sup>77,79</sup> Overuse of hand sanitisers in healthcare workers also has the potential to increase infection rates via contact dermatitis and the loss of the protective barriers of the skin.<sup>80</sup>

Hand hygiene data in Australian hospitals reveals poor rates of hand hygiene compliance in health care workers.<sup>81</sup> Hypervigilance through auditing and education has increased compliance, although rates are still low.<sup>82</sup> This is seen in practice as missed moments of hand hygiene.<sup>81</sup> Inadequate application and contact time of alcohol based hand rubs are also an ongoing concern to the efficacy of these agents.<sup>83</sup> Compliance rates with post contact moments over pre-patient contact may also indicate a self-preservation rate of hand hygiene over the reduction of transfers to others.<sup>82</sup> Although this data precedes the hypervigilance of COVID-19, it is likely that this hypervigilance will be difficult to maintain long term once complacency sets in and people become less concerned with their personal safety. Additionally, the levels of hand hygiene exhibited by healthcare staff in an environment of known contaminant risk are unlikely to be achieved by the general public with less knowledge of and direct visual reminders of infection risks.

## Plant based sanitisers

A recent media release from a company that develops novel handwashing stations has declared the incorporation of an unknown plant-based antiviral improves outcomes in terms of viral clearance when utilizing their device.<sup>84</sup> This novel approach demonstrates a potential market for plant-based antiviral topical solutions. In addition to antiviral components, many hand sanitisers contain additional agents to increase their retention time and limit the damage of active agents to the skin. The ongoing use of petrochemical surfactants in hand hygiene solutions and soaps has raised concerns of environmental contamination, further supporting the search for biodegradable plant-based solutions.<sup>85</sup>

## Existing data on plant based sanitisers

Despite being commonly incorporated in cosmetic based topical agents, limited studies have been conducted on plant extracts as direct agents for sanitation. Green tea has been investigated for activity against influenza virus as a standalone agent for hand sanitation.<sup>86</sup> When looking at plant constituents, saponins are the most widely studied plant-based surfactants.<sup>85</sup> Saponins from *Quillaja saponaria* have been shown to poses antiviral activity against numerous viral species including HIV. *Bupleurum marginatum* and *Parisipolyphylla* are effective against influenza A and the saikosaponin constituents of *Bupleurum marginatum* have demonstrated coronavirus activity.<sup>85</sup> *In-vitro* data of these agents against the coronavirus species and specifically for SARS-CoV-1, is needed before these agents can be utilised in the place of existing surfactants.

*Aloe vera* is an established cosmetic agent as a humectant, it has been shown to poses antiviral activity against previous coronavirus outbreaks, influenza and HIV.<sup>85</sup> Essential oils such as resveratrol from grape seeds and lemon balm oil are candidates for SARS-CoV activity although the yield could make them economically unattractive for hand sanitizer use.<sup>85</sup>

A plant based topical agent incorporated in an alcohol-based hand rub may extend the time of antiviral therapy via synergism, reducing infection rates due to lapses in hand hygiene moments, whilst reducing the potential of environmental contaminants from petrochemical additives.

## CONCLUSION

COVID-19 is the most recent warning of impending zoonotic viral illness. Its dramatic impact on the general public's quality of life and the financial stability of global markets places antiviral research at the forefront of both public and government sentiment. Vaccine candidates are currently being rolled out across the globe in response to this pandemic. Financial support for research in this domain is likely to continue from both the public and private purse. Pharmacognosy has a role to play in the management of this and future viral pandemics. The support of researchers in this domain is needed to combat viral pandemics via arming clinicians with a broader range of options for prevention and treatment of viral illness on a global scale.

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## CONFLICT OF INTEREST

The author declares no conflicts of interest.

## ABBREVIATIONS

**ACE2:** Angiotensin converting enzyme 2; **ARDS:** Acute respiratory distress syndrome; **COVID-19:** Coronavirus disease of 2019; **MERS:** Middle east respiratory syndrome; **RNA:** Ribonucleic acid; **SARS-CoV:** Severe acute respiratory syndrome coronavirus species; **SARS CoV-1:** Severe acute respiratory syndrome coronavirus -1; **SARS-CoV-2:** Severe acute respiratory syndrome coronavirus -2; **siRNAs:** Small interfering ribonucleic acids.

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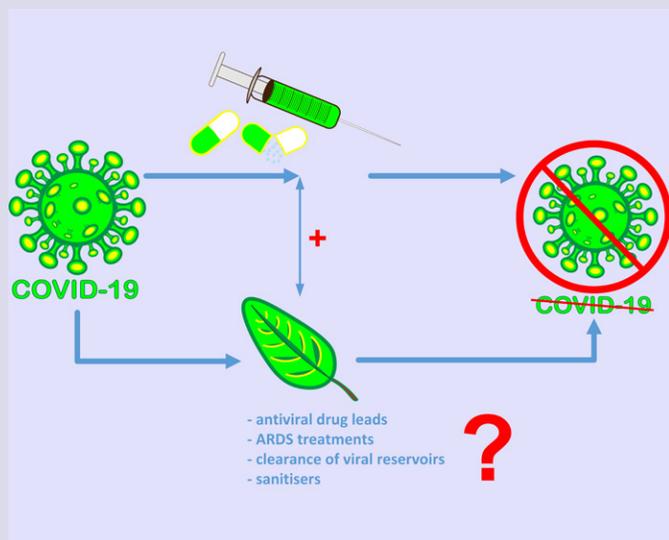
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## SUMMARY

- The COVID-19 pandemic caused by SARS-CoV-2 has triggered a rapid expansion of antiviral drug discovery.
- Vaccine development has been a primary focus of pharmaceutical and academic institutions with many vaccines currently entering the market. In order for a vaccine approach to be successful in isolation of other approaches. Vaccines must have extremely high efficacy and be rolled out to a large proportion of the global population to achieve global herd immunity.
- Antiviral drug discovery approaches are more limited with some novel agents in development and many studies investigating the re-purposing of older drugs.
- This narrative review and commentary discusses plant-based approaches; as viral drug leads, as agents for managing the cytokine storm associated with acute respiratory distress syndrome, as agents for elimination of human and zoonotic viral reservoirs and as agents in hand sanitisation.
- Plant based antiviral approaches may be beneficial in adding to the current drug discovery effort and providing adjunctive approaches to the vaccines currently entering the market. Pharmacognosy has a role to play in the management of this and future viral pandemics. The support of researchers in this domain is needed to combat viral pandemics via arming clinicians with a broader range of options for prevention and treatment of viral illness on a global scale.

PICTORIAL ABSTRACT



ABOUT AUTHORS



**Mr Sean Alcorn** has a clinical background in both Hospital and Community Pharmacy with special interest in Antimicrobial Stewardship. He is a lecturer in pharmacotherapeutics at Griffith University where he takes a keen interest in developing students to become critical thinking health practitioners. He has worked in project management in the field of Antimicrobial Stewardship and has extensive experience in antimicrobial stewardship, clinical governance and medication safety within the hospital environment. Mr Alcorn's active engagement with a network of clinical practitioners ensures he remains well versed in the challenges of clinical practice.