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## **When fear and misinformation go viral: pharmacists' role in deterring medication misinformation during 'infodemic' surrounding COVID-19**

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## **Abstract**

The world has faced an unprecedented challenge when coronavirus (COVID-19) emerged as a pandemic. Millions of people have contracted the virus and a significant number of them lost their lives, resulting in a tremendous social and economic shock across the globe. Amid the growing burden of the pandemic, there are parallel emergencies that need to be simultaneously tackled: the proliferation of fake medicines, fake news and medication misinformation surrounding COVID-19. Pharmacists are key health professionals with the required skills and training to contribute to the fight against these emergencies. Primarily, they can be a relevant source of accurate and reliable information to the public or other fellow health professionals thereby reducing the spread of COVID-19 medication misinformation. This can be achieved by providing accurate and reliable information based on recommendations given by relevant health authorities and professional associations to make sure the community understand the importance of the message and thus minimise the detrimental consequences of the pandemic. This commentary aims to summarise the existing literature in relation to the promising treatments currently under trial, the perils of falsified medications and medicine-related information and the role of pharmacists in taking a leading role in combating these parallel global emergencies.

**Key words: Coronavirus; misinformation; COVID-19; Pandemics; Pharmacists**

## **Introduction**

Our world has moved into uncharted territory as it fully succumbs to a novel coronavirus disease (COVID-19) after it was initially reported in Wuhan, China in late December 2019. COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), one of the most contagious and virulent viruses this world has witnessed in recent times. Although coronaviruses were responsible for the previous epidemics such as Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS), COVID-19 is the first one to spread to the entire globe, putting the whole world into an unprecedented level of anxiety. Unlike the previous coronaviruses, and despite having a 79% genomic similarity with SARS CoV, COVID-19 seems to transmit very rapidly and efficiently,<sup>1</sup> contributing to its global occurrence. As of April 29, more than 3 million people have contracted the virus worldwide, with nearly 220,000 people lost their lives within just four months. As a result, several countries have now implemented aggressive public health measures – including the enforcement of social distancing and total lockdowns, aiming to limit the transmission of the disease.

The clinical manifestations of COVID-19 include flu like symptoms, such as headache, fever and persistent dry cough, and atypical pneumonia that can lead to life-threatening acute respiratory distress.<sup>2</sup> While most patients with COVID-19 present with mild symptoms, this disease can cause hospitalisation, intensive care unit admission and death, particularly in older adults and those with comorbid conditions.<sup>3</sup> The case fatality rate of the disease is currently estimated at 2.7% and could be as high as 13% in older adults aged over 80 years.<sup>4</sup>

## **Therapeutics for COVID-19**

Research into potential vaccines and treatments for COVID-19 commenced immediately after the outbreak, with the aim to prevent infection, reduce the transmission and/or manage the severe outcomes of the disease. The usual process of vaccine development is a long, complex process typically takes about 6-10 years to reach the markets – but currently researchers and

regulators around the globe are working to accelerate this process. Nonetheless stopping this new virus may require a more aggressive approach. Repurposing existing drugs with good safety profiles and have activity against HIV, hepatitis C or similar virus strains might be the most feasible and timely approach. To this end, several clinical trials are currently underway, including in Australia, China, Japan, Europe and the USA to test the effectiveness of various drugs previously approved for other diseases for use against COVID-19.

The drugs under investigation aim to do either of two things: kill the virus or limit the severity of the disease to increase chances of survival. Their antiviral activities are produced by targeting one or more of the proteins that are essential for SARS-CoV-2 to bind and cause infection. To have a greater understanding of these potential drugs, it is imperative to understand how the virus works and its mechanism of transmission. SARS-CoV-2 is a ribonucleic acid  $\beta$ -coronavirus and, like SARS and MERS, encodes non-structural proteins (such as 3-chemotrypsin-like protease, helicase, and RNA-dependent RNA polymerase), structural proteins like spike glycoprotein and other accessory proteins.<sup>5</sup> The spike proteins are responsible for host cell-surface binding via angiotensin converting enzyme 2 (ACE2).<sup>6</sup> Another human protein, TMPRSS2, cleaves the spike protein, allowing the virus to fuse with the cell and start to replicate inside it.<sup>7</sup> These proteins are among targets for promising drug candidates currently under investigation for COVID-19 treatment. Importantly, most of these proteins, including the drug binding pockets of this virus, have strong similarity with those observed in SARS and MERS, highlighting the potential use of previously developed small-molecule therapeutics for COVID-19.<sup>8</sup>

Despite many pre-clinical and clinical studies on drugs against COVID-19, there is currently no evidence to make a definitive conclusion as to the most safe and effective COVID-19 treatment option. The ongoing large-scale trials on the potential treatments are hoped to reveal the most effective treatments for COVID-19. Available pre-clinical and clinical evidence on the drugs with potential activity against COVID-19 is summarized in Table 1.

**Table 1.** Summary of preclinical and clinical evidence on drugs with potential activity against COVID-19

Drug/indication	Anti-infective mechanism	Preclinical and clinical Evidence	Major safety concerns	Drug interactions
<b>Antivirals with potential activity against SARS-CoV-2*</b>				
<b>Lopinavir/ritonavir (LPV/r)</b>	A fixed dose combination medication indicated for the treatment and prevention of HIV/AIDS (HIV-1 Protease inhibitor)	<ul style="list-style-type: none"> <li>• <i>In vitro</i> and animal studies demonstrated LPV/r activity against /benefit for the treatment of MERS-CoV 2,<sup>9,10</sup> but more study is need on its <i>in vitro</i> &amp; <i>in vivo</i> activity against SARS-CoV-2.<sup>9</sup></li> <li>• A retrospective study reviewed records of hospitalised COVID-19 patients (n=323) in Tianyou Hospital, Wuhan, China from 8 January to 20 February 2020, and reported that 46% (13/28) of patients receiving LPV/r developed favourable outcomes (full recovery and discharge, progression from critical/severe to non-severe disease status, PCR positive to negative, and/or maintenance of non-severe status).<sup>11</sup></li> <li>• A retrospective study investigated duration of viral shedding in hospitalised COVID-19 patients (n=298) in Hubei Province, China, between 31 January 2020 and 9 March 2020, reporting that median duration of viral shedding was shorter in the LPV/r treatment group (n=78) than that in no LPV/r treatment group (n=42) (median, 22 days vs 28.5 days, p=0.02). Only earlier administration of LPV/r treatment (≤10 days from symptom onset) could shorten the duration of viral shedding.<sup>12</sup></li> <li>• A study conducted on hospitalised COVID-19 patients (n=298) in Guangdong Province, China between January 11, 2020 to February 11, 2020 reported that there was no difference in viral clearance time between patients who received antiviral therapy (LPVr or favipiravir, 15 days, IQR 10-19) and those who did not receive antiviral therapy (14 days, IQR 10-19). 10.7% were admitted to intensive care with no mortality was recorded.<sup>13</sup></li> <li>• A randomized, open-label trial comparing LPV/r vs standard care in adult patients (n=199) hospitalized with severe COVID-19 demonstrated LPV/r treatment did not significantly accelerate clinical improvement, reduce mortality, or diminish throat viral RNA detectability.<sup>14</sup></li> <li>• A retrospective cohort study in adults (n=33) evaluated use of LPV/r with or without umifenovir, and concluded including umifenovir</li> </ul>	Although data on the use of LPV/r (alone or in combination with other antivirals) for COVID-19 treatment is accumulating, <sup>16-18</sup> there is a need for more studies to ascertain its safety and clinical benefits in COVID-19 patients.	Extensive drug interaction profile, including with drugs metabolised by CYP3A and CYP2C19

Drug/indication	Anti-infective mechanism	Preclinical and clinical Evidence	Major safety concerns	Drug interactions
<b>Remdesivir</b> <b>Experimental drug for Ebola virus infection</b>	A broad-spectrum antiviral agent (investigational nucleoside analogue that may block viral nucleotide synthesis to stop viral replication)	<p>might delay the progression of lung lesions and lower the possibility of respiratory and gastrointestinal transmission.<sup>15</sup></p> <ul style="list-style-type: none"> <li>• <i>In-vitro</i> studies reported that remdesivir inhibits SARS-CoV-2 replication in Vero E6 cells with EC50 under 100 µM,<sup>19</sup> and it acts by inhibiting RNA synthesis.<sup>20</sup></li> <li>• A small non-controlled study on compassionate use of remdesivir reported clinical improvement in hospitalised patients<sup>21</sup></li> <li>• A phase 3 randomized, open-label trial aiming to evaluate safety and efficacy of remdesivir in patients with moderate COVID-19 (n=600) compared with standard care has begun recruiting patients.<sup>22</sup></li> </ul>	Several randomised clinical trials evaluating safety and efficacy are being conducted.	
<b>Camostat mesilate/nafamostat mesilate</b> <b>Treatment for pancreatitis</b>	Serine protease /TMPRSS2 inhibitor	<ul style="list-style-type: none"> <li>• In mice, camostat mesilate dosed at concentrations akin to the clinically achievable concentration in humans reduced mortality following SARS-CoV infection from 100% to 30-35%.</li> <li>• <i>In vitro</i> studies demonstrated that camostat mesilate can block SARS-COV-2 entry into human lung cells through inhibition of a host enzyme (TMPRSS2) that the virus uses to fuse with host cell membranes.<sup>7</sup> However, there is no sufficient data to support the use of this drug to treat COVID-19 in clinical practice.</li> </ul>	A randomized, placebo-controlled trial exploring the impact of camostat mesilate on COVID-19 Infection has begun recruiting patients (n=180) to provide key insights into the safety of camostat mesilate in COVID-19 patients.	
<b>Favipiravir (favilavir)</b> <b>Approved drug for novel influenza</b>	Inhibitor of viral RNA-dependent RNA polymerase, causing chain termination and preventing RNA elongation	<ul style="list-style-type: none"> <li>• An open level non-randomized study comparing the effects of favipiravir (FPV) plus IFN-α by aerosol inhalation (n=35) versus lopinavir/ritonavir (LPV/r) plus IFN-α by aerosol inhalation (n=45) in COVID-19 patients showed significantly better treatment effects of FPV in terms of disease progression and viral clearance.<sup>23</sup></li> <li>• A randomized open-label multicentre trial involving adult patients with COVID-19 (n=240) aimed at exploring the efficacy of conventional therapy plus umifenovir (n=120) versus conventional therapy plus favipiravir (n=120) revealed no significant difference (P=0.1396) in clinical recovery rate between favipiravir (71/116) and umifenovir (62/120) at Day 7.<sup>24</sup></li> </ul>	Several randomised clinical trials evaluating the safety and efficacy of this drug are being conducted.	
<b>Antimicrobials with potential activity against SARS-CoV-2</b>				
<b>Azithromycin</b> <b>Antibacterial agent</b>	A macrolide antibiotic with some <i>in vitro</i> activity against	<ul style="list-style-type: none"> <li>• It has been used as adjunct therapy in the treatment of viral respiratory tract infections such as influenza,<sup>28,29</sup> albeit with contradictory evidence.<sup>30</sup></li> </ul>	Risk of cardiac arrhythmias (such as QT prolongation) and psychiatric disturbances	Azithromycin causes additive toxicity with

Drug/indication	Anti-infective mechanism	Preclinical and clinical Evidence	Major safety concerns	Drug interactions
	influenza A, H1N1, Zika viruses <sup>25-27</sup> and some immunomodulatory and anti-inflammatory effects. It may prevent bacterial superinfection.	<ul style="list-style-type: none"> <li>A retrospective, single-centre case series of hospitalized COVID-19 patients (n=138) used azithromycin for antibacterial coverage,<sup>31</sup> although the available evidence is insufficient to establish safety and benefit of adjunct azithromycin use in patients with COVID-19.</li> </ul>		amiodarone hydrochloride
<b>Chloroquine</b> <b>Antimalarial agent</b>	May interfere with ACE2 receptor glycosylation thus preventing SARS-CoV-2 binding to target cells <sup>32</sup>	<ul style="list-style-type: none"> <li>Chloroquine is active against various viruses including SARS-CoV-2<sup>33-35</sup> and reported to have immunomodulatory activity.<sup>32</sup></li> <li>Currently, limited data and clinical experience is available to substantiate the efficacy and possible benefits of chloroquine in patients with COVID-19.<sup>36</sup></li> <li>Although the pharmacokinetics and toxicity profile of chloroquine is well-established in malaria treatment (the use of high dose for short period or low dose for longer duration),<sup>32</sup> additional data are needed to determine optimal dose and duration as well as toxicity profile when used in patients with COVID-19.</li> </ul>	Risk of cardiac arrhythmias, retinal damage (long term use); caution in patients with glucose-6-phosphate-dehydrogenase deficiency and diabetic patients.	Chloroquine may increase ciclosporin's concentration and risk of toxicity (creatinine concentration may increase even with low doses of ciclosporin); cimetidine reduces metabolism of chloroquine
<b>Hydroxychloroquine</b>	Hydroxychloroquine (hydroxyl analog of chloroquine) has similar antiviral mechanism as chloroquine. <sup>37</sup> This may include inhibition of viral enzymes or processes and ACE2 cellular receptor inhibition.	<ul style="list-style-type: none"> <li>Hydroxychloroquine is also active against SARS-CoV-2<sup>33,34</sup> and, unlike chloroquine, is better tolerated when used at high doses for longer duration.<sup>32</sup></li> <li>However, multiple clinical trials have already been initiated across the globe<sup>38</sup> and early findings from China reported good prognosis for patients who received hydroxychloroquine sulfate 400 mg daily for 5 days.<sup>39</sup></li> <li>A randomized, controlled open-label trial compared the efficacy of standard treatment (oxygen therapy, antiviral agents, antibacterial agents, and immunoglobulin, with or without corticosteroids) vs standard treatment plus oral hydroxychloroquine in patients in COVID-19 patients (n=68) from February 4–28, 2020. Time to clinical recovery, body temperature recovery time and the cough remission time were significantly shortened with hydroxychloroquine.<sup>40</sup></li> </ul>	Ocular effects (retinopathy),  Rarely, cardiac toxicity, severe hypoglycaemia, agranulocytosis, thrombocytopenia	Have relatively better drug interaction profile compared with chloroquine, but it may interact with drugs affecting blood glucose concentration

Drug/indication	Anti-infective mechanism	Preclinical and clinical Evidence	Major safety concerns	Drug interactions
<b>Hydroxychloroquine with azithromycin</b>	See above for information about each agent.	<ul style="list-style-type: none"> <li>• A comparative observational study designed to emulate a randomized clinical trial using real-world data collected from the routine care of hospitalised COVID-19 patients (n=181) in France compared the efficacy of standard care alone (n=84) vs standard care plus oral hydroxychloroquine (n=97) but found no significant difference in admission to ICU or death at day 7 after hospital admission.<sup>41</sup></li> <li>• Preliminary findings from a small nonrandomized study showed that patients (n=36) who received hydroxychloroquine with azithromycin had a higher percentage of negative PCR results in nasopharyngeal samples at day 6 than those who received hydroxychloroquine alone.<sup>36</sup></li> <li>• A pilot uncontrolled non-comparative observational study in Marseille, France investigated the efficacy of hydroxychloroquine with azithromycin in mild COVID-19 patients (n=80), and revealed that all except two patients (1 death, and 1 severe case) improved clinically at Day5.<sup>42</sup></li> <li>• While early research is promising, data is very limited, and more work is required to assess the clinical benefits and safety profile of this drug combination.</li> <li>• Emerging evidence suggests that the combination could have a severe QT prolongation, highlighting the need to do adequate cardiac assessment, especially coexisting conditions and use of other drugs causing QT prolongation.<sup>43</sup></li> <li>• Another study recently reported that azithromycin used alone has caused QT prolongation,<sup>44</sup> demonstrating the need for more evidence to clear the confusion in relation to the use of this combination drug and to understand the actual cause of the QT prolongation</li> <li>• <a href="#">Sarayani et al (2020)</a> analysed data from FDA’s Adverse Event Reporting System (more than 13 million cases), and concluded that Hydroxychloroquine/chloroquine use was not associated with a safety signal while azithromycin used alone was associated with TdP/QT prolongation.</li> </ul>	See above for information about each agent. Both drugs are associated with QT prolongation, <sup>45</sup> raising concerns regarding the safety of this drug combination.	See above for information about each agent.
<b>Other agents**</b>				

Drug/indication	Anti-infective mechanism	Preclinical and clinical Evidence	Major safety concerns	Drug interactions
<b>Ibuprofen and other NSAIDS</b>		<ul style="list-style-type: none"> <li>• A letter published in <i>The Lancet Respir Med</i><sup>46</sup> reported a link between use of thiazolidinediones and ibuprofen and an increased ACE2 expression, resulting in worsened outcomes in COVID-19 patients. However, as of April 1, there is no compelling published evidence to support an association between ibuprofen and poor outcomes in patients diagnosed with COVID-19.</li> <li>• On March 18, the WHO communicated, via Twitter, that there is lack of strong evidence on this issue and that it does not recommend against the use of ibuprofen.</li> <li>• Similarly, the US FDA issued a statement on March 19 that all NSAIDS, through reducing inflammation and fever, may affect the utility of diagnostic symptoms in detecting infections, but there is no scientific evidence connecting these drugs with worsening of COVID-19 symptoms.</li> </ul>	<p>GI ulceration or bleeding; salt and fluid retention, hypertension</p> <p>Renal impairment, hyperkalaemia, heart failure</p>	<p>NSAIDs may reduce antihypertensive effect of ACEIs and may increase risk of renal impairment and hyperkalaemia</p>
<b>ACE Inhibitors and Angiotensin II Receptor Blockers (ARBs)</b>		<ul style="list-style-type: none"> <li>• It is hypothesised that because human pathogenic coronaviruses bind to their target cells through ACE2,<sup>46-48</sup> increased expression of ACE2, facilitated by ACE inhibitors or ARBs, may potentially worsen COVID-19 infections.<sup>46</sup></li> <li>• Conversely, it has also been hypothesised that the use of ACEIs/ARBs could be beneficial if given to patients with COVID-19, particularly in those ACEI/ARB naïve patients.<sup>49</sup></li> <li>• There remains a lack of conclusive evidence on the benefit or harm of these drugs in COVID-19 infection. Continuation of treatment with ACE inhibitors or ARBs is recommended for patients who are currently prescribed such agents.<sup>50,51</sup></li> </ul>	<p>Renal impairment, hyperkalaemia, angioedema, hypotension, persistent cough</p>	<p>Interacts with NSAIDs, increasing the risk of hyperkalaemia and renal impairment</p>

Drug/indication	Anti-infective mechanism	Preclinical and clinical Evidence	Major safety concerns	Drug interactions
<b>Nitric oxide (inhaled)</b>	A selective pulmonary vasodilator with demonstrated benefit in the treatment of acute respiratory distress syndrome (ARDS), one of the serious complications of COVID-19. <sup>52</sup>	<ul style="list-style-type: none"> <li>• There is <i>in vitro</i> evidence of direct antiviral activity of nitric oxide against SARS-CoV.<sup>53</sup></li> <li>• Clinical trials evaluating the use of inhaled nitric oxide in the management of mild-to-moderate COVID-19 are underway.<sup>54</sup></li> <li>• At this time there is no strong evidence to support its use clinically for COVID-19</li> </ul>	Thrombocytopenia, hypokalaemia, hyperbilirubinemia	Its effect could be increased by sildenafil, leading to severe drug interactions, although there is only anecdotal evidence
<b>Ivermectin</b>	Anti-parasitic drug with anti-viral activity. Has a nuclear transport inhibitory activity may be effective against SARS-CoV-2	<ul style="list-style-type: none"> <li>• An <i>in vitro</i> study showed a potential for ivermectin against SARS-CoV-2.<sup>55</sup></li> </ul>	Safe at a dose for anti-parasitic use, but from <i>in vitro</i> study and IC50 it is not possible to achieve the required SARS-CoV-2 IC50 (2µM) even with 3 times the highest dose approved for ivermectin. Clinical safety data at these doses is not available.	Relatively safe from drug interactions point of view

\*Other antivirals active against influenza viruses such as baloxavir<sup>56</sup> and neuraminidase inhibitors (oseltamivir)<sup>57</sup> are currently under investigation for potential use in the treatment of COVID-19; \*\*Other drugs currently being evaluated for potential use in the management of patients hospitalized with severe COVID-19 include disease-modifying anti-rheumatic drugs such as sarilumab, immunosuppressive agents such as sirolimus, general corticosteroids, and high dose ascorbic acid. **NB: The information contained in the table is emerging and rapidly evolving and reflects the evidence at the time of writing this piece (April 25, 2020)**

## **Surge of Fake Medicines and ‘Infodemic’ – Parallel Global Emergencies**

Although there is no approved treatment for COVID-19, nearly 800 clinical trials have been registered by the World Health Organisation’s (WHO) International Clinical Trials Registry Platform, with over 85% of the trials originated from China.<sup>58</sup> It is likely that 90% of new entrants into clinical trials never make it to the market. The drugs being investigated range from repurposed flu treatments to failed Ebola drugs, to antimalarial agents to immunosuppressants that have been developed decades ago.

Coronavirus pandemic also fuelled a surge in counterfeit medicine sales — a parallel pandemic of fake “essential” medicines (including the COVID-19 candidate drug chloroquine and hydroxychloroquine) and other medical supplies. Since COVID-19 was declared as a pandemic, a global pharmaceutical crimes police unit has captured tens of thousands of counterfeit medicines and medical supplies claimed to cure the coronavirus. This is mainly attributed to a decline in the production capacities of world's two largest producers of medical supplies, China and India, following lockdown. After hydroxychloroquine was claimed effective for COVID-19 treatment, there was a surge in the demand for the drug and a decline in international supplies,<sup>59</sup> posing risk of drug shortages. The African nations will especially be affected if this trend continues because Indian companies supply up to 20% of all medical supplies to Africa, where the region carries a high share of global malaria burden (>90% of global cases and deaths).<sup>60</sup> Also, reports of distribution of faulty coronavirus testing kits and substandard protective gears have dominated the news amid the COVID-19 pandemic.

Another equally pressing and parallel emergency is medication information overload and misinformation surrounding COVID-19. The WHO has described that the outbreak of and response to COVID-19 “has been accompanied by a massive ‘infodemic’ – an over-abundance of information.” An ‘infodemic’ refer to the perils of excessive volume of information in relation to COVID-19 (including false prevention measures or cures) that pose concerns for the public to distinguish fact from fiction, and for government agencies to conduct evidence-based policy-making. As COVID-19 turns into a full-fledged global public health crisis, several unsubstantiated claims regarding cures and transmission and/or exposure have taken hold on the internet and social media. Such misinformation and conjecture are of great concern as they represent a serious challenge in tackling the pandemic. Moreover, medication misinformation in the absence of scientific validation can potentially spread unnecessary fear and panic,

undermining the public's willingness to follow legitimate public health advices and to take proven precautionary measures.<sup>61</sup>

The current rush to search for the magic drug without adequate safety guarantees has already become a source of medication-related misinformation, causing public confusion and panic. A classic example is the recent media announcements that hydroxychloroquine and chloroquine are the “game changers” and potential cure for COVID-19, prompting inappropriate stockpiling and use by the public. Inappropriate stockpiling of hydroxychloroquine has also resulted in substantial shortages affecting arthritis or lupus patients— conditions for which it has been proven effective.<sup>62</sup> Moreover, people in many countries are being confused into taking unproven and at times poisonous “cures” for COVID-19 including ingesting methanol (which resulted in hundreds of deaths in Iran), using cocaine, taking Brazil's chloroform and ether based drug ‘loló’, exposure to the sun or to temperatures higher than 25 °C, and widely circulated myths on social media around taking Ibuprofen (Advil, Motrin), naproxen (Aleve) and other non-steroidal anti-inflammatory drugs (NSAIDs), vitamins: C, D or a hot bath.<sup>63</sup>

### **The Emerging Role of Pharmacists in Fighting the ‘Infodemic’**

Healthcare professionals are expected to be up to date with accurate and reliable information in order to provide information with utmost accuracy and clarity. Being located at the heart of the community and easy accessibility, community pharmacies can be a valuable source of reliable and evidence-based information for consumers. Pharmacies are also among essential business sectors that continue to serve the public despite the declaration of total lockdowns in several countries. Community pharmacists are vital part of the public health response and, in many instances, are the first point of contact given the nature of access to the pharmacies. They carry a shared responsibility to keep the public and other healthcare professionals informed on emerging evidence, especially in relation to potential treatments.

In addition to their regular activities, pharmacists are well equipped to educate the community about the nature of the pandemic, symptoms, mode of transmission, promoting prevention and infection control procedures in line with the public health guidelines. Pharmacists are involved in identifying patients with symptoms and act as a point of referral at the community level. Adequate understanding of the symptoms of COVID-19 and being able to differentiate these symptoms from seasonal influenza is instrumental in early detection and referrals for further assessment, as required. This involves team-based care and proactively collaborating with other

health workers within the pharmacist scope of practice whilst performing additional responsibilities.

We have identified and discussed how pharmacists can serve the community during the fight against these global health emergencies, using the Australian system as a case in point. The Pharmaceutical Society of Australia (PSA) and The Pharmacy Guild of Australia have developed valuable practical resources that can be used by pharmacists during this pandemic.<sup>64,65</sup>

### **Stewardship of Off-label and Supportive Treatments for COVID-19**

The media suggestions on the potential efficacy of certain drugs, such as chloroquine and hydroxychloroquine, have resulted in hoarding of the drugs in many countries. In Australia, this was accompanied by an increase in off-label prescribing and concerns about the potential shortage of hydroxychloroquine. Given the limited evidence on efficacy and safety of hydroxychloroquine, the Therapeutic Goods Administration (TGA) implemented restrictions on the medical specialists that can initiate hydroxychloroquine prescribing. Further to this, TGA has released a statement highlighting the absence of approved medicines for COVID-19 treatment, therefore prescribing of any drug for this indication is considered off-label use.<sup>66</sup> Pharmacists are in the front-line to act as stewards, and at the local level, they are involved in updating the prescribers with new legislative changes implemented by the TGA. In addition to hydroxychloroquine, there has been an increased demand in relation to adjunct treatments, such as salbutamol, ibuprofen, and paracetamol as well as pressure from the public to get more refills leading to shortages at various locations across Australia. This has resulted in enforcing new limits on dispensing of prescription and sales of over-the-counter medicines to one-month supply or one unit by the TGA in liaison with the Pharmacy Guild of Australia and the PSA. Again, pharmacists are on the front line enforcing these new restrictions whilst educating consumers the need for such changes during the pandemic in order to avoid medicine shortages. It is therefore imperative for pharmacists become aware of such developments to provide evidence-based information in a timely fashion.

### **Ensuring Safety and Continuity of Service**

Pharmacists provide an essential public service in the supply of medicines and pharmaceutical care and continuing these services without interruption is even more important during the pandemic. In addition to continuing these essential services, pharmacists are empowered with extended capabilities to reduce the burden on general practitioners and support social distancing and self-isolation measures employed by the authorities. National, state and territory governments have put in place continued dispensing arrangements providing authority to pharmacists for the ongoing supply of medicines without a prescription until 30 June 2020.<sup>67</sup> This has increased responsibility of pharmacists to monitor and follow up patients, at times in liaison with their medical practitioner. In order to promote social distancing and self-isolation especially in vulnerable patients, home delivery services for Medicare subsidised medicines are implemented by the Department of Health. The Pharmacy Guild of Australia and the PSA in liaison with health authorities have provided guidance to pharmacies on how to set up these services. This programme has leveraged a previously existing payment process for pharmacy services. In addition, there is ongoing work in liaison with pharmacists, general practitioners, and state and territory authorities to enable therapeutic substitution by pharmacists in the event of a shortage. This will allow community pharmacists to substitute dose strength or form without prior approval from the prescriber, if a prescribed medicine is not available at the time of dispensing. These measures highlight the important role pharmacists can play in enabling and maintaining access to medicines for people in need throughout the COVID-19 outbreak.

### **Stewards for Seasonal Influenza Vaccination**

Given that Australia is entering the influenza season, health authorities are urging Australians to have the influenza vaccine to reduce the risk of doubling-up of seasonal influenza and COVID-19. Pharmacists in Australia are well placed with appropriate background knowledge and training to educate, encourage and provide vaccination to the public. Provision of vaccinations by pharmacists<sup>68</sup> has increased the vaccination uptake and reduced the burden on general practitioners; in the current context, this reduces unnecessary visits to general practitioners and ensures their availability to focus on other important aspects of pandemic healthcare. In Australia, when a vaccine against SARS-COV-2 becomes available, pharmacists will be a key provider in the vaccination rollout. Pharmacists are acting as stewards on the frontline encouraging the public to get their annual immunisation on time so that the healthcare system will not be over-stretched in dealing with influenza cases during the pandemic period.

In developing countries, pharmacists' responsibilities are beyond fighting medication misinformation. The International Pharmaceutical Federation (FIP) has prepared a guidance document for pharmacists on newly available evidence and recommendations,<sup>69</sup> including position statement on the safety concerns raised with some of the frequently mentioned drugs (such as non-steroidal anti-inflammatory drugs, ACEIs/ARBs and corticosteroids).<sup>70</sup> These resources should be used along with locally relevant guidelines to provide sustainable benefits for the communities. Right now, people living in these settings are facing an extreme shortage of hand sanitizers or antiseptic hand-rub products. The pharmacist can play a key role through the formulation and supply of these products from local easily accessible chemicals and promoting their appropriate application and usage e.g. through social media.

Depending on speciality and scope of practice, pharmacists can make substantial contributions in the fight against the pandemic including identifying, preventing and treating medication-related problems<sup>71</sup> managing minor ailments<sup>72</sup>, early detection and appropriate referral of possible cases of the COVID-19<sup>73</sup>, and in combating medication misinformation.<sup>74</sup> A summary of the potential role of pharmacists to fight against medication misinformation and other aspects around COVID-19 is provided below.

- Provide updated and evidence-based scientific advice on vaccines or treatments under investigation to the community and other health-care professionals.
- Provide proper counselling and appropriate information through social media or other appropriate virtual platforms which can easily be accessed by the community and establish a conducive environment to encourage the public to seek advice or clarifications on COVID-19 preventive and therapeutic measures.
- Counsel communities on therapy and medications for the treatment of minor symptoms associated with COVID-19.
- Guide the public towards authorized national and local information distribution and dissemination channels within each country.
- Participate actively in COVID-19 hygiene and infection control initiatives or strategies.
- Conduct health-education campaigns that promote the appropriate use of medication information.
- Collaborate with other health professionals, health-professional societies and associations to facilitate educational and behavioural interventions that will assist the community to

comply with standards/procedures aimed at combating the spread of COVID-19 and misleading information.

- Aid preventive measures through the preparation of sanitizers or antiseptic hand-rub products from locally available chemicals, and promote their appropriate application and usage.
- Advise the community of risks with procuring drugs from unregistered internet retail shops, in particular with the risks of falsified medicines.
- Examine products for suspicious appearance, and constantly monitor medicine product alerts.
- Confirm the reliable sourcing of drugs with their respective National regulatory authorities (NRAs), e.g. drug registration with official NRAs, this is particularly important in resource limited communities, in the shadow of a global crisis.
- Community education to reduce the risk of transmission of emerging pathogens from animals to humans in live animal markets or animal product markets including consumption of raw meat, milk or animal organs.

## **Conclusion**

Pharmacists around the globe are currently engaged in serving their communities and helping patients cope with COVID-19 pandemic. While they are faced with this unparalleled public health crisis — fighting on multiple fronts, their authorities to test and treat are inconsistent across different jurisdictions. In addition to their routine roles, pharmacists are contributing significantly towards the overall COVID-19 pandemic control. These include rapid point of care tests for COVID-19 (varied depending on jurisdictions) and vigilant surveillance measures on suspected cases; proactive steps in identifying, mitigating drug shortages, and ensuring the medicine quality; prioritized availability of up to date, reliable COVID-19 information to their communities via flyers and social media platforms; and ensuring education and home care for individuals, suspected patients, and related family members while in self isolation, including appropriate referrals for psychological support. However, COVID-19 presents the world with a parallel pandemic of falsified medicines, medical supplies and ‘infodemic’ of misinformation. While collaborative efforts and global partnerships are required to fight these pandemics, pharmacists are uniquely positioned in this battle along with other frontline health professionals.

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DAE conducted the research and wrote the first draft of the manuscript. WT contributed in initial idea development, data synthesis, writing and editing. SA, JT, KS, MS and SAB supported in writing and editing the manuscript.

## **Declaration of interests**

All authors declare that there is no actual or potential conflict of interest.

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