Coronavirus Disease 2019: A Comprehensive Review on Recent Clinical Updates and Management Tools for Pharmacists

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ABSTRACT

In the Hubei region of China, a pneumonia outbreak occurred in December 2019, which was confirmed to be caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). It quickly became known as Coronavirus Disease 2019 or simply COVID-19, a pandemic that continues to devastate countries across the world. Through this COVID-19 pandemic, pharmacists across the globe have continued to offer direct patient care and provided frontline service to society. However, while the frontline staff is heralded, they are relegated to the background and overlooked most of the time. The most reachable healthcare providers are pharmacists because they can provide direct medical services despite tight regulations and restrictions related to the pandemic. During this pandemic, the involvement of pharmacists to handle COVID-19 and its complications proved to be crucial in alleviating the burden on the already strained healthcare system. They have provided very important services such as distributing medications to patients, encouraging adherence to medications for better control of chronic diseases, consulting on minor illnesses, clarifying myths regarding COVID-19, and contributing to COVID-19 screening. The treatment or management of COVID-19 was based on initial findings but is now being updated several times based on viral mutation, different studies across the globe, etc. This review focuses on recent clinical updates and tools that would help pharmacists with a more systematic approach to properly handling COVID-19 and its complications.

Keywords: Pharmacist, COVID-19, Infodemic, OTC products, Coronil

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INTRODUCTION

On 29th December 2019, four individuals showed up at a hospital in Wuhan, China. They all had pneumonia and worked in a particular market of seafood and live animals, which was a coincidence enough to attract local health experts two days later. The Chinese authorities have alerted the World Health Organization (WHO) to a new potentially serious respiratory virus and are now well known to be responsible for millions of atypical respiratory infections worldwide¹. The disease caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), is named as coronavirus disease 19 or simply COVID-19, has quickly spread at an unprecedented rate across the world and was declared a pandemic by WHO on March 11, 2020². Unfortunately, as more has been discovered, the number of people infected with COVID-19 and dying from COVID-19 is huge. Worldwide, 97.6 million cases and 2.09 million deaths have occurred; the United States is the leading country in both categories, with 24.6 million cases and 410,383 deaths as of 22 January 2021, with figures rising every day³. These statistics are sobering. Each number represents a person—parents, co-workers, siblings, friends, and health care providers. Although a multitude of concerns remains about this disorder, scientists and health care professionals have discovered more knowledge about its pathophysiology, clinical presentation, and treatment over the past year to include evidence-based guidance⁴.

MECHANISM OF COVID-19 INFECTION

Coronaviruses earned their name based on distinctive spikes around the large, single-stranded RNA virus, which gives them the appearance of a solar corona⁵. SARS-CoV-2 is the third coronavirus to cause severe respiratory disease, after SARS-CoV, which emerged in November 2002⁶. While cases disappeared in 2004, and Middle East respiratory syndrome (MERS-CoV), which was reported in September 2012 and continues to cause sporadic yet controlled outbreaks⁷. SARS-CoV-2 structural spike proteins get attached to angiotensin-converting enzyme II (ACE-II) receptors that allow the virus to invade bronchial cells, nasal cells, and pneumocytes at early stages⁸. As viral replication occurs in the later stages of infection, the virus infects pulmonary capillary endothelial cells and the inflammatory cascade begins. The fulminant

activation of coagulation and diminution of clotting factors occurs in severe infections, most often leading to death^{9,10}. Viral transmission mostly occurs through respiratory droplets¹¹. Recent studies have shown that transmission may also occur in pre-symptomatic patients between 48% and 62% of the time^{12,13}.

Symptoms of COVID-19 in terms of common laboratory/radiologic findings have been depicted in Fig 1¹⁴. However, symptom severity can differ greatly, especially among older and younger adults as well as ethnic and racial minorities. Studies have reported that older age increases the risk of severe COVID-19 illness and hospitalization, with 8 of 10 COVID-19 deaths occurring in adults aged older than 65 years¹⁵. Older adults may have comorbid or underlying medical conditions, such as heart failure, cancer, or diabetes, that place them at increased risk for severe illness and complications of COVID-19 infection, depicted in Table 1¹⁶⁻¹⁹. Likewise, individuals with poorer socioeconomic status, especially people of color, are more likely to have untreated comorbid conditions, including asthma, diabetes, and cardiovascular diseases, which can contribute to more severe symptoms of COVID-19²⁰. These populations also experience significant variability in social determinants of health, such as lower-income, less education, and fewer options for access to quality health care. These inequities in access to health care are additional contributing factors to the higher risk of COVID-19 infection and often stem from being uninsured, holding lower-paying jobs designated as essential, and having to rely on public transportation to get to appointments²¹. Such circumstances increase an individual's risk of exposure but reduce their ability to seek timely and quality medical care²⁰. Rates of hospitalizations and death from COVID-19 have consistently been higher in locations with higher rates of ethnic and racial diversity and lower median incomes²². Across multiple studies, researchers have reported that Black Americans have been disproportionately affected by COVID-19 compared with White populations, with one study estimating infection rate among Blacks to be three times higher and mortality rate to be 6 times higher than Whites²². Further reviews have shown the factors that are associated with increased risk of more severe illness among older adult and minority ethnic and racial populations²³.

MANAGEMENT OF MILD COVID-19 SYMPTOMS

Patients can experience a spectrum of symptoms with COVID-19 and these can range from being

asymptomatic and mild cold or influenza-like symptoms that can be managed at home to more severe symptoms, such as pneumonia and hypoxia, that require hospitalization ²⁴.

Fig 1: Clinical Presentation and Common Laboratory/Radiographic Findings of COVID-19

The Centres for Disease Control and Prevention (CDC) provides several recommendations for how someone with COVID-19 should take care of themselves, including with hydration, managing symptoms with over-the-counter (OTC) products, and learning how to monitor symptoms to recognize emergency warning signs²⁵. Patients should be aware of symptoms that may require emergent attention, including difficulty breathing, persistent chest pain/pressure, delirium, difficulty staying awake, and cyanosis^{18,25}.

Patients who do not have more severe symptoms can follow quarantining guidelines and manage symptoms with self-care and OTC products²⁶. The guidelines for quarantining are being revised and updated continuously as more information on COVID-19 becomes available, so pharmacists

should reinforce that patients check for the most up-to-date recommendations²⁷.

COVID 19 AND NSAID USE

On March 11, 2020, *The Lancet* published a letter describing a hypothesis that COVID-19 binds to target cells through ACE-II receptors ²⁸. The researchers stated due to ibuprofen's properties on increasing ACE-II receptors, ibuprofen may increase a person's risk of being infected with COVID-19. This information quickly went viral with the sentiment becoming to avoid ibuprofen. Following the release of this publication, the World Health Organization (WHO) tweeted on March 18, 2020, "At present, based on currently available information, WHO does not recommend against the use of ibuprofen"²⁹.

The WHO added that between consulting with providers who are managing patients with COVID-19 as well as clinical/population-based data, no reports were found that supported avoiding ibuprofen in patients with COVID-19. On the same date, The European Medicines Agency (EMA) released a statement in which it affirmed, "There is

currently no scientific evidence establishing a link between ibuprofen and worsening of COVID-19. When starting treatment for fever or pain in COVID-19, patients and healthcare professionals should consider all available treatment options including paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs).

Tables 1: Factors Associated with Increased Risk of More Severe Illness

Factors	Associated Risks
Increasing age	<p>Person aged > 85 years are at greatest risk for severe COVID-19 illness</p> <p>Compared with adults aged 19-29 years.</p> <ul style="list-style-type: none"> Adults aged 65-74 years have 5x higher risk for hospitalization, 90x higher risk for death. Adults aged 75-84 years have 8x higher risk for hospitalization, 220x higher risk for death. Adults aged >85 years have 13x higher risk for hospitalization, 630x higher risk for death
Comorbidities	<p>Increase risk of severe illness</p> <ul style="list-style-type: none"> Cancer Chronic kidney disease COPD Heart conditions such as heart failure, coronary artery disease, or cardiomyopathies. Immunocompromised state (weakened immune system) from solid organ transplant Obesity (BML >/ 30kg/m² but <40 kg/m²) Severe obesity (BMI >/40 kg/m²) Pregnancy Sickle Cell Disease Smoking Type 2 Diabetes <p>Might be at increased risk:</p> <ul style="list-style-type: none"> Asthma (moderate to severe) Cerebrovascular disease (affects blood vessels and blood supply to the brain) Cystic fibrosis Hypertension or high blood pressure

- Immunocompromised state (weakened immune system) from blood or bone marrow transplant, immune deficiencies, HIV, use of corticosteroids, or use of other immune-weakening medicines.
- Neurologic conditions, such as dementia
- Liver Disease
- Overweight (BMI ≥ 25 kg/m² but <30 kg/m²)
- Pulmonary fibrosis (having damaged or scarred lung tissues)
- Thalassemia (a type of blood disorder)
- Type 1 diabetes

Socioeconomic background Underlying disparities in the social determinants of health including

- Limited access to health care due to lack of transportation.
- Communication or language barriers
- Inability to secure childcare or time off work.
- Lack of health insurance
- Higher risk of exposure to COVID-19 due to essential work settings

Living in multigenerational households making it challenging to follow prevention or distancing strategies.

BMI: Body Mass Index; COPD: Chronic Obstructive Pulmonary Disorder

Fig 2: NSAIDs: Timeline of Information

Each medicine has its benefits and risks which are reflected in its product information”³⁰. The following day, on March 19, 2020, the US Food and Drug Administration (FDA) issued a similar response, expressing, “The FDA is not aware of scientific evidence connecting the use of NSAIDs, like ibuprofen, with worsening COVID-19 symptoms”. All of the agencies stated that they were continuing to investigate these claims, depicted in Fig 2³¹ documents the timeline of information about the use of NSAIDs from these organizations³².

Several studies have been conducted since the reports from early on in the pandemic implicating the use of NSAIDs, specifically ibuprofen, in causing negative effects in patients with COVID-19³³. Published results have evaluated the role of NSAIDs. Yet, almost 10 months later, the debate remains at large and the findings remain the same as well: there is no conclusive evidence to avoid the use of NSAIDs, including ibuprofen, in patients with COVID-19. This started with a theoretical basis on how ibuprofen works *in vitro*, that it may upregulate ACE-II receptors, leading to an increased entry into the cells of the virus^{31,34}. At the same time, it was suggested that patients with hypertension or diabetes who were taking angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARBs) also had an increased risk, due to the same mechanism of up-regulation of ACE-II receptors³⁵.

Researchers started asking questions and leading organizations started issuing statements about the relationship between COVID-19 and NSAIDs, covering topics such as whether the use of NSAIDs (1) makes it more likely for the person to be susceptible to becoming infected with COVID-19; (2) worsens outcomes in patients with COVID-19; (3) helps manage symptoms in a patient with COVID-19; and (4) whether the evidence shows that there is no connection with the use of NSAIDs and COVID-19³⁶.

Soon after, studies showed that there was no impact of the use of ACEI or ARBs on infection frequency; some even showed there may be a potential that the opposite was true and that ACE-II receptors up-regulation was protective³⁴. Although that statement is not conclusive, it was determined that ACEI/ARBs should be continued as per usual care³⁷. With ibuprofen, the theoretical determination was made by one animal study and the thought became chronic use of NSAIDs may increase the virus penetration into cells^{38,39}. However, research that

further studied exposure to medications such as NSAIDs and the prevalence or severity of COVID-19 did not reveal any correlation with elevated rates of infection or negative outcomes^{40,41}. Another consideration was whether the use of NSAIDs could mask the symptoms of the virus. At this time, as there is no specific treatment for this virus, masking the symptoms should not be of concern⁴². A recent study suggests that ibuprofen and other NSAIDs may prevent COVID-19 complications by blocking the diffuse inflammation produced by the virus⁴³. Although this also is a scientific theory, without clinical trials in humans, it is a good example of how scientists are researching many pathways that may impact COVID-19 related transmission, infections, and outcomes.

The current evidence at-hand is not indicative in showing a link between ibuprofen causing harm in patients with COVID-19, depicted in Table 2^{38,39,42-46}. However, with the theoretical mechanisms and previous implications, some patients and health care providers may be hesitant in choosing an NSAID to treat the fever or pain related to COVID-19. The clinical guidance that is utilized in determining which medication to use remains the same. Using NSAIDs at the lowest effective dose for the shortest duration is prudent. Patients should be evaluated holistically, is taking into consideration comorbidities and renal function to determine the optimal advice on which medication to take to relieve fever and symptoms causing aches and pain⁴⁷.

Considering NSAIDs are associated with numerous adverse effects and have many precautions and contraindications as well as drug-drug interactions, it is prudent that a thorough medical and medication history is taken to ensure the patient is a candidate to use an NSAID, as a fever or pain reliever. Additionally, if a patient has been prescribed an NSAID for other conditions, it may be appropriate to continue it with a COVID-19 diagnosis, unless risk due to other considerations outweighs the benefits, which would then warrant a conversation with the patient's provider. The approach that pharmacists have always taken when choosing an OTC product for fever and pain management should be utilized in the same way. Table 3 offers a quick review of the use of these agents^{48,49}.

VACCINES TO COMBAT SARS-CoV-2

On January 11, 2020, the genetic sequence of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was published, eliciting a rush of

research and collaboration among scientists and biopharmaceutical companies. Vaccines are discovered and manufactured using a variety of methods. The New York Times Coronavirus Vaccine Tracker lists three vaccines in emergency use in the United States as of April 6, 2021. Several other vaccines have been approved for full use (in

countries other than the United States), and 22 vaccines are currently being tested in phase 3 clinical trials around the world⁵⁰. On January 2, 2021, the Central Drugs Standard Control Organization (CDSCO) approved vaccines developed by Bharat Biotech and the Serum Institute of India (SII).

Table 2: Summary of Selected Clinical Trial Results that Reviewed the Use of Ibuprofen For symptomatic COVID-19 Support

Author	Objective	Design/Method	Result	Conclusion
Sodhi, July 2020	Examined pneumonia complications in patients who had taken NSAID before the onset of symptoms were identified and assessed the quality of evidence in these studies.	A systematic review to evaluate the role of NSAIDS on the pneumonia complications	10 studies: 5 nested case-control studies, 2 population-based case-control studies. 3 cohort studies: 59,724 adults included from 4 studies; positive association between use of NSAIDs and the risk of pneumonia-associated complications reported in all studies; moderate or serious risk of confounding, misclassification of exposure, and protopathic biases in all studies.	Results should not be extrapolated as evidence of harm for NSAIDs due to the number of biases present.
Rinnott, June 2020	Examined the use of Ibuprofen in individuals with COVID-19 associated with more severe disease compared with individuals using paracetamol or no antipyretics	A retrospective cohort study examined any use of ibuprofen from 1 week before the diagnosis of COVID-19 through the disease. Primary outcomes: mortality and the need for respiratory support, including oxygen administration and mechanical ventilation.	403 confirmed cases of COVID-19; median, 45 years; 44 patients (11%) required respiratory support and 12 (#%) died; 179 (44%) patients had fever with 32% using acetaminophen and 22% using ibuprofen. In the ibuprofen group, 3 (3.5%) patients died, 9 (10.5%) required support. In the non-ibuprofen group, 9 (2.8%) patients died (P=.95) and 35 (11%) (P=1.0) required respiratory support	Ibuprofen use was not associated with worse clinical outcomes compared with paracetamol or no antipyretic
Kragholm, September 2020	Examined the risk of severe COVID-19	Registered-based study of patients with COVID-19 in	Of 4002 patients, 264 (6.6%) had ibuprofen prescription claims	No significant association between ibuprofen

	between ibuprofen prescribed and non-ibuprofen patients with COVID-19	Denmark between February 2020 and May 16, 2020, excluding patients with HF or using other NSAIDs: outcome was a 30-day composite of severe COVID-19 diagnosis with an acute respiratory syndrome, intensive care unit admission, or death.	before COVID-19. Age, sex, and comorbidities were comparable between groups. Standardized absolute risks for composite outcome: ibuprofen-prescribed versus non-ibuprofen patients were 16.3% (95% CI, 12.1-20.6) vs 17.0% (95% CI, 16.0-18.1); P = .74	prescription claims and severe COVID-19.
Abu Esba, November 2020	Prospective cohort study between April 12, 2020, and June 1, 2020. Adults consecutively diagnosed with COVID-19 were included.	Information on NSAID use was collected through a telephone questionnaire, and patients were followed up with for COVID-19 infection outcomes, including death, hospital admission, severity, time to clinical improvement oxygen requirement, and length of stay.	Risk of mortality with acute use: HR, 0.632; 95% CI, .073-5.441; P = .6758 Risk of mortality with chronic use: HR, 0.492; 95% CI, 0.178-1.362; P = .1721	Acute or chronic use of ibuprofen and other NSAIDs was not associated with worse COVID-19 disease outcomes.

HF: Heart Failure; NSAID: Non-steroidal Anti-inflammatory Drugs

Table 3: Over the counter antipyretic and analgesics

Agent	Usual dose	Clinical considerations
Adults:		
Acetaminophen (APAP) (available in a variety of dosage forms, including effervescent, dispersible, and chewable tablets, suppositories, and liquid)	• Immediate-release products: 325-1000mg every 4-6 hours as needed	AEs: skin reaction
	• Extended-release products: 650-1300 mg every 8 hours as needed	DDI: alcohol, warfarin
	• Maximum 4000mg with HCP supervision; otherwise, 3000-3250 mg as self-treatment maximum	Hepatotoxicity warning at doses >4grams/day, taking combination APAP products, > 3 drinks/day
Children:		

10-15 mg/kg every 4-6 hours		
Acetaminophen 250 mg Ibuprofen 125 mg (available as caplets)	Adults and children >12 years: 2 caplets every 8 hours while symptoms persist	Please note clinical considerations for APAP and ibuprofen. AEs: GI including dyspepsia, heartburn, nausea, anorexia, epigastric pain, ulcers, or bleeding: associated with a higher risk of MI, HF, HTN, stroke. DDI: aspirin, phenytoin, bisphosphates, digoxin, SSRI, P2Y12 inhibitors, β -blockers, ACE-I, vasodilators, diuretics, anticoagulants, methotrexate; <i>Ways to mitigate risk</i> Evaluate patients to determine if a higher risk of certain NSAID-related AEs, start at low dose/frequency for the shortest duration of time; Ulcers/stomach bleeding: risk factors include age >60 years, previous ulcer disease, concurrent use of anticoagulants, higher dose, longer duration of treatment, >/3 alcoholic drinks/day; CV risk: increase with no selective NSAIDs, higher dose, longer duration, underlying comorbidities including HTN, HF, and diabetes; The warning label states, "NSAIDs may cause an increased risk of serious CV thrombotic events, MI, and stroke, which can be fatal. This risk may increase with the duration of use. Patients with CV disease or risk factors for CV disease may be at greater risk".
Naproxen sodium (available as immediate- and delayed-release tablets and capsules)	Initial dose: 2 tablets within the first hour, then 220 mg every 8-12 hours as needed (maximum 660 mg)	

ACEI: Angiotensin-Converting Enzyme Inhibitor; AE: Adverse Effect; CV: Cardiovascular; DDI: Drug-Drug Interaction; GI: Gastrointestinal; HCP: Health Care Provider; HF: Heart Failure; HTN: Hypertension; MI, Myocardial Infarction; NSAID: Non-steroidal Anti-inflammatory Drug, SSRI: Selective Serotonin Reuptake Inhibitor

This enables the vaccines — Covishield from SII, which is based on the Oxford AstraZeneca vaccine, and Covaxin from Bharat Biotech — to be made available to healthcare workers and frontline workers in India⁵¹.

OTHER OTC SUPPORTIVE PRODUCTS

As noted, many of the symptoms of COVID-19 that appear in patients resemble other types of cold or influenza virus infection. When mild signs and symptoms of COVID-19 occur, they can be monitored at home and multiple OTC agents are available to relieve symptoms^{55,56}. Symptomatic

relief can be achieved with antipyretics and analgesics discussed previously, cough suppressants, and decongestants, as well as vitamins or dietary supplements⁵⁷. Pharmacists should always take a thorough history, think through a differential diagnosis, ensure there are no contraindications to the recommended products, and provide thorough patient education that includes details about how to safely and effectively take the recommended product, non-pharmacologic options, expected duration of use, and when it is required for the patient to contact their primary health care provider and/or go to the emergency department. At the time of this writing, there is no cure for COVID-

19, and only supportive care is available to patients⁵⁸.

Cough Suppressants

In late February 2020, a Joint Mission between the WHO and China was established to enhance understanding of the novel virus. A report of the Joint Mission's findings identified early symptoms of the disease, such as fever and dry cough⁵⁹. Coughs are classified as "wet/moist" or "dry," though their description by patients can be subjective. Coughs may be secondary to other viruses, allergies, and medical conditions, such as heart failure, asthma, or chronic obstructive pulmonary disease, or an adverse effect from medication taken. If the cough is thought to be of viral origin, including because of COVID-19, symptomatic relief of dry cough can be achieved with antitussives containing dextromethorphan, which decreases the activity of the cough reflex for symptomatic relief but does not resolve the underlying pathophysiology of the virus^{60,61}. OTC products containing dextromethorphan are available as strips intended to dissolve on the tongue, chewable tablets, lozenges, or, most commonly, liquid formulations. Pharmacists should advise patients to administer the medication according to instructions on the product labelling, with special attention to dosing values using the measuring equipment provided with liquid medications and appropriate age-related considerations. Specific education should be provided to the patient in terms of how long to use the product and how to determine worsening symptoms that may require medical attention⁶².

Decongestants

Patients may present with nasal congestion that is due to COVID-19; however, a thorough history should be taken to determine a differential diagnosis, including allergies or sinus infections that may require antibiotics. OTC decongestant medications, including pseudoephedrine and phenylephrine, may be effective in relieving upper respiratory symptoms⁶³. Contraindications and precautions to use, such as hypertension or drug-drug interactions, need to be considered before recommending these products. Specific education should be provided to the patient in terms of how long to use the product and how to determine worsening symptoms that may require medical attention⁶⁴.

Oral Rehydration Solutions

Some patients who experience gastrointestinal symptoms related to COVID-19, such as diarrhea, are at increased risk for dehydration, which can negatively affect lung function already compromised by COVID-19. The WHO recommends the use of oral rehydration products containing sodium, potassium, glucose, starch, citrate, and bicarbonate acids to maintain and restore fluid loss^{65,66}. Oral rehydration product formulas containing sodium bicarbonate or sodium citrate must meet the criteria set forth by the US Pharmacopoeia. Many oral rehydration solutions are available OTC as tablets, capsules, or powders to be mixed with water. General dosing for adults can be up to 750 mL/hour as necessary for dehydration⁶⁷. Specific education should be provided to the patient in terms of how long to use the products and what are worsening symptoms that may require medical attention. If diarrhea or the patient's dehydration status does not improve within 24 to 48 hours, it should be recommended to contact the patient's primary health care provider⁶⁸.

Coronil kit

An enormous amount of effort has been made to find a breakthrough to cure COVID-19 by some giants in every field, but it has not yet been successful. Antibiotics do not work on the virus, and current antiviral medications are unable to neutralize or destroy the virus. The most reliable way to stop the virus from infecting people has turned out to be "The Immune System"⁶⁹. Father of germ theory, Louis Pasteur once said on his deathbed, "A microbe is nothing. The terrain is everything"⁷⁰. Experts claim that if the immune system performs at its best, the speed of recovery from the infection will be greatly improved. As a consequence, improving immunity has been of the utmost significance during this pandemic⁷¹. Many organizations have shifted their attention to the production of immunity boosters. One such organization is Patanjali Ayurved Limited (PAL) in India, which has recently produced a package called Coronil kit. The coronil kit comprises three formulations, the following: Divya Coronil Tablet, Divya Swasari Vati, and Divya Anu Tali⁷². It was developed in the framework of collaborative research by the Patanjali Research Institute and the National Institute of Medical Sciences, Jaipur, India. As per Patanjali spokesperson, it is clinically approved and in just 3 days, 69 percent of patients

with COVID-19 tested negative during the trial, and 100 percent fully recovered within a week. The potency of this kit is believed to be attributed to certain potent herbal ingredients used in the manufacture of coronil⁷³. The coronil kit is prepared by adding a mixture of 100 potent herbal ingredients. A few of the main ingredients are Giloy (*Tinospora cordifolia*), Ashwagandha (*Withania somnifera*), Tulsi (*Ocimum sanctum*), Black Pepper (*Piper nigrum*), and Bhingraj (*Eclipta alba*). While all these herbs are highly capable of boosting the immune system, Giloy is the most potent natural immuno-stimulant on planet Earth. They are also effective in minimizing symptoms such as cough, cold, sore throat, and fever⁷⁴.

Claims and Controversy

At first, Patanjali Ayurved Limited claimed that this kit was a cure for COVID-19, but the Ministry of AYUSH (Ayurveda, Yoga, Unani, Siddha, and Homeopathy) in India rejected this claim because no substantial research or large-scale clinical trial was suggesting that the drug could cure COVID-19. Patanjali has been given strict guidelines that they can only sell this kit as an immune booster. With all this, Patanjali Ayurved Limited claimed that the coronil kit would be an immunity booster and would have some excellent medicinal properties, such as anti-viral, anti-inflammatory, anti-oxidant, and bronchodilator⁷⁵.

THE USE OF DIETARY SUPPLEMENTS IN COVID-19

Various dietary supplements are being utilized for the prevention of COVID-19 and/or mitigation of symptoms in those infected with the virus. A myriad of social media reports describe these supplements to be beneficial, and some companies are taking advantage of these reports by marketing with false or misleading claims. The FDA has issued warning letters against the companies that are participating in this fraudulent activity, and anyone coming across these companies or claims is encouraged to report them⁷⁶. Largely, treatment guidelines stated there are insufficient data to recommend for or against the use of these agents for the treatment of COVID-19⁷⁷. The following paragraphs will briefly review some of the more widely discussed dietary supplements in COVID-19, namely vitamin C, vitamin D, and zinc.

Vitamin C

Vitamin C is a supplement that has been touted for its use in the prevention of colds⁷⁸. One prevalent belief involves drinking orange juice to prevent or fight colds. Numerous research studies have examined the effect of vitamin C on preventing or reducing the duration of colds⁷⁸. A meta-analysis that included 29 trials and 11,306 participants found that taking vitamin C regularly did not have an impact on cold incidence. Within this review, a comparison of 31 studies that included 9745 common cold episodes determined use of vitamin C in colds was associated with reducing cold duration by 8% in adults and by 14% in children⁷⁹. Based on published trials reviewed, this meta-analysis did not conclusively show that routine use of vitamin C in therapeutic trials was effective; however, more research is warranted based on findings from regular supplementation trials demonstrating effectiveness.

Research suggests vitamin C may have an antiviral effect, immuno-modulatory effects (improving T-cell function and increasing immune-globulins), anti-inflammatory, and antioxidant effects. Numerous studies are being conducted on the impact of vitamin C in the prevention and treatment of COVID-19⁸⁰. There is evidence that shows a decrease in the duration of mechanical ventilation and shorter intensive care unit stays. Intravenous vitamin C is being used in hospitalized patients, and higher doses are utilized to meet their metabolic requirements. The recommended daily dose of vitamin C in the United States is 90 mg/day, with the upper limit being 2 grams/day⁸¹. High doses (>10 grams/day) are being utilized in inpatients and clinical trials with no serious adverse effects, although doses above 2 grams can be associated with gastrointestinal adverse effects, and doses greater than 10 grams/day may cause oxalate nephropathy, kidney stones, and interfere with the accuracy of blood glucose readings (falsely elevating them) masking potential hypoglycemia⁸². Doses should be adjusted in patients with renal impairment, and higher doses should be avoided in patients with glucose-6-phosphate dehydrogenase deficiency. In general, while the official recommendation states there is insufficient evidence for or against the use of vitamin C in critically ill patients with COVID-19, experts are stating that the potential benefit of vitamin C seems promising and is unlikely to cause serious adverse effects⁸¹. In terms of patients who are not critically ill with COVID-19, the rationale is the role of vitamin C

is unclear as these patients are less likely to be experiencing oxidative stress or inflammation^{83,84}.

Vitamin D

Vitamin D is effective in supporting the immune system in a variety of ways. It contributes to maintaining the integrity of the cell physical barrier, antimicrobial peptide expression through macrophages/monocytes, and works with dendritic cells and T cells to help with inflammation⁸⁵. Low vitamin D levels are linked with negative outcomes, including acute respiratory tract infections⁸⁴. The risk of acute respiratory tract infections was reduced with oral vitamin D supplementation, especially in those with lower baseline levels of vitamin D or who were taking daily or weekly supplements versus bolus doses⁸⁶. Recommendations from experts have suggested maintaining adequate vitamin D levels may have a role in the management of COVID-19; however, there is not sufficient scientific evidence to support this. Epidemiologic studies show a relationship between low vitamin D levels and a higher rate of infection with COVID-19, but there may be a relationship to other confounding factors as well and, therefore, cannot be deemed to be a causal relationship⁸⁷. In general, the recommended daily intake of vitamin D is age-dependent, ranging from 15 mcg/day in people aged 70 years and younger to 20 mcg/day in people aged 71 years and older⁸⁸. The Endocrine Society released a joint-guidance statement of the role of vitamin D during this COVID-19 pandemic with recommendations for individuals to get 15 to 30 minutes/day of direct sunlight exposure on the skin while being careful not to get a sunburn and obtain recommended amount of vitamin D (400-1000 IU in adults >18 years) through food and supplementation⁸⁹.

Zinc

Zinc is another dietary supplement that is often thought of in connection with the prevention and reduced duration of respiratory viruses⁹⁰. It is thought to work by inhibiting viral replication and in vitro is shown to lead to apoptosis with a zinc ionophore, such as chloroquine⁹¹. The recommended daily allowance of elemental zinc is gender-specific, with recommended values of 11 mg/day in males and 8 mg/day in non-pregnant females⁹². There are many adverse effects associated with long-term or high-dose zinc supplementation, including reversible hematologic

defects and neurologic defects that can be potentially irreversible. The current recommendations are against using zinc supplements above the recommended daily allowance for the prevention of COVID-19 outside of clinical trials⁹³.

THE ROLE OF THE PHARMACIST

It is well known and accepted that pharmacists are some of the most trusted and accessible health care professionals, which means people often rely on them to answer drug-related questions. During this time where there is a mixture of information, misinformation, and scarcity of information all at once, pharmacists must be up-to-date about COVID-19 related developments, especially about medications to treat, prevent, or mitigate symptoms. Examining the data that support or refute claims about any medication's role in COVID-19, answering questions, educating patients, advocating the appropriate use of non-pharmacologic therapies, and being the expert on the interprofessional health care team are crucial responsibilities every practicing pharmacist should uphold^{94,95}.

Recommending an Appropriate Treatment Plan for the Management of COVID-19 Symptoms

Pharmacists can apply the patient-centered Pharmacists' Patient Care Process (PPCP) to ensure patients achieve optimal health and medication-related outcomes⁹⁶. The steps in the PPCP are readily applied to counseling patients and/or family and caregivers about the management of COVID-19. Table 4 outlines the process and how it can be applied in managing patients with COVID-19⁹⁷⁻¹⁰⁰ (Table-5).

Navigating the Infodemic Era

Countless outlets dispersing excessive information about COVID-19 have given rise to an infodemic of typically unreliable information that is misleading or inaccurate. Although social media can be a beneficial way to share information, it can also be destructive when false information is passed from one person to their networks and beyond¹⁰¹. Behavioral scientists are trying to understand the infodemic phenomenon and exploring potential ways to counteract this spreading of misinformation¹⁰². While some information is blatantly true or completely false, a lot of information

that is shared among people falls in a grey, in-between area on the continuum of true and false. This information requires in-depth understanding,

context, or additional explanations to avoid inappropriate conclusions¹⁰³.

Table 4: Examples of vaccines, their platforms, attributes, doses, and manufacturers⁵²⁻⁵⁴.

Platform	Attributes	Doses	Vaccine Candidate (Manufacturer)
Whole-Virion Inactivated Vero Cell	Medium development; high manufacturing scale	2	BBV152 (Bharat Biotech)
Adeno virus vector	Medium- to-fast development; high manufacturing scale	2	ChAdOx1 nCoV- 19 (Serum Institute of India)
mRNA	Fast development speed; low- to-medium manufacturing scale	2	BNT-162b2 (Pfizer, BioNTech); mRNA-1273 (Moderna)
DNA	Fast development speed; medium manufacturing scale	2	INO-4800 (Inovio)
Viral vector	Medium development; high manufacturing scale	1 or 2	AZD-1222 Ad5-CoV (AstraZeneca; Oxford University); Ad26.COV2.S (Johnson & Johnson)
Protein subunit	Medium- to-fast development; high manufacturing scale	2	NVX-CoV2373 (Novavax)

In a published report, 48% of 8914 Americans surveyed stated that they heard “at least some [COVID-19–related] made-up news and information”¹⁰⁴. There are countless examples of false information that has spread across the United States, and there is no one person who is immune to either receiving this information and/or spreading it. Pharmacists need to recognize their role during this time in promoting accurate beliefs and encouraging safe and healthy behaviors¹⁰⁵.

In addition to the massive quantity of information, the underestimated impact of low health literacy has been highlighted during this pandemic. Health literacy is defined as the ability to obtain, process, and understand health information and services; this goes beyond the ability to read. People may be literate and still have low health literacy and are thereby unable to either comprehend or use the available information¹⁰⁶. Further information from the WHO will be outlined next to summarize ways pharmacists can help address the infodemic. Some strategies to ensure effective communication with patients regardless of their health literacy levels include using patient-friendly language, using the teach-back method, and ensuring any hand-outs

provided to the patient are developed keeping health literacy concepts in mind and are given in conjunction with verbal education. As always, pharmacists should ask patients what questions they have and address their concerns in a person-centric way¹⁰⁷.

The WHO has developed strategies for how the infodemic curve can be flattened and individuals can do their part by not sharing rumors in group chats, getting news from trusted sources, double-checking facts, and asking how the information is known to be true. All of these tactics can help contain misinformation. Patients receive information from a myriad of sources; it is the pharmacist's responsibility to discuss optimal places for the patient to go to receive accurate information and how to differentiate accurate versus misinformation. During this time of uncertainty, health care professionals also need strategies to separate what is accurate, what is inaccurate, and the in-between information. Pharmacists can use the following strategies provided by the WHO for themselves as well as patients¹⁰⁸:

Assess the source:- Who is sharing the information, and from where are they getting the information?

Typically, on websites, there is a “Contact Us” page to get this information.

Read beyond the headline:- The headlines only tell the most sensationalized part of the story. The entire article should be read for the main information.

Determine the author:- Does this person or group have expertise in the area or topic on which they are reporting?

Check the date:- Especially with this pandemic, new information is being released almost daily.

Look for the evidence:- Some articles can be opinion pieces. Credible authors use facts, additional resources, and evidence to support their claims.

Be aware of personal biases: Biases may impact the lenses through which information is interpreted.

Review the accuracy:- If the information appears dubious or there are no sources for the information, turning to a fact-checking organization to have the information evaluated can help determine its accuracy.

Table 5: Covid-19 Treatment Plan

Pharmacists' Patient Care Process Components	Application in COVID-19
Collect	Gather pertinent + and – subjective and objective findings: symptoms, temperature, comorbidities that may impact the outcomes, health maintenance (i.e. vaccinations), personal/ social history, review of systems, medication
Assess	Is the patient a candidate for self-treatment or are there exclusions present? Consider the severity of symptoms to determine if the patient needs to be seen by another HCP or go to the led: Consider comorbidities or drug-drug interactions that may be present with the treatment options.
Plan	Recommended an appropriate treatment plan that may include OTC medications for symptom relief or referral to another HCP. Discuss goals of therapy and what to do if symptoms do not improve or worsen. Stress the importance of quarantining and avoiding contact with others and self-care strategies: rest, warm teas to soothe the throat, how to sanitize high-touch surfaces, avoiding sharing personal household items, how to wash properly, the importance of social distancing and quarantine requirements.
Implement	Help select and/or verify the selected products are appropriate: connect patient with appropriate HCPs as necessary
Follow-up Monitor and Evaluate	Follow up with the patient as possible and/or let the patient know how to contact you with questions as well as stress when a patient may need to follow up with a primary care provider.

ED: Emergency Department; HCP: Health Care Provider; OTC: Over the Counter

Masks, Hand washing, Social Distancing, and Other Recommendations to Flatten the Curve

The CDC has many readily accessible resources that embrace health literacy standards on best practices for protecting oneself and others. Pharmacists can share these ideas and resources with their patients. While many of these

recommendations are well known, between people making personal choices based on their logic of risk assessment and the potential misinformation that may be influencing their decisions, pharmacists can have important person-centered conversations to help patients reduce their risk of getting or spreading COVID-19¹⁰⁹. Additionally, sometimes having a conversation with a patient will allow for them to

personalize the recommendations to their own lives¹¹⁰.

Masks

Always wearing masks in any public place continues to be a recommendation. A wide variety of masks are available, and patients should be counseled to choose masks with two or more layers and that fit securely around their nose and mouth¹¹¹. Children aged two years and younger or people who have trouble breathing should not wear masks. If a reusable mask is wet or dirty, it should be placed in a sealed plastic bag and washed as soon as possible so that it does not get contaminated with mold. Paper bags should be used for masks and needs to be stored temporarily¹¹². Masks should be washed after every use, at least daily, in the washing machine or by hand with the use of laundry detergent, and they can be dried in the dryer or hung up to air dry. The CDC includes a tutorial on how to make a mask in the most effective way using tightly woven cotton fabric and elastic¹¹³.

Hand Sanitizer

While washing hands with soap and water is the optimal recommendation to prevent the spread of the virus, hand sanitizers may be used as well for convenience and at times when hand washing is not feasible. Hand sanitizers should contain at least 60% alcohol and be rubbed on all parts of the hands and fingers until hands are dry¹¹⁴. Ensure the hand sanitizers are not on the FDA's "should not use" list. This list includes hand sanitizers that have been found to have toxic ingredients. Hand sanitizers that are packaged in food or beverage containers should be avoided as people sometimes mistake them for food or drink, which, if ingested, can be very dangerous¹¹⁵.

Social Distancing

Staying 6 feet away from people who are not of household contacts continues to be the recommendation¹¹⁶. Describing ways to practice social distancing with patients may be helpful, including guiding them to the most appropriate resources for the latest local public health recommendations, providing options for safe social activities (as social isolation can be detrimental to mental health), discussing ways to limit contact while running errands (best times to go grocery shopping

or other options to get groceries, using drive-thru or curbside pick-up), and ways to remain active and go outside while simultaneously being safe¹¹⁷.

CONCLUSION

In the battle against COVID-19, our primary defence is healthcare infrastructure, and our fighters are healthcare professionals such as pharmacists. COVID-19 has not allowed pharmacists to stop working; in fact, they have stepped up to take on additional responsibilities. As frontline workers, their efforts should not be disregarded. Their frontline efforts are desperately required to tackle the COVID-19 pandemic, particularly now that the second wave is wreaking havoc in India and other parts of the world. It is important to provide them with more facts and awareness about the disease. It would undoubtedly make them more competent and assist them in carrying out their duties, which is the sole objective of this article. Pharmacists are front-line professionals and should be treated as such and treated with dignity.

FUTURE PROSPECTIVE OF THE STUDY

As frontline health care workers, pharmacists connect with patients uniquely. During this pandemic, there have been many lessons learned and lessons that continue to be taught. When counseling patients seeking self-care for symptoms of COVID-19, pharmacists should always take a thorough history, think through a differential diagnosis, and ensure that there are no contraindications to the use of the recommended OTC product. Patient education should include details about how to safely and effectively take the recommend OTC product, non-pharmacologic options, expected duration of use, and when to contact their primary health care provider and/or go to the emergency department if symptoms worsen. Pharmacists can reinforce that patients check for the most up-to-date recommendations and provide thorough, unbiased, and evidence-based information in a way that is meaningful and applicable to each patient. The massive number of organizations and a plethora of media outlets that are releasing information by the minute are very difficult for anyone to navigate through to ensure the information is accurate and context is readily apparent. By knowing which sources to rely on, how to obtain accurate and timely information, and how to actively guide patients by providing answers and

resources to them, pharmacists can continue to embrace their roles in this pandemic.

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