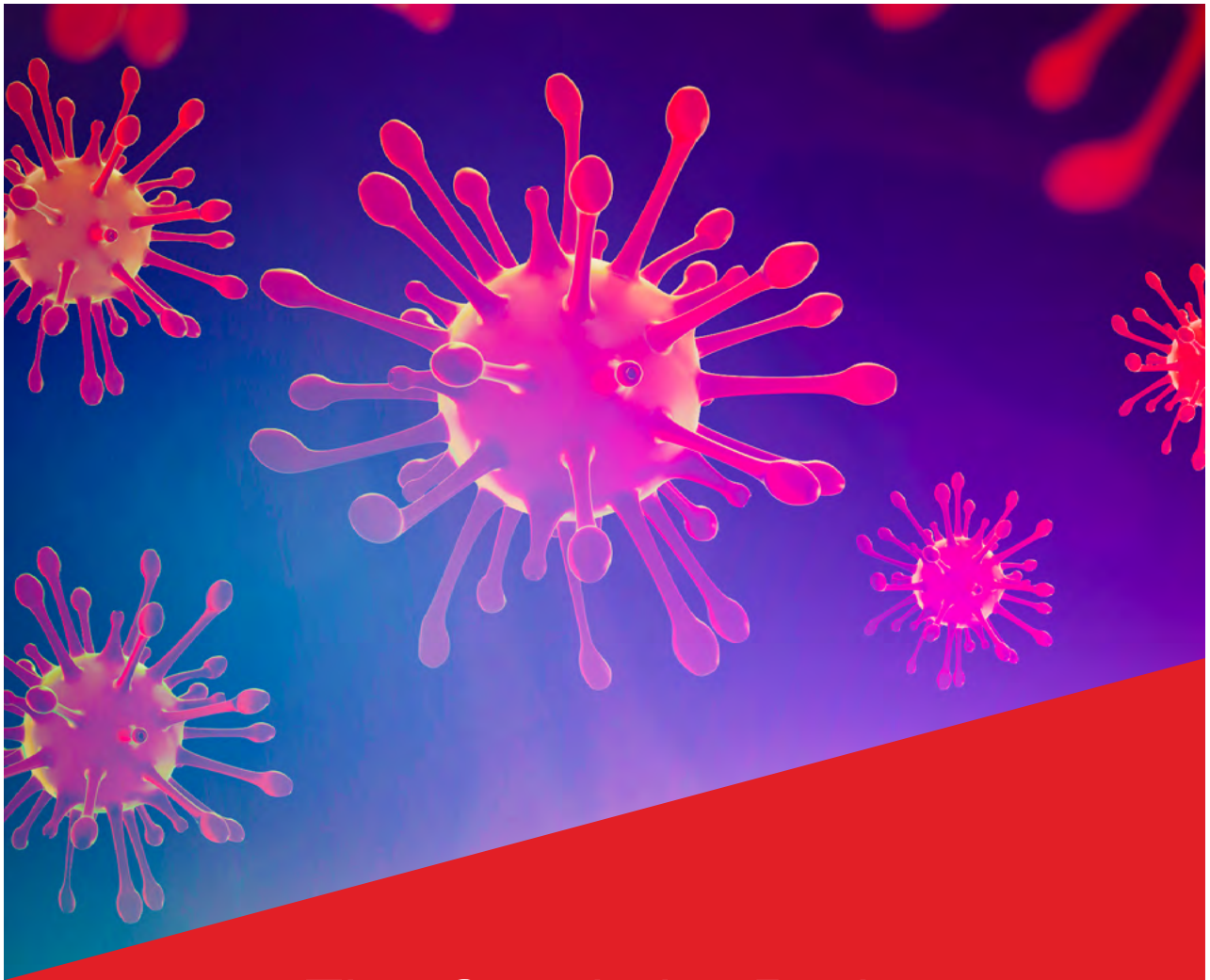




# The Good, the Bad, and the Ugly

Alternative therapies in the prevention  
and treatment of COVID-19

Hilary Henly

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## Introduction

Since the COVID-19 pandemic began, both approved and unapproved pharmaceutical drugs and products have been used to prevent infection with and treat symptoms of COVID-19. Many of these purported treatments are extremely unsafe or simply ineffective. This report discusses alternative methods that people have turned to in an effort to stave off or treat infection. Alternative medicines and non-prescription treatments may be disclosed by applicants applying for life cover, and it is important to understand the impact that they can have on health and mortality.

## Hydroxychloroquine

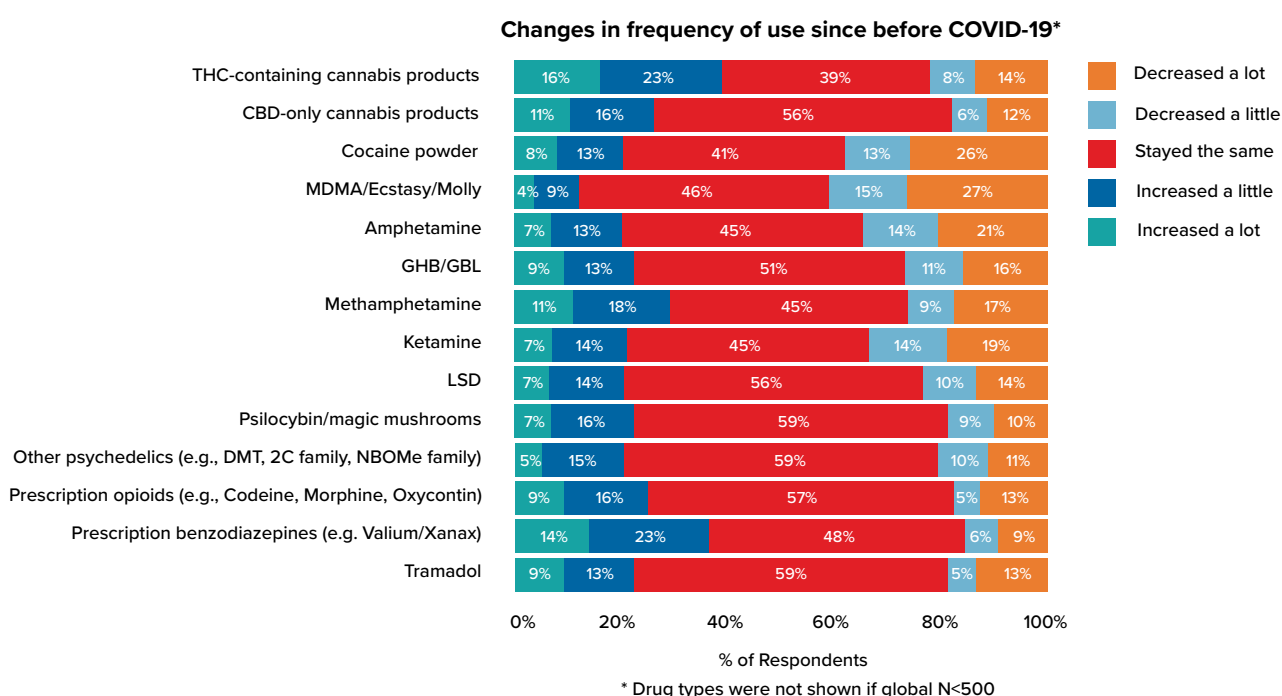
Hydroxychloroquine, a less toxic metabolite of chloroquine, is approved for use in the treatment of rheumatoid arthritis, systemic lupus erythematosus (SLE), and juvenile arthritis, while chloroquine is used to prevent and treat malaria. In March 2020 hydroxychloroquine was given an emergency use authorization (EUA) by the U.S. Food and Drug Administration (FDA) for the treatment of COVID-19, with doses often exceeding 800mg daily, more than double the daily dose used in the setting of rheumatological diseases.<sup>1</sup>

At the end of April, the FDA issued a Drug Safety Communication (DSC) recommending that the drugs not be used outside of the hospital setting due to the risk of arrhythmias. Even moderate doses of the drug can cause depression, psychosis, coma, and even death.<sup>1</sup> Of 385 COVID-19 patients who received hydroxychloroquine or chloroquine, 109 patients suffered a serious cardiac event, of which 73% had QT prolongation, 13% had ventricular arrhythmia, and 23% died.<sup>2</sup> Both the Solidarity and RECOVERY trials showed that the drugs appeared to have little or no effect on mortality in the treatment of COVID-19, and the FDA revoked the EUA on June 15, 2020. [See the COVID-19 Brief by RGA's Dr. Radhika Counsell.](#)

## Non-prescription drugs

While not specifically used for prevention or treatment of COVID-19, several large studies have examined the impact of the pandemic on drug consumption and found that substance use associated with home or private use such as cannabis and benzodiazepines has increased, while substance use associated with social events such as MDMA, cocaine, amphetamine, and ketamine has decreased. The quantity and frequency of alcohol use have increased by 43% and 36%, respectively, compared to before COVID-19, resulting in 35% of respondents to the Global Drug Survey reporting poorer mental health. However, of those who increased their cannabis use, 26% reported an improvement in mental health.<sup>3, 4</sup>

**Figure 1: Global Drug Survey COVID-19 special edition key findings report<sup>4</sup>**



## Methanol

The pandemic caused a huge spike in demand for ethanol as a topical antiseptic, which has led to its being unscrupulously replaced by methanol in hand sanitizers and alcoholic drinks. Ingesting hazardous and toxic chemicals such as methanol can lead to blindness, organ toxicity, and poisoning.<sup>5</sup> Per the FDA, methanol is not an acceptable ingredient in alcohol-based hand sanitizer (ABHS), which should contain at least 60% ethanol or 70% isopropanol instead. The World Health Organization (WHO) states that ABHS should be made up of 80% ethanol or 75% isopropanol, 1.45% glycerol, and 0.125% hydrogen peroxide.<sup>6</sup>

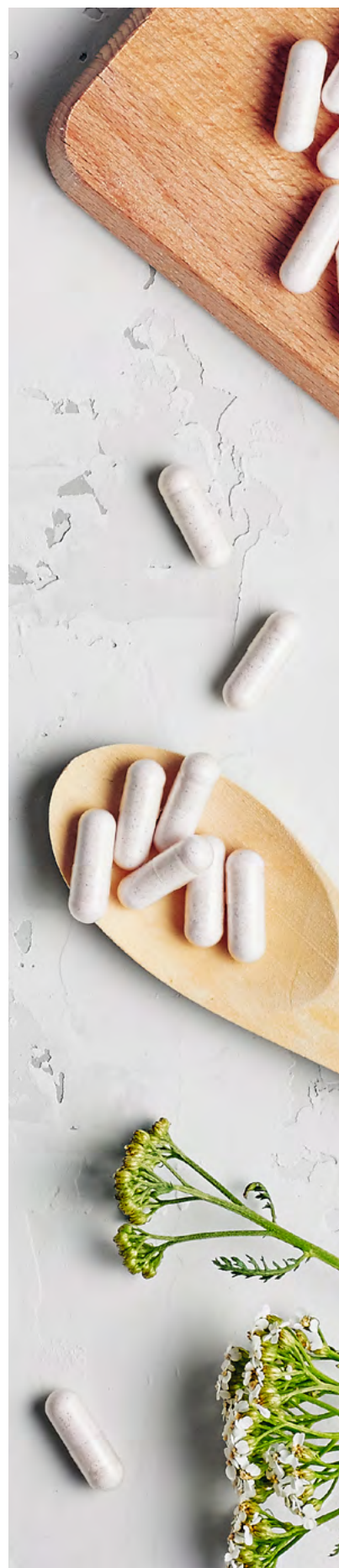
Although symptoms of ethanol and methanol poisoning are similar, methanol can cause anion gap metabolic acidosis (when the body produces too much acid), seizures, and blindness and can ultimately be fatal. Laboratory-based findings include elevated anion gap levels (normal = 3-10 milliequivalents per liter [mEq/L]), low serum bicarbonate concentrations (normal = 22-28 mEq/L), and low blood pH (normal = 7.35-7.45).<sup>6</sup>

In Iran, where selling and consuming alcohol is illegal, misinformation that drinking alcohol can protect people from COVID-19 led to an upsurge in sales of black-market alcohol. As a result of drinking methanol-based alcohol, more than 5,000 people were poisoned and/or suffered permanent visual damage, and over 700 people died as a result between February 20 and April 7, 2020.<sup>7</sup>

## Herbal medicines

There has been a significant increase in the number of people consuming herbal medicines to prevent or treat COVID-19 since the pandemic began. Herbal products are used worldwide to alleviate symptoms of or treat disease, but many people are unaware of the potential harmful effects of some of the ingredients in these products. While some herbal compounds demonstrate antiviral activity, they can also contain other active ingredients that are not fully understood. Herbal products have been found to contain undeclared plant or animal material, as well as pharmaceutical ingredients such as warfarin, dexamethasone, diclofenac, cyproheptadine, and paracetamol, and heavy metals such as arsenic, lead, and cadmium.<sup>8</sup>

In April 2020, China announced that three herbal drugs, Lianhuaqingwen capsules, Jinhuaqinggan granules, and injectable Xuebijing, had been approved for use in the treatment of COVID-19. It was claimed that they could relieve symptoms and reduce the severity of disease, but these findings were unsupported by any clinical trials. Elsewhere, the Ministry of AYUSH (Ayurveda, yoga and naturopathy, unani, siddha, and homeopathy), which is responsible for alternative medicine systems in India, has promoted the use of traditional medicines to treat COVID-19. Guidelines issued to traditional practitioners were subsequently challenged by the Indian Medical Association, as they were unsupported by any clinical evidence to show that traditional medicines were effective against COVID-19. Overconsumption of such products can cause gastric upset and other side effects such as low blood pressure and hyperthyroidism.<sup>9</sup>



Turmeric, a product of the *curcuma longa* plant, has been used in Ayurvedic traditional medicine for centuries and is a widely used spice in South Asian and Middle Eastern cooking. Curcumin, an active compound of turmeric, has been reported to have anti-inflammatory, antibacterial, and antiviral activity and be beneficial against influenza A virus, HIV, enterovirus 71 (EV71), herpes simplex virus, hepatitis C virus (HCV), and human papillomavirus (HPV). Laboratory studies to date have shown that curcumin inhibited the growth of SARS-CoV-2 and demonstrated protective effects in cases of acute respiratory distress syndrome (ARDS) by enhancing the function of regulatory T-cells<sup>10</sup>

Cannabidiol (CBD) is being investigated as a potential therapy in the treatment of ARDS in adults with COVID-19. A recent study which mimicked the symptoms of ARDS in mice showed that CBD treatment improved oxygen levels and reduced inflammation and lung damage. Levels of apelin, a peptide known to reduce inflammation, fall during COVID-19 infection, but the study found that apelin levels increased 20 times when CBD was administered.<sup>11</sup>

Other plant-based extracts such as oleandrin, liquorice, and *nigella sativa* have been investigated for their potential antiviral activity, but overconsumption of these substances can cause potassium levels to fall, blood pressure to rise, and ultimately lead to heart failure and death.

### Vitamins, minerals, and probiotics

Vitamins and minerals can help maintain a healthy immune system; however, there is little evidence to date to show that when there is no deficiency, taking extra multivitamins improves any immune response in fighting off infections.

A 2013 Cochrane review found that high doses of vitamin C administered to adults showed no consistent effect on the duration or severity of the common cold. Normal plasma vitamin C levels range between 0.6 and 2 mg/dL, which can be maintained on a daily intake of about 0.1 g/day. In fact, high levels of vitamin C can lead to the development of kidney stones. Vitamin C levels are often depleted in critically ill patients, and a recent meta-analysis published in the *Journal of Intensive Care* in 2020 found that administering vitamin C to critically ill patients shortened the length of mechanical ventilation on average by 14%. In five of the studies included in the analysis, a dosage of 1-6 g/day of vitamin C shortened ventilation time by an average of 25%.<sup>12</sup>

Vitamin D is made by the body in the presence of UV light and is obtained from foods such as fish and fortified milk products. The recommended daily adult intake is 15-20 micrograms (mcg)/600-800 international units (IU). The best measure of vitamin D in blood levels is in a form known as 25-hydroxyvitamin D, described in either nanomoles per liter (nmol/L) or nanograms per milliliter (ng/mL), where 1 nmol/L = 0.4 ng/mL. Levels below 30 nmol/L (12 ng/mL) are too low for bone or overall health, and levels above 125 nmol/L (50 ng/mL) are regarded as high. Levels of 50



nmol/L or above (20 ng/mL or above) are recommended for most people. Several studies have shown that low vitamin D levels are linked to a higher risk of respiratory infection and severe symptoms of COVID-19. Grant et al.'s study suggested that the risk of contracting COVID-19 could be reduced in people with vitamin D deficiency when vitamin D<sub>3</sub> concentrations were raised above >40-60 ng/mL (100-150 nmol/L).<sup>13</sup> However, a recent study by Murai et al. on the effect of vitamin D<sub>3</sub> supplementation versus placebo in patients with severe COVID-19 found that it did not significantly reduce length of hospital stay (HR 1.12) or confer therapeutic benefits on the rate of mortality (7% versus 5.1%), admission to the intensive care unit (ICU) (15.8% versus 21.2%), or mechanical ventilation requirement (7% versus 14.4%).<sup>14</sup>

Minerals such as zinc play a supportive role in the immune system but taking unnecessary additional zinc over a long period of time can lower immunity and cause low levels of copper and high-density lipoprotein (HDL) cholesterol. Elderly people are often zinc-deficient and this can be a risk factor for developing pneumonia.<sup>15</sup> Barnett et al. reported that patients with serum zinc concentrations of >70 micrograms per deciliter of blood (µg/dl) had a lower incidence of pneumonia, lower duration of disease, and less need for antibiotics than patients with zinc concentrations <70 µg/dl.<sup>13</sup> A recent study of patients admitted to a Barcelona hospital with COVID-19 found that serum zinc levels lower than 50 µg/dl at admission were associated with worse symptoms, longer duration to reach stability (25 days versus eight days), and higher mortality (21% versus 5%) than those whose zinc levels at admission were >50 µg/dl.<sup>16</sup>

Recently, colloidal silver products have been fraudulently promoted as health supplements that can boost the immune system, fight infection, and treat COVID-19. When it is consumed orally over months to years, it can cause skin discoloration and serious organ damage. Colloidal silver can also interact with prescription drugs such as penicillamine, antibiotics, tetracycline, and levothyroxine.<sup>17</sup>

Probiotics may have a role to play in a prevention strategy against COVID-19 and are potentially beneficial to people suffering from respiratory infections. The National Administration of Traditional Chinese Medicine and the Chinese National Health Commission have recommended the use of probiotics to control coronavirus infection, and a number of studies have been registered on ClinicalTrials.gov (a database of clinical studies conducted globally) to evaluate the efficacy of probiotics in COVID-19.<sup>13</sup>

### **Nasal saline irrigation and gargling**

The SARS-CoV-2 virus attaches to the upper respiratory epithelium and replicates in the throat, hence saline (salt) water gargling and nasal saline irrigation (NSI) may have a role to play in reducing viral transmission and severe symptoms of COVID-19. Gargling with saline water targets infectious organisms in the pharyngeal mucosa, while NSI is more effective against pathogens in the nasal mucosa. Both saline water gargling and NSI at concentrations of 1.5-3% have been shown to help protect against the common cold, and recent laboratory tests demonstrated that a 1.5% saline solution inhibited replication of the SARS-CoV-2 virus.<sup>18</sup>



A recent laboratory study on the use of saline solution in the prevention of SAR-CoV-2 in Brazil found that a 1.2% solution inhibited virus replication by 90%, and a 1.5% saline solution inhibited 100% viral replication in vitro, suggesting that it could be used as a prophylaxis and an alternative treatment for COVID-19 patients.<sup>19</sup>

There has been some discussion about the use of povidone-iodine, better known as betadine, as a nasal irrigation solution or gargling medicine. Betadine is sold as a gargling solution in Canada and as an antiseptic in Japan and is used to prevent colds and flu. In the U.S., it is sold as a skin disinfectant, but is not suitable for gargling.

The Japanese government strongly encourages gargling with betadine as a measure against COVID-19 infection. A small Japanese trial in a group of 41 patients with mild symptoms of coronavirus found that gargling with diluted betadine four times daily reduced the number of those testing positive after four days to 9.5%, compared with only 40% for those who gargled with water alone.<sup>20</sup> A Malaysian trial on viral clearance of SARS-CoV-2 among COVID-19 patients found that gargling with 1% povidine-iodine for 30 seconds three times a day achieved viral clearance of SARS-CoV-2 at day four and that the virus was still undetected at day 12.<sup>21</sup>



### Ultraviolet (UV) light

Using ultraviolet (UV) light as a preventative method against COVID-19 can lead to skin damage and increases a person's risk of developing skin cancer. UVA is primarily responsible for skin ageing, while UVB damages the DNA in skin cells, leading to sunburn and skin cancer. A third type, UVC, is known to destroy genetic material in humans and in viral particles and has been used for decades as a method of sterilization to kill microorganisms and to sanitize drinking water. China is currently using a form of UVC to sterilize public transport vehicles in the fight against COVID-19, while Chinese banks are using it to disinfect money. Studies to date have shown that it can be harnessed to prevent viral particles from making copies of themselves, with a new type of UVC called Far-UVC reported to kill flu viruses suspended in the air. It has not yet been tested in humans, and it is too early to know whether Far-UVC can kill coronavirus.<sup>22</sup>

## Conclusions

Currently, only a limited number of measures are considered effective against the SARS-CoV-2 virus, but there is some evidence to support the use of dietary therapy, herbal medicine, and saline water gargling and nasal irrigation in the prevention and treatment of COVID-19. While many of the products and treatments discussed above are approved for use in specific circumstances, others have been used outside the purpose for which they were intended, which has resulted in serious illness and death.

Insurers should be aware of the health complications that can result from the misuse of products and perceived remedies in the prevention and treatment of COVID-19 and pay close attention to any blood test results and disclosures around supplements and non-prescription therapies. ■

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