

## Use of herbal drugs to treat COVID-19 should be with caution

On April 14, 2020, a Chinese official announced at a press conference that indications of three patent herbal drugs were approved to be expanded to include COVID-19 symptoms.<sup>1</sup> This included Lianhuaqingwen capsules and Jinhuaqinggan granules for mild conditions, and Xuebijing (injectable) for severe conditions.

These drugs are widely used to treat COVID-19 in China. The official claimed the patent herbal drugs can effectively relieve symptoms, such as fever, cough, and fatigue, and reduce the probability of patients developing severe conditions, but without giving further details.<sup>1</sup> So far, no high-quality, rigorously peer-reviewed clinical trials of herbal drugs have been reported in internationally recognised journals. The approvals, based on in-vitro investigations and anecdotal clinical data, will probably lead to several worrisome consequences.

First, safety is the top priority. Advocates argue that herbal drugs are widely used and safe, but the truth is that all drugs carry risks. In the 1990s, Vanherweghem and colleagues<sup>2</sup> reported that some women who followed a slimming herbal remedy developed rapidly progressive renal failure and urothelial carcinoma. Further investigations highlighted the role of aristolochic acid, a compound found in many traditional herbs.<sup>2,3</sup> Certain batches of an injectable herbal drug called Xiyanping, which is recommended by the Chinese Diagnosis and Treatment Protocol of COVID-19,<sup>4</sup> have already been recalled after reports of adverse effects.<sup>5</sup> Although these patent herbal drugs have been used clinically for several years, when we apply them to a novel disease like COVID-19, especially in combination with other antivirals, antibiotics, and immune

suppressants, the safety should be cautiously evaluated.

Second, more evidence is required through controlled clinical trials to support the efficacy of these herbal drugs. Many traditional medicine practitioners believe that herbal remedies cannot be tested because they are tailored to each individual's syndromes. This argument is simply not convincing. Because the patent herbal drugs are produced in advance of any treatment and their composition is fixed, clinical endpoints including mortality, time to clinical improvement, and number of days in an intensive care unit can be used to evaluate the efficacy of the herbal drugs for COVID-19. Standardised trials might have methodological challenges, consuming time and effort, but that should not be the reason for lowering safety and efficacy standards. Thousands of years of usage and faith cannot be taken as evidence for efficacy of traditional herbs.

Third, the basic molecular mechanism is obscure. Lianhuaqingwen capsules have been shown to have wide-spectrum antiviral effects and anti-inflammatory activities,<sup>6,7</sup> but the active ingredients and the underlying mechanism of action are unknown. Herbal drugs usually contain many active ingredients, and it is important to better understand which ingredients are functional, and how they work. Limited experimental cell cultures and animal studies cannot guarantee safety and efficacy.

Finally, the public can easily purchase herbal drugs without a doctor's prescription. Driven by the claim that some patent herbal drugs can effectively treat COVID-19, some patients with flu symptoms who fear quarantine measures are likely to self-medicate with herbal remedies and avoid going to hospital, thus delaying the proper diagnosis and treatment of the disease, and hampering the government's testing, tracing, and quarantining efforts. At the end of January, 2020, rumours circulating on

social media suggested that a patent herbal drug called Shuanghuanglian, which contains honeysuckle and forsythia and is used routinely in traditional medicine to treat influenza and the common cold, helps ward off or even cure COVID-19. Millions of people nationwide crowded into drug stores to buy the herbal drug as a just-in-case remedy.

The current COVID-19 pandemic is an unprecedented challenge for the Chinese Government and the general public. Doctors and researchers are desperately seeking a proven cure for it. When the conventional drugs such as lopinavir, ritonavir, chloroquine, and hydroxychloroquine are not as effective as expected,<sup>8,9</sup> screening potential active components from traditional herbal medicine is a viable strategy that should not be dismissed. My colleagues and I have previously called for more attention to testing traditional herbal medicine for the treatment of COVID-19,<sup>10</sup> but a rushed judgment without sufficient scientific evidence should be cautioned against.

Given the formidable morbidity and mortality of COVID-19, it is understandable to see emergency use of unproven drugs, but the approval of a new indication for herbal drugs should still build on evidence. In the past decades, the Chinese Government has invested huge sums of money to promote the modernisation and standardisation of traditional medicine, carrying out sustainable basic and clinical research to get international recognition, but the rushed approval seems to be a backward step. The attempt to develop rigorously tested drugs from traditional herbal medicine should not be given up. It is the only way to protect our vulnerable patients.

I declare no competing interests.

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## Steam inhalation and paediatric burns during the COVID-19 pandemic

Steam inhalation is traditionally used as a home remedy for common colds and upper respiratory tract infections. The evidence base of the practice is weak, with unproven theories that the steam loosens mucus, opens nasal passages, and reduces mucosal inflammation, or that the heat inhibits replication of viruses.<sup>1,2</sup>

Scald injuries are the commonest cause of burns in children. Every day, more than 100 children present to the emergency department with burn injuries in the UK.<sup>3</sup> Since lockdown measures were implemented

last month, our Burns Centre at Birmingham Children's Hospital, Birmingham, UK, received a 30-fold increase in the number of scalds directly resulting from steam inhalation. The mechanism is most frequently accidental spillage of boiling water from a bowl or from a kettle. Children have occasionally been left unsupervised.

On average, our unit admits two patients per year with scalds related to steam inhalation. Over the past month alone, we have admitted six children with burn injuries due to this mechanism, with the youngest child aged 2 weeks, and the most severe case involving 8% of the child's total body surface area, requiring excision and skin grafting.

We surveyed Burns Services across England. With an 86% response rate, we found that 50% of centres have had an increase in scalds relating to steam inhalation. This correlated with regions of England with higher prevalence of COVID-19 (London and South East; West Midlands; North West). Two thirds of centres reported an association with Asian ethnicity (Indian, Pakistani, Bangladeshi, or Other).

The common misconception is that steam inhalation is beneficial in preventing and treating respiratory tract symptoms. Social media and home-made tutorials from unverified sources have a role in misleading parents into practising this dangerous habit.

Studies have shown that there is no additional symptomatic relief from the use of steam inhalation therapy to treat the common cold.<sup>1,4</sup> However, a survey of general practitioners in 2016 showed that 80% of general practitioners have recommended steam inhalation as a home remedy to their patients.<sup>5</sup>

Steam inhalation is a hazard to children. Resulting scalds can ultimately lead to hospital admission, surgery, and life-long disfigurement. Parental education is paramount to preventing these injuries. Clinicians should actively discourage steam inhalation and educate parents about alternative treatments for their child.

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## Health inequity during the COVID-19 pandemic: a cry for ethical global leadership

Widespread reports of disproportionate impact of the COVID-19 pandemic among already vulnerable communities worldwide, from New York City to New Orleans and Chicago, to the shocking pictures of bodies lying in the streets in Ecuador, represent a prelude of the impact in low-income and middle-income countries, home to more than 80% of the world's population. Disadvantaged people are at higher risk of infection and death from COVID-19, and they have less access to care due to systems that treat health as a commodity and not a human right. Furthermore, most health-care systems are not prepared to handle a pandemic of this magnitude. Overwhelmed European and US systems are ominous reminders of the challenges faced in poor countries.