

Medical Approaches to COVID-19 in The People's Republic of China: A Cross-Pollination of Traditional and Modern

Jesse Eugene Hoover, DOM, MS, Dipl OM

Co-Founder

erbcare, LLC

Santa Fe, NM 87505

Tel: (505) 690-9317

E-mail: jesse.eugene.hoover@gmail.com

Author Note

The opinions expressed herein are those of the author alone and do not necessarily reflect the opinions of any organization the author serves. The author has no financial conflicts of interest.

Abstract

Herbal formulations from traditional Chinese medicine have been used extensively to treat and prevent COVID-19 within the People's Republic of China (PRC). These treatments principally take place in a hospital setting and are used integratively with modern medical treatments. There is growing scientific evidence that traditional Chinese medicinals, in isolation and in combination, can address important biological aspects of acute, respiratory diseases, including COVID-19. Some of the most challenging aspects of COVID-19, such as “cytokine storm” and abnormal blood coagulation, may be mitigated with traditional medicinals, using a traditional approach. The traditional approach, while different from Western methods, is nonetheless gaining support from contemporary medical research. Traditional Chinese formulae appear to function through a complex, multi-target approach. Network pharmacology, informed by omics technology, is providing evidence that these formulations may well do what they are purported to do and more. By engaging traditional medicinals via modern research, patient narratives are becoming associated with actual biological events.

Keywords: COVID-19, Severe Acute Respiratory Distress Syndrome, cytokine storm, blood coagulation, traditional Chinese medicine, Chinese herbal medicine, network pharmacology, omics technology

Introduction

At the turn of the 20th century, there were more books written about Chinese medicine than all of the books published in the English language.

— Paul Unschuld
Historian of East Asian Medicine

As of mid-March 2020, reports from Hubei, China, indicated that 91.6 % of patients diagnosed with COVID-19 received traditional Chinese medicine (TCM). That number was slightly lower than the national figure of 92.4 % of patients, all of whom received Chinese medicine to treat COVID-19 (Zhang, 2020). These numbers reveal the extent to which China has relied on traditional medicine during the global pandemic.

This may be surprising to medical physicians and researchers in the United States and Europe, where traditional “remedies” have been removed from hospitals and clinics. In China, nearly every hospital has a robust department of herbal medicine that is used across the entire spectrum of conditions treated, either cooperatively with contemporary modern medicine, or as an independent and stand-alone therapy.

To be sure, there is a split within the consciousness of the Chinese people as to whether they are traditional or modern, and it naturally rolls over into healthcare. For example, until the COVID-19 outbreak, traditional medicinals were mostly preferred and used by older generations, while young Chinese people gravitated toward modern pharmaceuticals. However, new science could potentially be closing this schism. While China has been pursuing research in traditional medicine since the 1970s, it is only in the last 20 years that this program has greatly accelerated, both in terms of quality and quantity of published research. In 2000, very little high-quality research was available. Today, it has become the norm in both basic research and clinical trials (Moses *et al.*, 2015; Ali *et al.*, 2019; Potash, 2015), but also in terms of experimental research done with omics technology, that is, the capacity to determine how cells are responding, en masse, to the application of traditional herbs and formulae, especially in terms of gene expression. As has been commented in *Nature*, “As modern medicine becomes more personalized, using biological and genetic markers, it is inadvertently developing the tools to better test traditional medicines” (Grayson, 2011).

While many have noticed that China has reached a tipping point economically, very few have noticed that it is also reaching such a moment medically. While we struggled in the West to find anything that would slow the progress of COVID-19, in both individual patients and the general population, China was arguably far ahead. They quite literally have hundreds of anti-viral medicinals that are worth the attention of doctors and researchers, and they were practically and intellectually ready to apply a portion of them during the present crisis. However, the medicinals used are not the most important portion of China’s present achievement. Rather, it is the approach.

A Traditional Approach to COVID-19

In the West, practitioners have a clear sense that medicine prior to the twentieth century is archaic, which is another word for worthless. This is not true of China, where ancient medical texts are studied vigorously and applied daily. Their view is that the indubitable value of current medical treatments does not automatically and necessarily diminish the importance of pre-twentieth century approaches, which are, themselves, founded on empirical observation, a developed theoretical understanding, practical application, and a tradition that extends unbroken into prehistory. The stance of China is neither for Tradition nor Modernity but for both. Treatment protocols are oriented towards the integration of these disciplines, and physicians have a willingness to use both sets of tools (Huang *et al.*, 2020). However, the West knows a great deal about the modern approach, so perhaps it is the traditional approach that needs greater illumination.

This tradition dictates that patients are best served when their illnesses are differentiated into patterns of manifestation and treated accordingly. It is an approach that might be called “individualized.” However, the tradition also demonstrates that important, broadly effective formulations can be developed. Both of these philosophies (individualized treatment and broadly effective formulations) have been implemented in the current crisis.

The National Health Commission (NHC) of the People’s Republic of China (PRC) created a national guide for treatment entitled *Guidance for Corona Virus Disease 2019*, in which they make specific recommendations of herbal formulations to be used. However, this guide simultaneously recognizes that appropriate treatment will vary according to “disease condition, local climate, and physical conditions” [i.e., individual disease manifestation, living environment, and individual constitution].

In the United States, physicians typically follow “standards of care” when treating their patients. However, the specific language used by the NHC’s document is that doctors “can refer” to recommendations. This document assumes a great heterogeneity among physician approaches and it also defers to individual physician choice when engaging the specifics of individual patients. Physicians are given tremendous leeway within Chinese medicine because there is a tacit assumption that no patient is truly average. Even if physicians use the specific formulations recommended by the NHC, it is also their responsibility to modify these formulas depending on how a patient actually is. If, for example, a patient is already suffering from a variety of health complaints prior to contracting COVID-19, it is considered highly beneficial if these complaints are factored into the broad picture of their treatment. It is fundamental to this system of thought that pre-existing problems alter the course of future illness. As a result, doctors of Chinese medicine are expected to use formulations and herbs gracefully and flexibly.

Table 1 shows the various patterns of COVID-19 manifestation, all encoded in the language and theoretical perspective of Chinese medicine. This notion of “patterns” is often compared with our own notion of “syndromes,” although they are really quite different. A syndrome is defined when a disease diagnosis is lacking. Within Chinese medicine, though, patterns are thought to be the cornerstone of diagnosis. Like syndromes, a patient need not have every symptom of a pattern to be diagnosed with it. However, unlike syndromes, they are also dynamic. It is common for a patient to have 5-6 patterns simultaneously, and these patterns interact and reinforce each other in various ways. Patterns can also transform into other patterns.

Table 1. Seven Basic TCM Patterns Organized by COVID-19 Disease Severity (with number of identified therapeutic targets based on symptomatology)

Disease Severity	TCM Pattern
Mild	Cold-Dampness Stagnation in the Lungs Damp-Heat Accumulated in the Lungs
Moderate	Cold-Dampness Obstructing the Lungs Toxic-Dampness Stagnating in the Lungs
Severe	<u>Lungs Blocked by Epidemic Toxins</u> Fever, flushing, cough, yellow sputum with or without blood, wheezing, shortness of breath, fatigue, sticky dry mouth, nausea, anorexia, decreased and brown urine, Tongue: red with a yellow, greasy coat. Pulse: slippery. <u>Flaring Heat in Qi and Ying Levels</u> Severe fever, great thirst, labored breathing and panting, delirium, blurred vision, rash, possible epistaxis or vomiting of blood, possible convulsions. Tongue: little to no coat. Pulse: deep and slow or large and rapid.
Critical	Internal Block and Outward Desertion

As has been mentioned, effort has also been made to create a broadly effective formula for all COVID-19 cases. This was indicated in the 6th edition of the NHC guidance document and it is called *Lung Clearing and Detoxification Decoction*, known in Chinese as: *Qing Fei Pai Du Tang* (see Table 2). A breakdown of this formula will help the reader have a clear view of how Chinese researchers and physicians are combining traditional and modern medicine cohesively.

Notes on Ancient Formulas brought to Modern Light

One of the oldest existing clinical texts about Chinese medicine is called the *Shang Han Lun*. It was published in the 3rd century CE and is focused on the treatment of contagious disease. The NHC formulation *Lung Clearing and Detoxification Decoction* (aka *Qing Fei Pai Du Tang*) is a combination of four formulas from this ancient text, with some additional herbs added. This contemporary combination, used in the treatment of COVID-19, can be investigated in a number of different ways, not least of which is by examining the four formulas that compose it.

Table 2. Lung Clearing and Detoxification (*Qing Fei Pai Du Tang*) Composition

• <i>Ma Huang</i> (<i>Ephedra stem</i>) 9g • <i>Zhi Gan Cao</i> (<i>Prepared Chinese licorice root</i>) 6g • <i>Ku Xing Ren</i> (<i>Apricot seed</i>) 9g • <i>Shi Gao</i> (<i>Gypsum</i>) 15-30g • <i>Gui Zhi</i> (<i>Cassia twig</i>) 9g • <i>Ze Xie</i> (<i>Asian water plantain rhizome</i>) 9g • <i>Zhu Ling</i> (<i>Zhu ling sclerotium</i>) 9g • <i>Bai Zhu</i> (<i>bai-zhu atractylodes rhizome</i>) 9g • <i>Fu Ling</i> (<i>Poria sclerotium</i>) 15g • <i>Chai Hu</i> (<i>Bupleurum root</i>) 16g • <i>Huang Qin</i> (<i>Barbed skullcap root</i>) 6g • <i>Jiang Ban Xia</i> (<i>Pinellia rhizome cured with ginger</i>) 9g • <i>Zi Wan</i> (<i>Tartarian aster root</i>) 9g • <i>Sheng Jiang</i> (<i>Fresh ginger rhizome</i>) 9g • <i>Kuan Dong Hua</i> (<i>Coltsfoot flower bud</i>) 9g • <i>She Gan</i> (<i>Belamcanda rhizome</i>) 9g • <i>Xi Xin</i> (<i>Chinese wild ginger root & rhizome</i>) 6g • <i>Shan Yao</i> (<i>Chinese yam rhizome</i>) 12g • <i>Zhi Shi</i> (<i>Bitter orange immature fruit</i>) 6g • <i>Chen Pi</i> (<i>Tangerine dried rind</i>) 6g • <i>Huo Xiang</i> (<i>Chinese giant hyssop aerial part</i>) 9g

Note. Substances in italics form the base formula of Ephedra, Apricot Kernel, Gypsum and Licorice Decoction (*Ma Xing Shi Gan Tang*)

Of the four, the most important is put at the very top and is called *Ephedra, Apricot Kernel, Gypsum and Licorice Decoction*, known in Chinese as *Ma Xing Shi Gan Tang*. Many studies have been conducted on this formula; and TCM practitioners are aware of some of its properties from a modern research point of view. This combination of four herbs is able to activate a variety of immune-related cells, while simultaneously regulating multiple cytokines and disrupting the process of viral pathogens entering host cells (Ma *et al.*, 2014; Ye-fang Wang *et al.*, 2020; Yefang Wang *et al.*, 2020). It is also likely that *Ephedra, Apricot Kernel, Gypsum and Licorice Decoction* has an impact on coagulation, having an anti-platelet aggregation effect (Yang

et al., 2020). Given that intense blood coagulation is a known cause of morbidity in cases of COVID-19, this is potentially of great benefit.

It has been suggested that the anti-inflammatory effect of *Ephedra*, *Apricot Kernel*, *Gypsum* and *Licorice Decoction* is actually regulatory (Yang *et al.*, 2020). This would mean that it has an anti-cytokine effect only when there is excessive inflammation. In either case, since “cytokine storm” has also been cited as a leading factor in morbidity, this too could be of remarkable benefit.

Turning from this base formula to the entire formula, one can see that *Lung Clearing and Detoxification Decoction* (aka, *Qing Fei Pai Du Tang*) has been researched in many ways. These include human trials and animal trials, as well as through other interdisciplinary technologies, such as *in vitro* research, various omics technologies, network pharmacology, effects on gut microbiota, and various computer models, such as molecular folding and interaction with COVID-19 proteins or the bioavailability of compounds (Chen *et al.*, 2020; Xin *et al.*, 2020; Yang *et al.*, 2020; Jing *et al.*, 2020).

The results of human and animal trials are arguable in the best of times, but during a pandemic they are even more so. Animal trials are based on an artificial damage to lung tissue, which makes them an imperfect model. Human trials are more likely to compare modern medical treatments for COVID-19 with a combination of modern medicines and traditional formulations used together integratively. The reason for this is obvious: Having a “no-treatment” group is ethically unconscionable. In general, a benefit to integrative treatment is found in these trials. For example, one study on 63 patients found an improvement in the levels of C-reactive protein, creatine kinase, lactate dehydrogenase, and blood urea nitrogen in the treatment group (Xin *et al.*, 2020). There are some trials which use Chinese medicinals but have no control group. These trials are less convincing, especially because the survival rate for COVID-19 patients is already generally high.

The mechanisms by which *Lung Clearing and Detoxification Decoction* appears to treat COVID-19 are numerous. The intricacy of cumulative research is staggering. As a way of focusing and managing the science, research programs begin and end with traditional theory and method. For example, the study conducted by Yang, *et al.* identifies distinct therapeutic targets among COVID-19 patients based entirely on their symptoms as organized by the NHC (Table 1). This creates seven distinct studies within one, which are then compared for overlap. The study by Chen, *et al.* uses a different approach. This team broke *Lung Clearing and Detoxification Decoction* into five “functional units” as defined by the four traditional formulas which compose it, plus the additional herbs that were added. In both cases, it is the tradition that organizes research, and modern approaches are used to plumb this depth.

An example of this process can be seen in Figure 1, which illustrates a quantifiable relationship between various categories— disease, pattern, symptom, gene, therapeutic molecule, traditional medicinal, and known formulation. These relationships were explored numerically, using specific examples and via the Symmap database. The breadth of relationships is beyond what can be shown in a single chart, but many databases have been established which map them visually and dynamically. Symmap is produced by the Beijing University of Chinese Medicine and is available free online at: <https://www.symmap.org>.

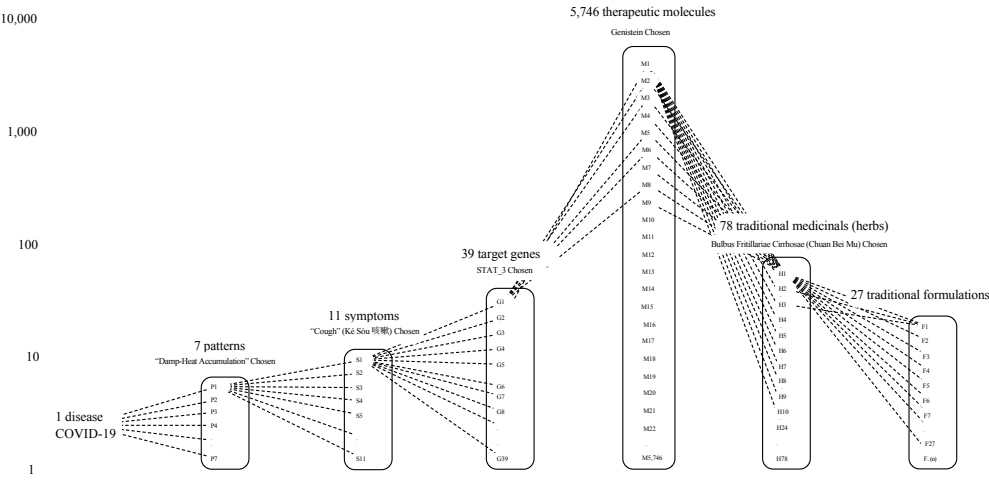


Figure 1. This figure demonstrates the basic relationships between categories—“disease”, “pattern”, “symptom”, “target gene”, “therapeutic molecule”, “traditional medicinal” and “formulation”, based on the database *symmap.org* with further extrapolations. A Log scale is used due to the vast difference in the number of items within each category. This chart mostly follows a single symptom “cough,” which is common among many patterns of COVID-19, but here the pattern of “Damp-Heat Accumulated in the Lungs” is used as an example, which itself has 11 symptoms. Also, the target gene STAT_3 (Signal transducer and activator of transcription 3) is highlighted because it is the most commonly activated gene within the identified group of the molecules that treat cough, having 8 connections. STAT_3, among other things, acts as a regulator of inflammatory response by regulating differentiation of naive CD4+ T-cells into T-helper or regulatory T-cells. Among the therapeutic molecules, Genistein was chosen, which up-regulates STAT_3 and is found within 24 traditional medicinals. Of these medicinals, *Bulbus Fritillariae Cirrhosae* (Chuan Bei Mu) was chosen, which is a medicinal commonly used for the pattern of “Damp-Heat Accumulated in the Lungs.” This herb is found in 27 commonly used formulations. Genistein also up-regulates gene HLA-DPB1, which binds peptides and presents them on the cell surface for recognition by the CD4 T-cells.

“Cough,” which is a common symptom of COVID-19, can be addressed via gene target STAT_3, through the molecule genistein, which is found in the traditional herb *Bulbus Fritillariae Cirrhosae* (called *Chuan bei mu*, in Chinese). However, the numbers presented by Symmap and other databases suggest that we should not expect such a simple reductionism of Chinese medicine. For example, *Bulbus Fritillariae Cirrhosae* contains 158 known molecules which collectively upregulate 210 gene targets and are capable of addressing 10 different symptoms of illness. Its use has been suggested for at least 131 different diseases.

The symptom of “cough” can be addressed by the upregulation of at least 39 target genes, which can be accomplished by any number of 5,746 molecules found scattered throughout 78 traditional medicinals. Rather than focusing on diseases, Patterns composed of Symptoms have long been the basic diagnostic framework for Chinese medicine. Here, this framework lends coherency to the data, and it rapidly moves research toward clinical application. We do not use *Bulbus Fritillariae Cirrhosae* for all instances of cough, because application is tempered by the kind of cough and also by the long list of *other symptoms* a patient is presenting.

Treatment of this sort is possible because it is standard for doctors of Chinese medicine to inquire about and differentiate many more symptoms than their counterpart physicians in the West. As an alternative to conducting tests, patient complaints are clarified in greater detail, through further questioning and physical examination. Symptom presentation is a ripe field for diagnostic inquiry, and it lends itself to treatment in a way that is distinct from the seeking of biochemical pathology.

Preventing the Disease

Faced with a global virus, many minds have turned to vaccinations. However, the other side of the healthcare coin is the individual reaction to viral exposure. As is known, most patients will not die from COVID-19. Many will even be asymptomatic. The Chinese medicine perspective on this difference is broadly known as “constitutional factors.” These factors include pre-existing patterns, which make a patient susceptible to infection and disease progression, and also to deep forms that an individual’s body has taken, created by both heritable qualities and the long-term consequences of lifestyle. These factors also broadly change with age, and as is known, children react to exposure in a manner substantially different from adults. A constitution is like a stage on which a drama is taking place. In lieu of a vaccine, the question becomes: What is the right kind of stage for a successful drama with the new coronavirus?

On March 16, 2020, the details of a successful case were published (Thevarajan *et al.*, 2020). Australian physicians treated a 47-year-old woman from Wuhan who contracted the virus. She was hospitalized in Australia with a fever of 101.3 degrees F, a rapid heart rate, and a positive viral load. However, other than giving IV fluids, the medical staff did little to intervene. Her body defeated the virus on its own, within seven days of her symptoms first appearing.

Specifically, this woman’s body responded in the following ways:

- There was an increase in the number of cells producing and excreting antibodies (ASC’s).
- There was an increase in the number of antibodies. These were immunoglobulin M and G (IgM and IgG) that attached to and bound the virus so that it could be destroyed.
- There was an increase in the number of T lymphocytes. These are white blood cells that search out and destroy invading pathogens and also increase the number of antibodies being produced. These were CD4+ (helper) T cells and CD8+ (killer) T cells, as well as follicular helper T cells.

China has a long, documented, clinical record of using herbs for infectious disease. Within this corpus, there are dozens of treatments for respiratory viruses. There is a special category of disease known as “pestilential qi,” which refers to pandemics; and there are preventive strategies developed. This tradition held true during the more recent outbreaks of Severe Acute Respiratory Distress Syndrome (SARS) and H1N1 influenza. A number of fairly large-scale studies conducted during those times (some with patients in the tens of thousands) show, with statistical significance, that those who took appropriate Chinese herbs were less likely to contract these viruses (Luo *et al.*, 2020). It should be noted, though, that these studies were of short duration and so do not describe the results of such treatments over longer periods of time.

Nonetheless, research generated by these outbreaks has been plentiful. As a result, there is something like a roadmap for the enhancement of our immune system. ASC's, IgM & IgG, helper and killer T cells--the factors identified in the Australian paper--are investigated and discussed in terms of the herbs and formulations that can actually increase their presence in the body, as known through *in vivo* research with both humans and rats (Xiaoguang & Zejing, 2014).

A great deal has been learned about another traditional formulation called *Jade Windscreen Powder*, known in Chinese as *Yu Ping Feng San*, first published in the year 1213. This formula was the most common "base" used by clinicians during both SARS and H1N1, and it was used in modified forms for several of the trials mentioned above. This formula has only three herbs in it--Astragalus/Huang qi, Saposhnikovia/Fang Feng, and Atractylodis/Bai Zhu. However, this small combination is able to increase the percentage of helper and killer T cells and stabilize the levels of immunoglobulin M and G. In other words, *Jade Windscreen Powder* (*Yu Ping Feng San*) can be used before an active infection to increase a person's odds of survival. It is worth mentioning that, based on this research, two of the three herbs in *Jade Windscreen Powder* were also added to *Lung Clearing and Detoxification Decoction* (*Qing Fei Pai Du Tang*), the formula discussed previously.

Reflection

In the West we view the endeavor of medicine as proceeding along a line, with progress moving in one direction. The Chinese are more likely to view this same process as having the shape of a circle or spiral, along which the problems and solutions of our ancestors are continually encountered, in a coherent sphere of human experience.

While the West has only one way of pursuing rational medical treatment, the Chinese have two. At the intersection of these two intellectual domains, intense friction has generated fertile soil. This notion is still beyond the general perspective of Western culture, which is committed to the belief that modern research, alone, is the way to finding effective treatments. Although our present tension with China could be described as a battle of cultures, in fact this would be inaccurate. They are churning a soil that contains the best parts of our and their medical cultures, while we hold resolutely to our own. China knows our medicine. We do not know theirs.

Their approach may have profound implications. Operating via direct observation of patients, and with a special emphasis on inquiry, the reasoning method of traditional Chinese medicine has always been language-based. Through precise definitions, researchers are now able to tie together words and biological events, not as one-to-one relationships, but via the complexity of network analysis. If their approach is validated, it will completely change the nature of medical treatment. Medicine will become personalized, not necessarily through invasive medical testing, but rather, through speaking with our patients.

In the West, through the process of medical reductionism, we have long neglected that which is being reduced, i.e., the human being. This entity, "the human," can be thought of as a top level of organization, what we call the "organism." It is the aspect we interact with daily, the people to whom we speak, but medical physicians do not make it overly important, preferring instead to engage with investigative data--images and tests--which describe lower levels of organization. Compared with this, Chinese medicine is the science of organism. While pulmonologists focus on the level of organs, histologists focus on the level of tissue, and

geneticists focus on the level of molecules, doctors of Chinese medicine focus on the level of organism. This is why they value their observations and why they value their patients' words.

Our scientific tradition dictates that we avoid the level of organism, and at least one important reason is that its complexity seems to confuse what is real and what is illusory. A man who seems to be perfectly healthy may actually have a malignant tumor. A woman with a typical fever and body aches may actually have COVID-19. However, perhaps there really was something to be seen and noticed in these patients, but Western tradition does not support our seeing it, and so our perceptions have atrophied. In this regard, omics and other technologies support our seeing with better clarity, but only if we step away from our own bias, which informs us that the best information is always hidden, and so only found through images and tests.

References

- Ali, S., Egunsola, O., Babar, Z. D., & Hasan, S. (2019). Clinical trials in Asia: A World Health Organization database study. *Perspectives in Clinical Research*, 10(3), 121-124 https://doi.org/10.4103/picr.PICR_109_18
- Bauer, Matthew (2004, August). An Interview with Dr. Paul Unschuld, Part 2. *Acupuncture Today*, 5(8). <https://www.acupuncturetoday.com/mpacms/at/article.php?id=28498>
- Chen, J., Wang, Y., Gao, Y., Hu, L.-S., Yang, J., Wang, J., Sun, W., Liang, Z., Cao, Y., & Cao, Y. (2020). Protection against COVID-19 injury by qingfei paidu decoction via anti-viral, anti-inflammatory activity and metabolic programming. *Biomedicine & Pharmacotherapy*, 129, 110281. <https://doi.org/10.1016/j.biopha.2020.110281>
- Grayson, M. (2011). Traditional Asian medicine. *Nature*, 480, S81. <https://doi.org/10.1038/480S81a>
- Huang, F., Li, Y., Leung, E. L.-H., Liu, X., Liu, K., Wang, Q., Lan, Y., Li, X., Yu, H., Cui, L., Luo, H., & Luo, L. (2020). A review of therapeutic agents and Chinese herbal medicines against SARS-COV-2 (COVID-19). *Pharmacological Research*, 158(104929), 1-12. <https://doi.org/10.1016/j.phrs.2020.104929>
- Jing, Z., Sai-sai, T., Jian, Y., & Jian-feng, L. (2020). Investigating the mechanism of Qing-Fei-Pai-Du-Tang for the treatment of Novel Coronavirus Pneumonia by network pharmacology. *Chinese Traditional and Herbal Drugs*, 4(51), 829-835.
- Luo, H., Tang, Q., Shang, Y., Liang, S., Yang, M., Robinson, N., & Liu, J. (2020). Can Chinese Medicine Be Used for Prevention of Corona Virus Disease 2019 (COVID-19)? A Review of Historical Classics, Research Evidence and Current Prevention Programs. *Chinese Journal of Integrative Medicine*, 26(4), 243-250. <https://doi.org/10.1007/s11655-020-3192-6>
- Ma, L.-Q., Pan, C.-S., Yang, N., Liu, Y.-Y., Yan, L., Sun, K., Wei, X.-H., He, K., Xiao, M.-M., Fan, J.-Y., & Han, J.-Y. (2014). Posttreatment with Ma-Xing-Shi-Gan-Tang, a Chinese Medicine Formula, Ameliorates Lipopolysaccharide-Induced Lung Microvessel Hyperpermeability and Inflammatory Reaction in Rat. *Microcirculation*, 21(7), 649-663. <https://doi.org/10.1111/micc.12144>

- Moses, H., Matheson, D.H.M., Cairns-Smith, S., George, B.P., Palisch, C., & Dorsey, E.R. (2015). The Anatomy of Medical Research: US and International Comparisons. *JAMA*, 313(2), 174–189. doi:10.1001/jama.2014.15939
- National Health Commission (NHC) of the PRC. Guidance for Corona Virus Disease 2019: Prevention, Control, Diagnosis and Management. Translated by Liang, Xiaofeng, *et al.* 2020. Accessed 7/29/2020. <https://mp.weixin.qq.com/s/nOAmosQ4YqkXHKdJbBE9GA>
- Potash, S. (2015). Research advances in China improve health globally. Global Health Matters Newsletter, NIH Fogarty International Center. 2015;12(5). Accessed 6/21/2020. <https://www.fic.nih.gov/News/GlobalHealthMatters/september-october-2015/Pages/china-global-research-impact.aspx>
- Thevarajan, I., Nguyen, T. H. O., Koutsakos, M., Druce, J., Caly, L., van de Sandt, C. E., Jia, X., Nicholson, S., Catton, M., Cowie, B., Tong, S. Y. C., Lewin, S. R., & Kedzierska, K. (2020). Breadth of concomitant immune responses prior to patient recovery: A case report of non-severe COVID-19. *Nature Medicine*, 26, 453-455. doi.org/10.1038/s41591-020-0819-2
- Wang, Ye-fang, Fei, Y., Zhao, B., Yin, Q., Zhu, J., Ren, G., Wang, B., Fang, W., & Li, Y. (2020). Ma Xing Shi Gan Decoction Protects against PM2.5-Induced Lung Injury through Suppression of Epithelial-to-Mesenchymal Transition (EMT) and Epithelial Barrier Disruption. *Evidence-Based Complementary and Alternative Medicine*, 2020, 1– 17. <https://doi.org/10.1155/2020/7176589>
- Wang, Yefang, Zhao, B., Fei, Y., Yin, Q., Zhu, J., Ren, G., Wang, B., Fang, W., & Li, Y. (2020). Ma xing shi gan decoction eliminates PM2.5-induced lung injury by reducing pulmonary cell apoptosis through Akt/mTOR/p70S6K pathway in rats. *Bioscience Reports*, 40(7), 1-15. <https://doi.org/10.1042/BSR20193738>
- Xiaoguang, W., & Zejing, L. (2014). Prevention and treatment of viral respiratory infections by traditional Chinese herbs. *Chinese Medical Journal*, 127(7), 1344-1350.
- Xin, S., Cheng, X., Zhu, B., Liao, X., Yang, F., Song, L., Shi, Y., Guan, X., Su, R., Wang, J., Xing, L., Xu, X., Jin, L., Liu, Y., Zhou, W., Zhang, D., Liang, L., Yu, Y., & Yu, R. (2020). Clinical retrospective study on the efficacy of Qingfei Paidu decoction combined with Western medicine for COVID-19 treatment. *Biomedicine & Pharmacotherapy*, 129, 110500. <https://doi.org/10.1016/j.biopha.2020.110500>
- Yang, R., Liu, H., Bai, C., Wang, Y., Zhang, X., Guo, R., Wu, S., Wang, J., Leung, E., Chang, H., Li, P., Liu, T., & Wang, Y. (2020). Chemical composition and pharmacological mechanism of Qingfei Paidu Decoction and Ma Xing Shi Gan Decoction against Coronavirus Disease 2019 (COVID-19): In silico and experimental study. *Pharmacological Research*, 157, 104820. <https://doi.org/10.1016/j.phrs.2020.104820>
- Zhang, Yangfei (2020). 6 effective traditional Chinese medicines for COVID-19. Chinadaily.com.cn; 3/17/2020. <https://covid-19.chinadaily.com.cn/a/202003/17/WS5e702f52a31012821727fa19.html>