



Review Article

THE IMPACT OF NATURAL COMPOUNDS IN THE FIGHT AGAINST COVID-19: A REVIEW

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ABSTRACT

Over 200,000 lives have been claimed by Covid-19 all over the world. The impact of this disease has led the World Health Organization (WHO) to declare COVID-19 as a global disaster. Diverse precautions have been established to wipe out this disease and hence, prevent it from causing severe damages on earth. However, these precautions could not fully eradicate the disease since there is still a lack of a preventive vaccine or any antiviral treatments. Hence, there is a crucial need to find a platform where novel antiviral drugs can be developed, and natural compounds serve as an excellent source where this discovery can be found. This brief study aims to provide a general review of some of the recent researches, in which natural compounds were studied for their antiviral effects.

Keywords: COVID-19, natural compounds, antiviral

INTRODUCTION

Just three months into the New Year (2020), the world has experienced one of its biggest crises in decades. Turning the busiest streets of Europe into deserts and grounding most of the African countries into their respective homes, Covid-19 has proven itself a force to reckon with. Claiming over 200,000 lives all over the world¹. Covid-19 is classified as one of the viruses that belong to the family of coronaviruses. These viruses are the source of diverse illnesses including the ones ranging from the common cold to more severe illnesses, among others: The Middle East respiratory syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV). Additionally, further studies have indicated that these viruses are classified into four major genera which are α -CoVs, β -CoVs, γ -CoVs, and δ -CoVs². Two of these groups (γ -CoVs and δ -CoVs) are zoonotic, while the other two can only infect mammals. Quickly, scientists have subsequently discovered that seven coronaviruses can infect humans and develop respiratory diseases. The first discovery of these viruses (HCoV, HCoV-229E, and HCoV-OC43) was found in the early 90 s but did not cause serious damages to humans.

However, Covid-19 or SARS-CoV-2 is the only virus in the family of coronaviruses that have never been previously identified in humans. It falls under β -CoVs genera and currently has a huge impact on earth. The first patient infected with Covid-19 was identified in December 2019 in the city of Wuhan in China³. Since there, the virus has killed more than 200,000 people globally. However, statistics have shown that the deadly airborne virus

mostly attacks fragile people (old people, smokers, people who have undergone surgical operations/chemotherapy, HIV-Positive people, people taking insulin for diabetes and people recovering from serious wounds). This could be attributed to the type of immune system found in humans. Many studies have reported that the viruses generally weaken people with a very low immune system^{4,5}. The impact of this virus on earth has led many countries to a total lock-down, resulting in fear; panic to the population; and a total pandemic in the world. Moreover, there are no vaccine or antiviral treatments that have been developed against Covid-19 up to date. All these features have raised debates, doubts and total panic in people's minds, resulting in much false news on social media and other platforms; while others have politicized the outbreak to a level where one thinks this could be a biological war between China and USA⁶.

Hence, there is an urgent need to find better alternatives that could bring a rapid solution to this pandemic. This is where natural compounds could play a vital role in the management of Covid-19. Thousands of studies have shown that natural compounds are a primary source of necessary medicinal properties including antiviral⁷. Natural compounds are considered as the reservoir of active compounds (phytochemicals) that could act as the human body's defense against viruses and pathogens. Most of these natural compounds interact with the viral life cycle, among others: viral entry, replication, assembly and release and finally focus on targeting virus-host-specific interactions⁸. This brief review aims at putting together a comprehensive platform on the importance of natural compounds in the battle against Covid-19 to minimize fear and confusion in people's minds.

The symptoms of Covid-19 and standard recommendations to prevent the spread of the virus

According to the World Health Organization (WHO), the most common symptoms of Covid-19 are as follow: respiratory symptoms, fever and cough, shortness of breath and breathing difficulties. However, symptoms range from mild to more severe illnesses depending on people. This could be due to the type of immune system as this plays an important role in the management of viruses. One of the major roles of the immune system is to protect humans from diseases that are mostly caused by viruses, bacteria, and toxins⁹. Different studies conducted in China and globally have shown that fragile people are the ones at high risk since most of them have a compromised immune system^{9,10}. This scenario is similar to what has been seen with other viral diseases such as Influenza. A study of more than 40,000 coronavirus patients showed that approximately 15% of patients older than 80 years old have passed away¹. Hence, the WHO has put in place a list of standard recommendations that could be used not only to minimize deaths among fragile people but also to prevent the spread of the virus in humans. These recommendations are as follow:

- Regular hand washing with soap for approximately 20-30 seconds.
- Use of sanitizer or disinfectant.
- Covering mouth and nose when coughing and sneezing.
- Wearing masks when necessary. This mostly concerns 3 types of people: Infected people; people who are treating infected people (either in hospitals or homes); people who are disinfecting public areas, etc.
- Avoid close contact with anyone showing symptoms of respiratory illness like coughing and sneezing.

However, these precautions could not fully silence the wind of Covid-19 since the spread of the virus continues to rise and the trend is ascertained to increase more rapidly. One should take note that these precautions were simply applied to prevent the spread of the virus but not to cure the disease. It generally takes 10-15 years to develop a vaccine against infection since many parameters are considered along the process such as Laboratory and Animal studies; Clinical studies with Human subjects; Approval and Licensure, etc¹¹. In this regard, the use of rapid alternatives could be very useful in the battle against Covid-19. The use of natural compounds is among the best route one should consider tackling this pandemic due to safety, efficacy and efficiency⁷. The antiviral effects of natural compounds have been studied for years by scientists and the results have been very promising. Here are some of the natural compounds that could be used as potential candidates to explore the possible cure of viral illnesses including Covid-19 with more ease:

Herbal Plants for Antiviral Applications

A. Saikosaponins (A, B₂, C and D)

Many herbal plants firstly undergo extraction before conducting further studies. The extracts emanating from the process are mostly used for different clinical studies. Saikosaponins is one of those plant glycosides and components of Xiao-chai-hu-tang (a traditional Chinese herbal medicine), which is extracted from the roots of *Bupleurum falcatum*⁷. In a study conducted by Cheng PW *et al*¹², the *in-vitro* studies were conducted to test the anticoronaviral activity of Saikosaponins (A, B₂, C and D) including their mode of

action. The main aim of the study was achieved using the 2, 3-bis[2-methoxy-4-nitro-5-sulfophenyl]-5-[(phenylamino) carbonyl-2H-tetrazolium hydroxide] (XTT) assay. The results revealed that all Saikosaponins used in the study showed antiviral activity at a concentration ranging from 0.25 to 25 micromol/L¹². However, Saikosaponins B₂ was found to be the strongest among all of them with a value of inhibition revealed to be $IC_{50} = 1.7 \pm 0.1$ micromol/L. The remaining saikosaponins (A and C) on the other hand did not show any cytotoxic effects on target cells at concentrations that achieved antiviral activity. Based on these results, it was reported that saikosaponins B₂ could be considered as a potential candidate in the fight against viral diseases. Therefore, this plant might produce promising results in the battle against Covid-19. This is attributed to the fact that Saikosaponins B₂ can interact with the viral life cycle such as the early stage of viral replication including absorption and penetration of the virus⁷.

Another study was conducted by Lee *et al*¹³, where Saikosaponins B₂ was used in combination with daclatasvir to investigate the resistance of these materials against the hepatitis C virus. Hepatitis C virus is also one of the viral diseases that mostly cause chronic hepatitis, cirrhosis and hepatocellular carcinoma. The results showed that Saikosaponins B₂ could easily inhibit viral entry, replication as well as translation¹³. All these findings highlight the fact that Saikosaponins (A, B₂, C and D) may have the ability to restrain SARS-CoV-2 infection.

B. *Lycoris radiata*

This herbal plant is mostly known by the name of red spider lily, hell flower, red magic lily and equinox flower. The plant belongs to the family of amaryllis and it is originated from the Asian countries, mostly in China, Korea, and Nepal¹⁴. A study conducted by Shi-You Li *et al*⁸, where more than 200 Chinese medicinal plants were investigated for the antiviral activities against Severe Acute Respiratory Syndrome-associated coronavirus (SARS-CoV). These authors used 3-(4, 5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium inner salt (MTS) as the main assay for virus-induced cytopathic effect (CPE). However, among all the herbal plants used in the study, it was found that only four could be considered as potential candidates in the fight against coronavirus. These plants include *Lycoris radiata*, *Artemisia annua*, *Pyrrosia lingua* and *Lindera aggregata*. All these plants exhibited an antiviral activity at the concentration ranging from 2.4 ± 0.2 to 88.2 ± 7.7 µg/ml and were all extracted using a common solvent – Ethanol, except for *Pyrrosia lingua* in which chloroform was used⁸. The results revealed that all the four plants exhibited an effective inhibition of virus-induced CPE when SARS-CoV strain BJ001 was used in screening. The bioactive compounds served as an obstruction against viral infection and allowed the cell to survive.

However, *Lycoris radiata* was the strongest among all the four candidates with an EC_{50} value of inhibition equivalent to 34.5 ± 2.6 µg/ml. This led them to further isolate a compound (s) from *Lycoris radiata* that could be the key behind the antiviral activity. After further studies, it was discovered that lycorine (Figure 1) was the anti-SARS-CoV component within the plant. This component had an EC_{50} value of 15.7 ± 1.2 nM, a CC_{50} value of 14980.0 ± 912.0 nM in cytotoxicity assay and finally a selective index (SI) greater than 900⁸. Based on these results, one might consider the idea of exploring lycorine along with the four other plants mentioned above for the development of a drug against Covid-19.

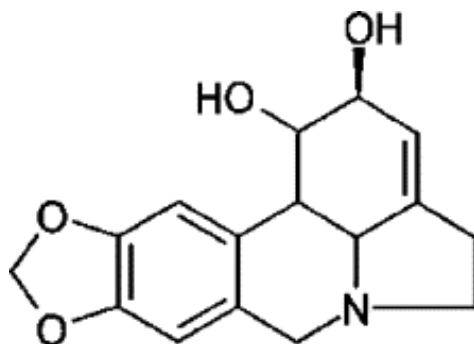
Figure 1: Chemical Structure of Lycorine⁸

Table 1: Antiviral effects of certain natural compounds and different mechanisms applied against SARS-CoV

Infection (s)	Herbal plants studied	Proposed mechanism (s)	References
Coronaviruses	Herbacetin – flavonoid compound that can be found in flaxseed against SARS-CoV.	SARS-CoV 3CL protease inhibitor.	15
	Rhoifolin – flavonoid compound found in citrus peels against SARS-CoV.	SARS-CoV 3CL protease inhibitor.	15
	Pectolinarin – flavonoid compound found in <i>Lantana camara</i> against SARS-CoV.	SARS-CoV 3CL protease inhibitor.	15
	Phenolic compounds of <i>Isatis indigotica</i> against SARS-CoV.	SARS-CoV 3CL protease inhibitor	16
	Myricetin and Scutellarein against SARS-CoV.	SARS-CoV helicase inhibitor.	17
	Houttuynia cordata water extract against SARS-CoV.	SARS-CoV 3CL protease inhibitor; viral Polymerase inhibitor.	18

Many other herbal plants have been studied by scientists and can, therefore, be used as potential candidates in the development of drugs against Covid-19. The table above is a representative of different natural products that were studied and considered as potential candidates in the fight against Severe Acute Respiratory Syndrome-associated corona virus (SARS-CoV).

The impact of natural compounds on public health has been known for centuries. Most of them have been known for their antiviral and anti-malarial activities. The history of anti-malarial began since the discovery of quinine, which is the active compound in Cinchona bark, the medicinal properties of which have long been known to the natives of South America in the tropical regions of the Andes and which was used against chills and fever. The Spanish conquerors introduced it to Europe in the 1960 s. Quinine was isolated in 1820 by Caventou and Pelletier from the bark of *Cinchona officinalis* L¹⁹.

Currently, due to the health emergency, chloroquine and hydroxychloroquine have been authorized in certain countries in Africa such as Burkina Faso and Benin, as well as the combination of chloroquine-azithromycin or the combination lopinavir/ritonavir for the treatment of patients affected by Covid-19. The efficacy of these anti-viral against Covid-19 has been proven *in vitro*²⁰ and *in vivo*^{21,22}.

Additionally, Burkina Faso is cooperating with neighboring Benin, which has also authorized the use of chloroquine for therapeutic purposes. The two countries are conducting an international clinical trial called Api-Covid-19. The study has been coordinated by a team from the Research Institute for Health Sciences (IRSS), which aims to assess the clinical and virological efficacy of herbal medicine called “Apivirine” in patients with Covid-19²³.

Covid-19 and Traditional medicine: Is it an immunity problem?

Traditional medicine is an effective method for eradicating an infectious problem, minimizing its intensity, shortening its course, as well as avoiding its recurrences. The effectiveness of traditional medicine is mainly due to the choice of products, which optimize the functioning of the immune system and strengthen its reactivity²⁴.

Immune stimulation is presented in the field of foods, food supplements, as an increase in the capacity to resist infection, for example, a viral or bacterial infection in winter, by an increase in the effectiveness or the extent of the body’s response²⁵.

Micro nutrition, trace elements, homeopathy, herbal medicine, aromatherapy, traditional Chinese medicine (TCM), all have an excellent reputation for stimulating the immune system and have been used as first treatments for infectious disease such as flu, colds, nasopharyngitis, sore, throat, angina, laryngitis, bronchitis, sinusitis²⁶. Here, we have picked some of the effective plants, known for their immunostimulatory and anti-infectious activities.

A. *Echinacea*

It is also known as *Echinacea purpurea* (L.) Moench; the plant is widely used by Indian tribes for its anti-infectious properties and has scientifically confirmed its empirical activities. It is widely used to strengthen the immune system and is very effective in preventing or at the onset of respiratory infection including the SARS virus. Clinical trials have confirmed the efficacy and safety of *Echinacea* in the treatment of respiratory infections in children²⁷.

B. Ginseng

Echinacea is also widely used in combination with Ginseng known and revered for 4000 years, known to boost, revitalize and energize, for natural defense reactions. The roots of two species (*Panax ginseng* C.A Mey. and *Panax quinquefolius* L.) are known as ginseng and used to reinforce the immune system against bacterial, viral infections and autoimmune diseases. These properties have been confirmed, in connection with the presence of substances such as ginsenosides and polysaccharides²⁸.

C. Garlic

The antimicrobial properties of several medicinal species against respiratory infections have been proven. A study published in 2009 in the Iranian Journal of Virology, indicated that the extract of garlic *in vitro* inhibits the proliferation as well as the cellular penetration of the Influenza virus (H1N1)²⁹.

D. Ginger

The protective potential of fresh ginger in inhibiting the human respiratory syncytial virus (RSV or HRSV) has been described by the Journal of Ethnopharmacology. HRSV is the most common respiratory infection in young children. The 300 µg/mL prescription for fresh ginger stimulated respiratory cells to secrete an antiviral protein called β-interferon³⁰.

E. Aromatherapy

It plays a vital role in the natural treatment of infectious diseases of viral or bacterial origin. Certain essential oils are indeed widely used in the prevention of respiratory infections. Eucalyptus and Ravintsara essentials are the two most known essential oils.

Eucalyptus essential oil

Eucalyptus is a plant native to Australia, which has been used since always by the aborigines to fight against infections and fever. It is emerged throughout the Mediterranean basin to dry up marshy areas. The ancients burned their leaves to disinfect

the premises and prevent the epidemic. Eucalyptus essential oil is very rich in eucalyptol (80-85%), widely used against respiratory problems, sanitizes the pulmonary phlegm. It is mostly used for frictions, inhalations, fumigations and diffusions in the atmosphere. The anti-infectious activities of this essential oil, as well as eucalyptol, have been scientifically proven³¹.

Ravintsara essential oil

Cinnamomum camphora (L.) J. Pesi is a tree of Asian origin, established late in Madagascar (mid-19th century). The essential oil obtained from the distillation of its leaves is a strengthening of the immune system. It has powerful antiviral and anti-infectious properties. It is indicated for prevention during Influenza epidemics and nasopharyngeal diseases³².

However, despite the success of all these therapies as a preventive and curative remedy for viral/infectious diseases, the scientific community remains skeptical since there is still a lack of scientific evidence showing the effectiveness of these natural compounds in the treatment of Covid-19.

Nevertheless, Traditional Chinese Medicine (TCM) has a tremendous reputation of having remarkable physiochemical and antiviral properties and, thus, plays a major role in the fight against Covid-19. According to Chinese tradition, the patient's immune system remains the crucial point to analyze in TCM.

In this context, a Covid-19 prevention program has been launched in 23 provinces of China. A study published in the Chinese Journal of Integrative Medicine recommended Astragalus root (*Radix astragali*), Licorice root (*Radix saponosifoliae*), Actractyl rhizome (*Rhizoma atractylodis* Macrocephalae), the Honeysuckle rhizome (*Lonicerae japonicae* Flos) and the Forsythia fruit (*Fructus forsythiae*) as a preventive against Covid-19³³. Later, a report was published by the National Health Commission (NHC) of the People's Republic of China that approximately 60.107 infected people (Covid-19 patients) have been treated with TCM³⁴. However, despite this enthusiasm, the scientific community remains skeptical, given the lack of rigor in clinical trials. Ensuring the efficacy and safety of a traditional remedy is necessary for the safety of treated patients. Nevertheless, on March 1st, 2020, more than 250 clinical trials were launched to test the efficacy and safety of treatments for Covid-19. TCM and western medicines are among the chosen therapeutics for clinical trials to test Covid-19 treatments³⁵. Up to date, the results are still pending, and we anticipate that the WHO would compare at least two or three therapeutics supported by scientific evidence. We cite 14 ongoing TCM clinical trials (Table 2); 19 most used TCM herbs (Table 3) for the prevention and treatment of Covid-19 (SARS-CoV-2) infection, as well as the TCM recommended by 6th editions Guidelines of Diagnosis and Treatment for Covid-19 (Table 4).

Table 2: Ongoing TCM Clinical Trials for the treatment of novel Coronavirus pneumonia (COVID-19)³⁵

Registration number	Design type	Title	TCM herbal medicine	Sample size	Phase
ChiCTR2000029432	CCT	A real-world study for the efficacy and safety of large dose Tanreqing Injection in the treatment of patients with novel corona virus pneumonia (Covid-19)	Tan Re Qing Injection	72	4
ChiCTR2000029434	RCT	A randomized, open label, blank-controlled trial for Lian-Hua-Qing-Wen Capsule/Granule in the treatment of novel corona virus pneumonia (Covid-19)	Lian Hua Qing Wen Capsule/Granule	400	4
ChiCTR2000029487	CCT	Clinical study for Gu-Biao Jie-Du-Ling in preventing of novel coronavirus pneumonia (COVID-19) in children	Gu Biao Jie Du Ling	200	0
ChiCTR2000029589	CCT	An open, prospective, multicenter clinical study for the efficacy and safety of Reduning injection in the treatment of novel corona virus pneumonia (Covid-19)	Re Du Ning Injection	60	0
ChiCTR2000029605	RCT	A randomized, open label, black-controlled, multicenter trial for Shuang-Huang-Lian oral solution in the treatment of novel corona virus pneumonia (Covid-19)	Shuang Huang Lian Oral Liquid	400	4
ChiCTR2000029780	RCT	A multicenter, randomized, open, controlled trial for the efficacy and safety of Shen-Qi-Fu-Zheng injection in the treatment of novel corona virus pneumonia (Covid-19)	Shen Qi Fu Zheng Injection	160	4
ChiCTR2000029781	RCT	A multicenter, randomized, open, and controlled trial for the efficacy and safety of Kang-Bing-Du granules in the treatment of novel corona virus pneumonia (Covid-19)	Kang Bing Du granules	160	4
ChiCTR2000029822	RCT	A randomized controlled trial for honeysuckle decoction in the treatment of novel corona virus pneumonia (Covid-19) infection	Jin Yin Hua Tang	110	0
ChiCTR2000029991	RCT	A randomized, open label, controlled trial for the safety and efficacy of Kesuting syrup and Keqing capsule in the treatment of mild and moderate novel corona virus pneumonia (Covid-19)	Ke Su Ting Syrup/Ke Qing Capsule	72	4
ChiCTR2000030043	RCT	Shen-Fu injection in the treatment of severe novel corona virus pneumonia (Covid-19): A multicenter, randomized, open label, controlled trial	Shen Fu Injection	300	4
ChiCTR2000030117	RCT	A multicenter, randomized, open, parallel controlled trial for the evaluation of the effectiveness and safety of Xiyanping injection in the treatment of common type novel corona virus pneumonia (Covid-19)	Xi Yan Ping Injection	348	4
ChiCTR2000030255	RCT	Efficacy and safety of Jing-Yin Granule in the treatment of novel corona virus pneumonia (Covid-19) wind-heat syndrome	Jing Yin Granule	300	4
ChiCTR2000030388	RCT	Efficacy and safety of Xue-Bi-Jing injection in the treatment of severe cases of novel corona virus pneumonia (Covid-19)	Xue Bi Jing Injection	60	0
ChiCTR2000029813	RCT	Clinical trial for Tanreqing Capsules in the Treatment of Novel Corona virus Pneumonia (Covid-19)	Tan Re Qing Capsules	72	0

Table 3: Most commonly Used TCM Herbs for the prevention of novel Coronavirus pneumonia (Covid-19)

Herbs (Latin name)	Herbs (Chinese Pin Yin)	Applicable regions	References
<i>Astragalus membranaceus</i> <i>Glycyrrhizae uralensis</i> <i>Saposhnikovia divaricate</i> <i>Rhizoma atractylodis</i> Macrocephalae <i>Lonicerae Japonicae</i> Flos <i>Fructus forsythiae</i> <i>Atractylodis rhizoma</i> <i>Radix platycodonis</i> <i>Agastache rugosa</i> <i>Cyrtomium fortune</i> J. Sm <i>Astragalus membranaceus</i>	Huangqi Gancao Fangfeng Baizhu Jinyinshua Lianqiao Cangzhu Jiegeng Huoxiang Guanzhzhong Huangqi	23 provinces covered Northwest, North Central (including Wuhan) South, East, Northwest, and Southwest Beijing, Tianjin, Shandong, Shaanxi, Gansu, Hebei, Shanxi, Henan, Hubei, Jiangxi, Hunan, and Yunnan Beijing, Tianjin, Shandong, Shaanxi, Gansu, Hebei, Shanxi, Henan, Hubei, Jiangxi, Hunan, and Yunnan	33
<i>Atractylodis rhizoma</i> <i>Eupatorii herba</i> <i>Agastache rugosa</i> <i>Ophiopogon japonicus</i> <i>Scrophularia ningpoensis</i> <i>Rhizoma phragmitis</i> <i>Adenophora stricta</i> Miq <i>Dendrobium nobile</i> Lindl.	Cangzhu Peilan Huoxiang Maidong Xuanshen Lugen Shashen Shihu	Five regions in southern China (Hubei, Jiangxi, Hunan, Yunnan, and Wuhan) Eight regions in northern China (Beijing, Tianjin, Hebei, Henan, Shanxi, Gansu, and Shandong)	36

Table 4: TCM recommended by 6th editions Guidelines of Diagnosis and Treatment for SARS-CoV-2³⁷

Stage of disease	Symptoms	Recommended Chinese patient medicine
Medical observation period	Fatigue with gastrointestinal discomfort Fatigue with fever	Huo Xiang Zheng Qi Shui Lian Hua Qing Wen Capsule, Shu Feng Jie Du Capsule, Jin Hua Qing Gan Capsule
Clinical treatment period (Confirmed patients)	Mild cases General cases Several cases Critical cases	Qing Fei Pai Du Tang Qing Fei Pai Du Tang Xi Yan Ping Injection, Xue Bi Jing Injection, Re Du Ning Injection, Tan Re Qing Injection, Xing Nao Jing Injection, Qing Fei Du Tang Xue Bi Jing Injection, Re Du Ning Injection, Tan Re Qing Injection, Shen Fu Injection, Shen Mai Injection, Su He Xiang Pill, An Gong Niu Huang Pill

Most of these herbal plants are the primary source of components that can inhibit the infection of SARS-CoV-2. An *in vitro* study conducted by researchers at Shanghai Institute of Drugs and Wuhan Virus Institute supported this statement since they found that Shuang Huang Lian Oral Liquid had the inhibitory effect on SARS-CoV-2³⁸. Further studies have shown that SARS-CoV, SARS-CoV-2 use receptor ACE2 for the cellular entrance³⁹. Therefore, compounds showing an effective activity to seal off ACE2 might as well prevent the infection of SARS-CoV-2. A molecular docking study on TCM was later conducted by Chen *et al*⁴⁰ and the results showed an interaction between AC2 and some of the TCM-derived compounds, among others: scutellarin, baicalin, hesperetin, glycyrrhizin and nicotianamine⁴⁰. We then expect these compounds or herbal plants containing such compounds to restrain the infection of Covid-19. Hopefully, ongoing clinical studies will confirm this hypothesis soon.

CONCLUSION

Despite all the precautions that have been developed so far to try to silence the wind of Covid-19. This virus remains a big threat to public health since there is no preventive vaccine or any antiviral treatments that have been structured up to date. However, natural compounds present a wide platform where new compounds/antiviral and effective remedies can be developed to eradicate Covid-19. Natural compounds contain active compounds that could serve as available weapons to fight Covid-19. Hence, the idea of exploring these materials would contribute to the development of drugs/derivatives in the treatment of Covid-19. Many derivatives have been developed in the past such as glycyrrhetic acid derivatives as new anti-HBV agents, acetoxime derivative from the Mediterranean mollusk *Hexaplex trunculus* playing a role of inhibitor against HSV-1 and caffeic acid derivatives as a novel type of influenza NA antagonist. However, many of these studies were not well-controlled and can, therefore, be considered as initial or preliminary assessments. Hence, conducting further studies like a characterization of the bioactive compounds; structuring a defined mechanism, purifying a single compound that contains an effective anti-corona viral activity and finally conducting *in-vivo* studies to assess the efficacy of the purified compound (s) is highly recommended. Moreover, one should also consider incorporating an active compound (s) from herbal plants into polymer materials to strengthen its efficacy. We are very persuaded that natural compounds will play a big role in the fight against Covid-19 and might help to successfully and diligently handle the current crisis.

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