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Herbal Medicine Used in Corona Treatment: An Ethnopharmacological Survey

Wahid Hussain¹, Hidayat Hussain² and Amjad Ali^{3*}

¹Department of Botany, GPGC Parachinar, District Kurram, **Pakistan**

²Department of Bioorganic Chemistry, Leibniz Institute of Plant Biochemistry Weinberg 3, D-06120 Halle (Saale), **Germany**

³Department of Sustainable Crop Production, Università Cattolica del Sacro Cuore, Via Emilia Parmense 84, **Italy**

*Correspondence: amjad.ali@unicatt.it Received 25-10-2020, Revised: 14-04-2021, Accepted: 15-04-2021 e-Published: 20-04-2021

The world has experienced various dangerous outbreaks of various intensities such as ebola, cholera, Spanish flu, American seasonal flu. Now we are facing an arguably a more dangerous viral endemic with COVID-19. The recent pandemic COVID-19 which arise from the Wuhan city of China spread around the globe and infected 137,011,754 people, killed 2,954,332 by 12th April, 2021 and only 110,173,254 patients have recovered which of total affected population. Being a novel virus and no availability of the treatment leading a fear in the people around the globe and the WHO declared emergency on 30 January 2020. Some antiviral drugs which are used from the ancient times for the treatment of Malaria and pneumonia are using for the treatment of COVID-19 such as chloroquine, lopinavir, oseltamivir, remdesivir and ritonavir. Different herbs are also used for the coronavirus, the recent COVID-19 was treated by using the *Ma Huang (Herba Ephedrae)* due to which the patients fell less chest pain by opening the chest cavity and also some other herbs such as *Zi Su Zi (Fructus Perillae)*, *Jiang Can (Bombay Batryticatus)*, *Di Long (Pheretima)*, *Fu Ling (Poria)* was used and it helped in decrease of patient temperature and decrease chest pain. Similarly the compounds from the *Nigella Sativa* "Nigellidine and α -hederin" may be used for the treatment of COVID-19.

Keywords: COVID-19, Ethnopharmacological, Chloroquine, Lopinavir, Oseltamivir, Ritonavir

INTRODUCTION

This severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), formerly known as the 2019 novel Coronavirus (COVID-19) is a single-stranded RNA beta-coronavirus whose genome encodes are structural proteins, non-structural proteins and accessory proteins (Rabi, 2020). Coronavirus are a large family of virus, which causes a disease, and developed symptoms depend upon their stages, they developed the symptoms from common cold to a severe disease. Corona viruses have 39 species, belong to family Coronaviridae, suborder Cornidovirineaea and order Nidovirales. All the SARS-CoV fall under the species severe acute respiratory syndrome-related

coronavirus and genus Beta-coronavirus. Most of the species under this head are enzootic and only a few of these species infect humans (Schoeman and Fielding, 2019; Vellingiri et al. 2020). It has globally already infected 3,065,778 people and killed 211,658 people by 28th April, 2020 and the casualties are growing exponentially. In the meantime, only 558,437 patients have recovered which is 25.30 % of total affected population. Chinese herbs combined with western medicine significantly improved symptoms of SARS, including decreasing body temperature, cough and breathing difficulties, dosages of corticosteroids, improving absorption of pulmonary infiltration, and quality of life (Li et al. 2020). The human

coronavirus also called Middle East respiratory syndrome coronavirus (MERS-CoV) which was first identified in Guangdong, China in 2002 and 2003 and in Saudi Arab when the first man died from the acute respiratory disorder in September 2012 (Memish et al. 2013). There are six species of coronavirus, which are known to cause human infection in human beings. Among these six species, four species cause simple cold and flu in immunocompetent individuals, while the two species MERS-CoV (Middle East respiratory syndrome coronavirus) and SARS-CoV (severe acute respiratory syndrome coronavirus) cause the severe respiratory disorder and cause fatalities (Memish et al. 2013).

The novel coronavirus, named 2019-nCoV or COVID-19 identified in December 2019, in the province of Wuhan, China in several patients with the symptom of pneumonia, which show the history of linkage with the seafood market. This novel coronavirus is completely different from the MERS-CoV and SARS-CoV and make the seventh member of the coronavirus family, which infect humans (Zhu et al. 2020). So due to the pneumonia of unknown aetiology the International Committee on Taxonomy of Viruses (ICTV) give named SARS-CoV-2, because it belong to the same species of SARS-CoV (Memish et al. 2013). Finally, the World Health Organization (WHO) name this virus coronavirus disease 2019 (COVID-19) (WHO, 2020). In China city Wuhan at 5 March 2020, there was a total case of 80,409 COVID-19 and the number of death was 3,012 deaths (3.75%) (Carlos et al. 2020). The rates of recovered patients were 52,045 (64.73%) and were quarantined at home for two weeks (Memish et al. 2013). Moreover, until 5 April 2020 case of COVID/19 reached to more than 1133 thousands and have taken life is 62.7 thousand people (Gorbalenya et al. 2020; Xing et al. 2020; Zhu et al. 2020)

MATERIALS AND METHODS

Objectives

To review updated literature available related to COVID-19 and safe use of drugs and medicinal plants for treatment of COVID-19. This article will enable the scientific community to find anti-Corona drugs, medicinal plants and other techniques used so for the treatment of COVID-19. This will boost further research on the medicinal plants for the treatment of pandemic COVID-19.

Methodology:

By using different online database such as Google scholar, Science Direct Navigator, ISI Web of Knowledge, Elsevier, springer link, Test databases, research gate and PubMed, data were retrieved by giving different keywords. Various keywords were used during the searching process in order to have detailed information of plants and their ethno-pharmacological studies for the treatment of COVID-19. Microsoft Word and Microsoft Excel were used in organization and tabulate.

RESULTS AND DISCUSSION

3.1 Herbal plants for corona treatment

The COVID-19 belong to *Beta coronavirus* as SARS and MERS and have no specific treatment (vaccine) but there are several existing antiviral drugs viz., ribavirin, interferon, lopinavir-ritonavir, corticosteroids which is used from the beginning for the treatment of SARS and MERS. Some of these antiviral drug show controversial behavior (Savarino et al. 2006; Shinwari et al. 2020; WHO, 2020; Wang et al. 2020; Zumla et al. 2016). The report from the (WHO, 2020), also showed that there are some allopathic medicines (chloroquine, oseltamivir and lopinavir-ritonavir) (Figure 1) that are very helpful in the control of malaria and shown a good result to treat Corona (COVID-19). In addition, there are lot of species of plant which are reported to effective in the treatment of Coronavirus (SARS-CoV), which are the main cause of serious pneumonia. Chloroquine are widely used for the treatment of malaria and autoimmune disease and this drug have ability to boost the immunity and also help in increasing endosomal PH that's required for the fusion between cell and virus, which may be help to resist the viral disease and clinically applicable used for the treatment of COVID-19 (Yan et al. 2013; Gao et al. 2020). Gao et al. 2020, reported that the chloroquine have a potential to treat anti-viral disorders that is why this drug may help to treat the COVID-19. It is noteworthy chloroquine is a cheap and easily accessible as well as safe drug which are being used from more than 70 years. The report from the Wang et al. 2020, also showed that remdesivir are highly effective in the treatment of COVID-19. From the report of (Sheahan et al. 2020), also showed that the remdesivir can help in the treatment of mice infected with MERS-CoV by improving the lung function as well as reduce the pathological. damage to lung tissue.

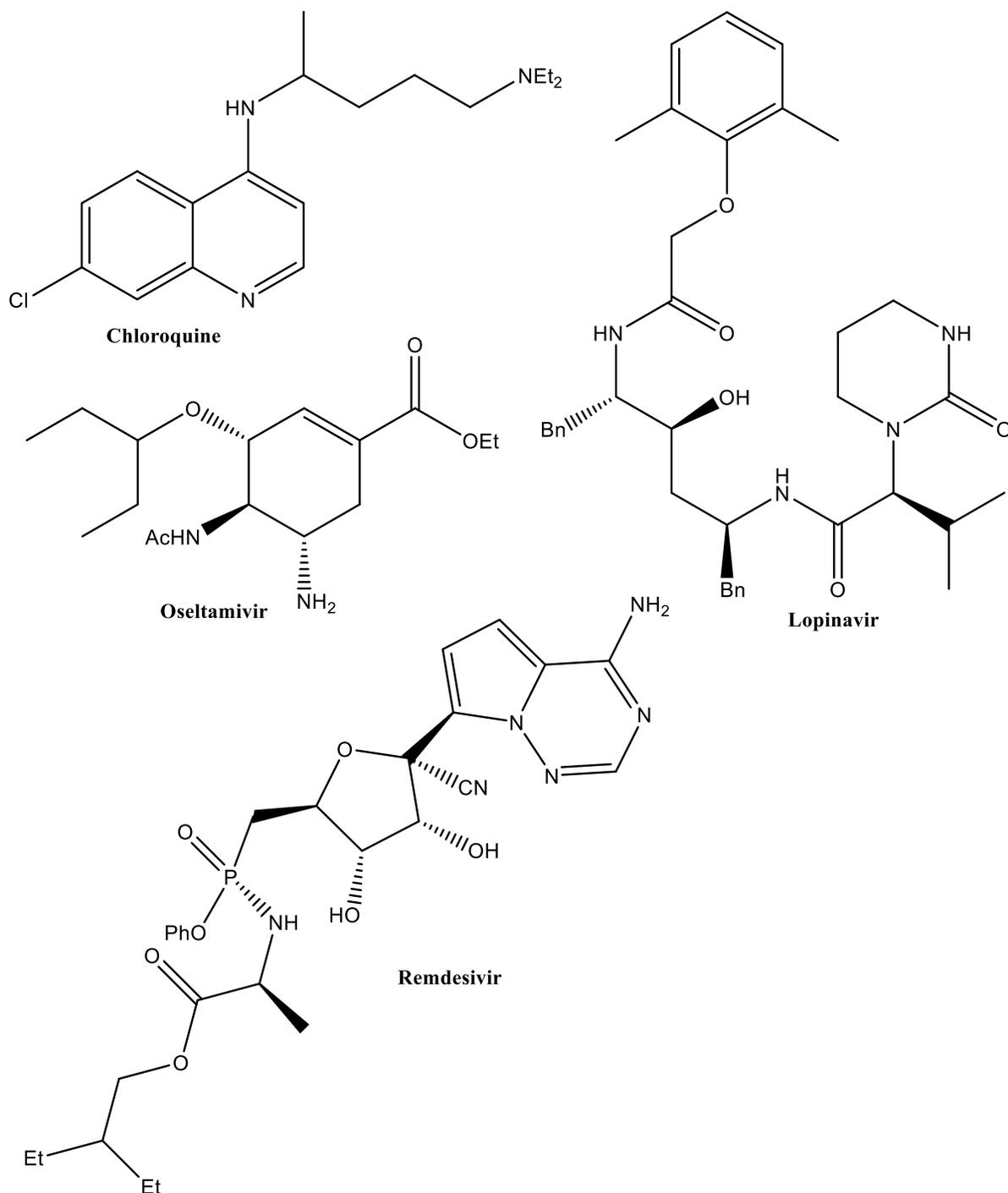


Figure 1: Structures of drugs used for COVID-19

Bouchentouf and Missoum, 2020, reported that with the help of molecular docking that the compounds of *Nigellia Sativa* such as Nigellidine and α - hederin (Figure 2) may be used for the treatment of COVID-19 by acting on the main

protease (M^{pro}). In addition from the report of (Ghahramanloo et al. 2017; Zhang, 2020), showed that the patients in China hospital of Guangzhou all 50 patients returned to a normal temperature and reduction noticed in the pneumonia after giving

Toujie Quwen granule as well as overall symptoms of COVID-19 improved significantly. Several traditional Chinese medicine such as Yupingfeng San, which made from three different herbs "*Astragalus*, *Fangfeng* and *Atractylodes*", is very helpful in the reduction of severe symptoms of COVID-19 patients by regulating body immune function (Ghahramanloo et al. 2017). Similarly from the same report, it showed that Sangju yin and Yinqiao san are used for the patient of COVID-19 with severe cough and these drugs are helpful in the reduction of phlegm and cough, clear lung heat and restore normal lung function and in addition Maxingshigan tang and Baihegujin tang also help in the treatment of COVID-19 patients with severe case especially the patients which face difficulty in breathing. Yupingfeng Powder also may be used for the treatment of COVID-19 because they have the properties of antiviral, inflammatory and immunoregulatory effects and used for the treatment of respiratory infectious diseases in ancient (Liu et al. 2020; Xu and Zhang, 2020).

As due to non-availability a specific therapies for the treatment of novel corona virus that's why in China and now in some other countries such as Italy, France, Spain used the compassionate use therapies that's hydroxychloroquine, chloroquine, lopinavir-ritonavir, azithromycin, favipiravir, interferon, convalescent plasma, remdesivir, ribavirin, steroids, and anti-IL-6 inhibitors, based on either there in vitro antiviral or anti-inflammatory properties. All these therapies used widely by given controls except for several randomized trails performed in China also most recently used in US (Delang, 2018; Kalil, 2020). Convalescent Plasma (using plasma from the recovered patients) to treat the patients in Shenzhen Third People's Hospital, China. Although these patients also received several drugs lopinavir/ritonavir and interferon but by using the plasma from the recovered patients the patients seemed to improve their clinical status such as decrease in the body temperature after using the Convalescent Plasma as well as improvements in Sequential Organ Failure Assessment scores was observed (Gonzalez-Paz et al. 2020; Roback and Guarner, 2020). The bioinformatica tools curcumin, capsaicin and piperine have ability to strongly binding to 3CL-protease of COVID-19, which can promote the structural changes in the viral proteases and induce the enzymes folding and all these techniques may be help in the treatment of

covid-19 (Gonzalez-Paz et al. 2020). Also the lopinavir and ritonavir are antiviral-drug candidate is combination of the HIV protease inhibitors which acts against the viral 3CL protease used from the ancient time of SARS-CoV-2 which also may be used for the treatment of recent pandemic of COVID-19 (Baden and Rubin, 2020; Ren et al. 2020). Some other traditional Chinese medicine which are helpful and suggested to be effective in the treatments of 2019-n CoV pneumonia patients such as *qingfei paidu* decoction (QPD), gancaoganjiang decoction, sheganmahuang decoction, *qingfei touxie fuzheng recipe*, etc. QPD which consisted of *Ephedrae Herba*, *Glycyrrhizae Radix et Rhizoma Praeprata cum Melle*, *Fructus Immaturus*, *Armeniaca Semen Amarum*, *Gypsum Fibrosum*, *Cinnamomi Ramulus*, *Alismatis Rhizoma*, *Polyporus*, *Atractylodis Macrocephalae Rhizoma*, *Poria*, *Bupleuri Radix*, *Scutellariae Radix*, *Pinelliae Rhizoma Praepratum cum Zingibere et Alumine*, *Asteris Radix et Rhizoma*, *Zingiberis Rhizoma Recens*, *Farfarae Flos*, *Belamcandae Rhizoma*, *Asari Radix et Rhizoma*, *Dioscoreae Rhizoma*, *Aurantii*, *Citri Reticulatae Pericarpium*, *Pogostemonis Herba*, *Xuanfei Touxie*, *Qingre Jiedu*, *Xuanxie Feire*, *Kaibi Gutuo*, *Huiyang Jiuni*, *Qingjie Yure*, *Yiqi Yangyin* (PDP, 2020; Pang et al. 2020; NHC, 2020). By using the QPD in China the 130 case was cured and discharged in 701 confirmed cases with COVID-19, and the reminder patients also improved their clinical symptoms after using QPD. In addition the QPD also help in the improvement of lung activity which is the main target of COVID-19 as well as the above mentioned herbs in combine with QPD help in inhibiting the replication of multiple ribosomal proteins (Wu et al. 2020; Xu et al.

. 2020; Zhao et al. 2020). Also from the report of Zhao et al. (2020) showed that the QPD could inhibit and alleviate excessive immune response as well as it can eliminate the inflammation which occur in the COVID-19 patients by regulating the cytokine and immune related pathway with the help of molecular docking it showed that the patchouli alcohol, ergosterol and shionone may have a good anti COVID-19 activity which can also open the door for the development of drug against COVID-19 (Shen et al. 2020).

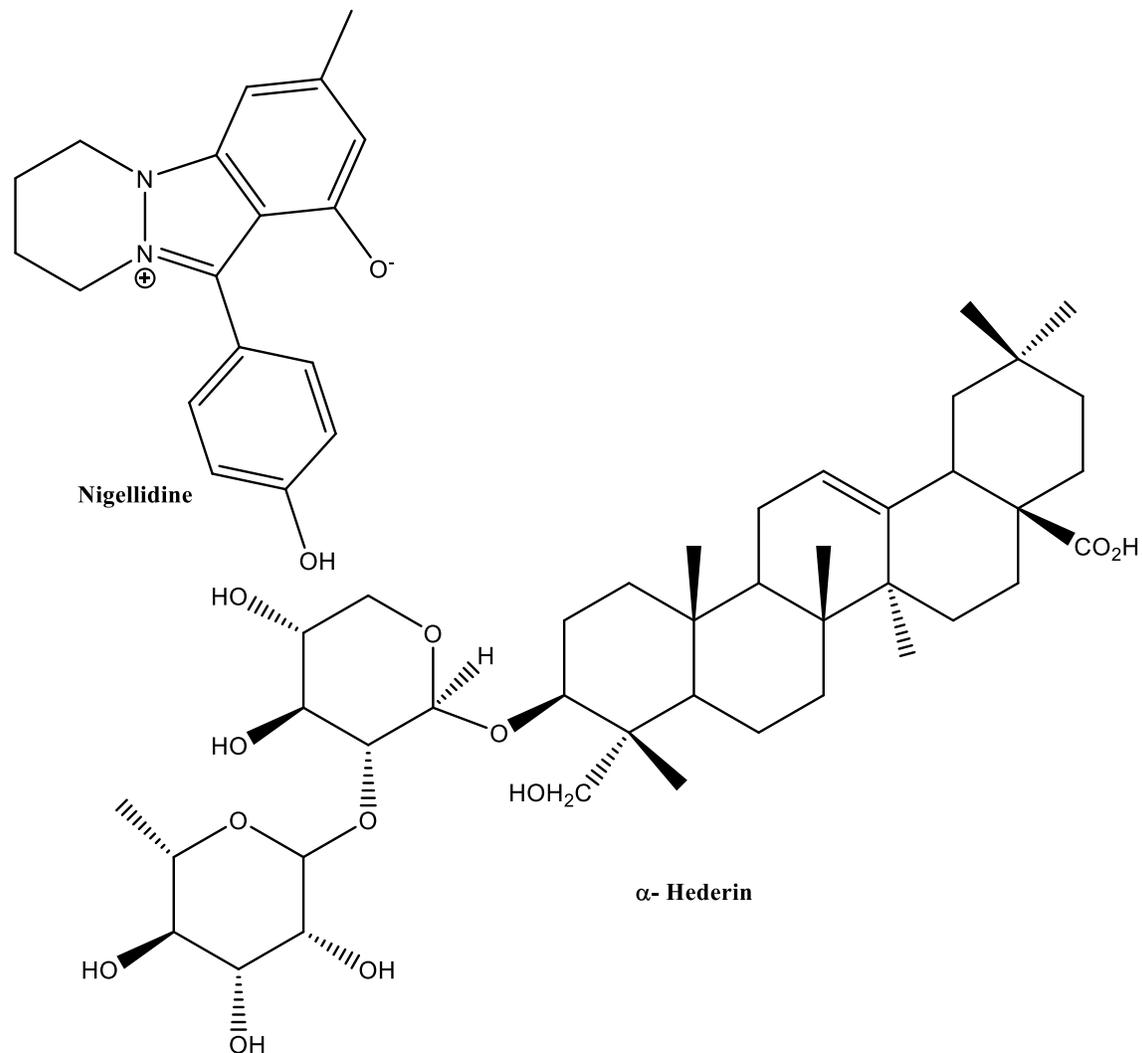


Figure 2: Structures of nigellidine and α -hederin

The five patients with critical situations in China with COVID-19 and acute respiratory distress syndrome (ARDS) was treated with the inoculation of convalescent plasma containing neutralizing antibody from the COVID-19 patients after giving mechanical ventilation antiviral agents and methylprednisolone. They noticed that after the plasma inoculation the body temperature of the patients normalized within 3- 5 days and improvement was occur in the patient's condition (Shen et al. 2020). Bacillus Calmette-Guérin (BCG) vaccination in the childhood decrease the mortality and morbidity rate from the COVID-19 (Chhikara et al. 2020; Miller et al. 2020). Miller et al. 2020, reported that those countries which have no universal policies of BCG vaccination such as

(Italy, Nederland, USA) have more mortality rate as compered then other countries so it may be the possible treatment of the novel pandemic COVID-19. The effective drugs used so for the treatment of COVID-19 in different parts of the world viz; Azithromycin, Cepharranthine, selamec, mefloquine Glucocorticoids, IL-6, antagonist, JAK, inhibitors, chloroquine/hydroxychloroquine, Chloroquine, hydroxychloroquine, Cepharranthine, selamectin, mefloquine, Qingfei paidu, Baricitinib, fedratinib, ruxolitinib, Remdesivir, Lianhuaqingwen, Renin-AngiotensinSystem (RAS)inhibitors, ribavirin, penciclovir, nitazoxanide, nafamostat (Chhikara et al. 2020; Fan et al. 2020; Gordon et al, 2020; Hameed et al. 2019; Stebbing et al. 2020; Tang et al, 2020; Yao et al. 2020). Recently, few researchers have identified that the SARS-CoV-2 has mainly two

types of strains, which are the 'L' and 'S' strains. Among these strains the L strain is more common and may have evolved from the S strain; additionally, this L strain has a higher rate of replication inside the human host cell, which has resulted in the escalation of the infection in limited time. Hence, it has become a big challenge to analyze the condition and offer therapy at the short time available. Due to the high mutation rate, it has been harder to understand the genomic organization and host interaction of the virus (Ganjhu et al. 2015; Habibzadeh and Stoneman, 2020; Zhang et al. 2019).

In addition, several plants are used for the treatment of Coronavirus. For instance, the *Silybum marianum*, which used for the treatment of Hepatitis virus but it, also expected to be useful for the treatment of Coronavirus. Similarly, *Glycyrrhiza glabra* also used for the treatment of Coronavirus (Chan et al. 2020; Damle, 2014; Feng et al. 2013; Hussain et al. 2017 Keyaerts et al. 2004; Li et al. 2005). In addition, the different extracts of various plants used for SARS-COV treatment. For instance, the ethanol extract of *Lycoris radiata*, *Artemisia annua* and *Lindera aggregata* and the chloroform extract of *Pyrrosia lingua* used to treat SARS-COV. The parts used of above-mentioned plants are stem, whole plant, root and leaf, In another report Chan et al. (2020) showed that the use of *Herba ephedra* are helpful in the treatment of COVID-19 by opening the chest activity of patient and open the water passageway above the lungs to enter the water. In this investigation the authors concluded that by increasing water intake the alternately cause more urine without experiencing thirst and the patients feel lighter and energetic. In addition Chan et al. (2020) also demonstrated that some other herbs other than *Ma Huang (Herba Ephedrae)* were used viz., *Zi Su Zi (Fructus Perillae)*, *Jiang Can (Bombyx Batryticatus)*, *Di Long (Pheretima)*, *Fu Ling (Poria)* which were helpful in the control of temperature and chest pain in the patients of COVID-19. Similar from the report showed that *Allium sativum*, *Glycyrrhiza glabra* might inhibit the SARS virus by inhibition the viral replication (Fiore et al. 2008; Liu et al. 2020). Some more herbs can be used for the treatment of SARS-CoV-2 such as *Boerhaavia diffusa*, *Clerodendrum inerme Gaertn*, *Clitoria ternatea*, *Coriandrum sativum*, *Cynara scolymus*, *Cassia occidentalis*, *Coscinium fenestratum* and *Embellia ribes* (Khan and Kumar, 2019; Liou et al. 2018; Maity et al. 2012; Panday et al. 2011; Prathapan et al. 2013). The plant *Vitex trifolia* and *Andrographis paniculata* might be used for the

inhibition activity of SARS-CoV (Liou et al. 2018). *Strobilanthes callosa* and *Strobilanthes cusia* Human coronavirus NL63 and these herbs might be helpful in the treatment of recent pandemic COVID-19 (Tsai et al. 2020; Vellingiri et al. 2020). Bouchentouf and Missoum, 2020, reported that with the help of molecular docking that the compounds of *Nigellia Sativa* such as Nigellidine and α -hederin (Figure 2) may be used for the treatment of COVID-19 by acting on the main protease (M^{pro}). In addition from the report of (Ghahramanloo et al. 2017; Zhang, 2020), showed that the patients in China hospital of Guangzhou all 50 patients returned to a normal temperature and reduction noticed in the pneumonia after giving Toujie Quwen granule as well as overall symptoms of COVID-19 improved significantly. Several traditional Chinese medicine such as Yupingfeng San, which made from three different herbs "*Astragalus*, *Fangfeng* and *Atractylodes*", is very helpful in the reduction of severe symptoms of COVID-19 patients by regulating body immune function (Ghahramanloo et al. 2017). Similarly from the same report, it showed that Sangju yin and Yinqiao san are used for the patient of COVID-19 with severe cough and these drugs are helpful in the reduction of phlegm and cough, clear lung heat and restore normal lung function and in addition Maxingshigan tang and Baihegujin tang also help in the treatment of COVID-19 patients with severe case especially the patients which face difficulty in breathing. Yupingfeng Powder also may be used for the treatment of COVID-19 because they have the properties of antiviral, inflammatory and immunoregulatory effects and used for the treatment of respiratory infectious diseases in ancient (Lu et al, 2020; Xu and Zhang, 2020).

CONCLUSION

Although there is no specific treatment for the COVID-19, but by using the ancient drugs and from the previous drugs which is used for the treatment of SARS-COV which have the antiviral properties and the traditional Chinese medicine which are used in the Chinese hospital for the treatment and the patients was improved the clinical symptoms. The high rate of mutation and replication of strain L inside the human host cell, which has resulted in the escalation of the infection in limited time. Hence, it has become a big challenge to analyze the condition and offer therapy at the short time available. Due to the high mutation rate, it has been harder to understand the genomic organization and host interaction of the virus. So by using and by exploring further the drugs and antiviral herbs

might be useful for the treatment around the globe and open a door for finding the treatment of novel corona virus.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS

W.H and A.A wrote initial draft of manuscript while H.H worked mainly on structure drawing and help in revision of manuscript. All the authors have approved the final draft.

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