



Review on Some Plants' Therapeutic Actions Against Novel Coronavirus (COVID-19) with Gastroenteritis as Contributory Factor

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Abstract

Coronavirus is an enveloped, multinucleated virus with capability of causing respiratory and enteric ailments in both humans and animals. It resulted to an epidemic SARS with an almost 10% fatality rate. The main aim of the review, is to access some important metabolites or compounds from plants that have therapeutic actions against the novel Coronavirus. Search engines have been utilized in looking for updated findings in regards to this review, so as to provide a sound and reliable information. Moreover, other important CoV including: transmissible gastroenteritis virus of swine (TGEV), porcine epidemic diarrhoea (PEDV) virus and crystal structure of transmissible gastroenteritis virus (TGEV) which resulted to many severe cases and similar to SAR-CoV which antagonised the host innate immune responses. Coronavirus (Covid-19), occurred in the late 2019 at Wuhan, China and later to other countries within a shorter period. The novel virus, triggered in the search of new compounds from various plants species, so as to develop a valuable drug that can get rid of its problems. Many compounds from medicinal plants have clearly shown to be therapeutically active against the viral replications. Some formulations granted to COVID-19 confirmed patients were good in curtailing the tragic Coronavirus infections in China, which were also recommended for future used. So many environmental factors have contributed towards its emergence, where by serious actions need to be taken to get rid of.

Keywords: Medicinal Plant; Novel-Coronavirus (Covid-19), Severe Acute Respiratory Tract Syndrome (SARS), Therapeutic Action; Transmissible Gastroenteritis Virus (TGEV)

Introduction

The coronaviruses belong to the order Nidovirales; Family Coronaviridae; subfamily Coronavirinae and genus Coronavirus. Coronaviruses happened to be more diverse group with an enveloped Positive RNA strands, about 30,000 nucleotides, they are also spherical in shape, with an approximate diameter of 100-160nm which have the capability of causing respiratory and enteric ailments in both humans and animals as pinpointed by (Bellini & Us, 2007). They are also classified into three (Hu *et al.*, 2017). genera based for both mammals and birds: Mammals (Alpha- and Beta coronavirus) and for birds (Gamma coronaviruses) (Drexler *et al.*, 2010). In the humans type, there are different prototypes which resulted to an epidemic severe acute respiratory tract syndromes (SARS) with an almost 10% fatality rate (Drexler *et al.*, 2010). Moreover, other important CoV including: transmissible gastroenteritis virus

of swine (TGEV), porcine epidemic diarrhoea (PEDV) virus and crystal structure of transmissible gastroenteritis virus (TGEV) which resulted to many severe cases and similar to Severe acute respiratory tract syndromes Coronavirus (SAR-CoV), that antagonised the host innate immune responses (Drexler *et al.*, 2010) and (Hu *et al.*, 2017). Subsequently, Coronaviruses having to be transmitted from wild and domestic animals to human as well as human to human transmissions which served to be major field of concerns nowadays. They usually infect respiratory organs, gastrointestinal organs, liver as well as the central nervous system of human, livestock, birds, bat, mouse and wild animals (Chen, Liu & Guo, 2020). It has also being captured that many out breaks of coronaviruses happened in the Middle east by the year 2012 as emerging incidence (Chen, Liu & Guo, 2020). In China, traditional herbal formulations were used with modern medicine to treat SARS. It has come to the notice that, more than 200 Chinese medicinal herbs extracts having some the screened metabolites were capable of killing many viruses, by inhibiting the viral replication including SARS-CoV. The metabolites contained in the natural plants include; dimethylthiazol, carboxyphenyl, sulfophenyl and tetrazolium (Li, *et al.*, 2005). Plants species performed vital roles in both local and cities to cutter for their health problems. Plants became familiar as medicine due to the ancient ideologies and believed. Entire plant parts served as medicines for so many tremendous ailments including gastrointestinal ailments, because of their constituents they made up of, to address so many problems in the wellbeing of living entity (Per.comm).

The novel Coronavirus (2019-nCoV) emergence

The novel coronavirus (2019-nCoV) has been revealed at Wuhan, China as human to human transmitted infectious disease in December, 2019 (Mizumoto *et al.*, 2020). It has also affected many people in China and other countries within a very short period. It also lead to a declaration of international recommendations as a public health emergency (Mizumoto *et al.*, 2020). However, the novel coronaviruses were compared with SARS and MERS coronaviruses' protein cotes in searching for an effective natural compounds so as to reduce the risk of the novel coronaviruses (Mizumoto *et al.*, 2020). Furthermore, it has come to the notice that informally, SARS-CoV and MERS-CoV were subgrouped into Sarbecovirus and Merbecovirus due to their prototypes (Coronaviridae Study Group., 2020).

Subsequently, about 13 different natural compounds were recommended from the plants' metabolites to bring the end of the novel coronaviruses outbreaks (Mizumoto *et al.*, 2020). However, the human coronaviruses were common cause of acute respiratory tract infections which linked with the severe acute respiratory tract syndromes (SARS)-CoV since 2003, which served to be novel as described by (Wong & Yuen, 2008). Laboratory workers and animal handlers were more vulnerable to pneumonia and not responded to standard antibacterial coverage as well, some precautionary measures need to be taken as it recorded severity signs and mortality rates (Wong & Yuen, 2008).

Nevertheless, the emergence of Coronaviruses having to be sporadic which became a severe global threat and unavoidably occurred due to the changes of climate changes, ecological settings and how people interact with animals, with such a threat, and urgent need to be in place for the development an effective therapies against the CoVs incidences (Chen, Liu & Guo, 2020). Emerging infectious diseases and re-emerging infectious diseases, were kind of diseases that occur in the past and also re occur in near future. Certain factors contributed towards their occurrences, which include: Ecological factors, human demographic changes & behaviour as well as technology and industries as pointed out by (Abdallah, 2019).

Coronaviruses causing gastroenteritis

Gastrointestinal ailments were not only caused by bacteria and parasites but also caused by some coronaviruses types. Among the one capable of causing the ailments include: Transmissible gastroenteritis virus (TGEV) and enteropathogenic coronaviruses (CoV) of porcine, which resulted to lethal watery diarrhoea and plain dehydration in piglets that resulted to myriad losses in swine industries across the globe (Zhou *et al.*, 2017).

Moreover, TGEV infection also caused acute enteric disease which categorized by lethal diarrhoea, dehydration, high mortality rate and lead to losses in an economic stability, this is in line with their positive-sense RNA genome contents (Zhou *et al.*, 2017). As such, some transmissible gastroenteritis coronaviruses were susceptible among the baby pigs herd at farrowing time which were not unusual to lose most, despite its actions in causing diarrhoea and economic losses (Hu *et al.*, 2017).

However, study has shown that common coronaviruses are well known to be transmissible via fomites and also capable for surviving on an ordinary surfaces for some hours (Feied, 2004). It also shared similar features on surviving on an ordinary surfaces as well as transmitting from one to another, the organisms include; *E. faecalis*, *E. faecium* and *Chlamydia* spp (Feied, 2004). Coronavirus can stay for up to 4 days in a patients' stool with diarrhoea which is in line with the higher PH more than the normal PH. So also, the samples' suspensions (SARS-CoV) have a larger duration than the solid one (Feied, 2004). Emerging viral infections (e.g. SARS-CoV), have revealed a profound diversity of viruses as well as the how they were transmitted from one host to another, which caused a serious global catastrophe as reported in the metagenomic (Sheahan *et al.*, 2012). Nevertheless, among the clinical symptoms of SARS (Viral pneumonia) include: Fever, chills, myalgia, malaise, quickest respiratory worsening, sore-throat, Rhinorrhoea and watery diarrhoea (Cheng *et al.*, 2007).

Recently, China through its National Health Commission has reported that, as at February 2, 2020, 14,488 cases, including about 304 deaths have put in place and also 23 other countries have been reported with the case of coronaviruses (Zhang *et al.*, 2020). Based on the ongoing pandemic, it is an urgent for looking forward to the lasting therapeutic agents so as to minimize the occurrences through vaccines formulations and enacting laws to the populace (Zhang *et al.*, 2020). SARS-CoV, has become a life threatening form of pneumonia which infected a larger number of people (8000) since around 2002 to 2003 worldwide, where China having the larger number since then, due to the lack of western orthodox, *Houttuynia cordata* thumb as a traditional medicine for many years, known to be capable of addressing any lung related ailments, was very useful and active as well (Lau *et al.*, 2008). Moreover, the 10% iodophor solution that contain 1% iodine usually caused oxidation of cysteine, iodination of some essential acids which leads to the bacterial cell wall damage and effective against fungi and viruses e.g.; Transmissible gastroenteritis virus Rabies virus (Coronavirus) (Lim & Kam, 2008).

Plants therapeutic actions against Coronaviruses

Plants are essential not only for food but also for medicine especially managing many ailments caused by microbes including potential cure against COVID-19 outbreak. Active compounds contained in plants as metabolites in fighting the foreign bodies (Redeploying plant defences, 2020). It is just recently that, Chloroquine phosphate can inhibit the viral replication, which were parts of plant extracts, especially quinine derivatives that play a vital role in ; ethnobotany and phytochemistry two integral parts in drug discovery for fighting deadly disease like coronavirus (Redeploying plant defences, 2020). However, Ontario public health dedicated in carrying out many works so as to come out with good findings to help the front-line health workers and researchers around the globe against Coronavirus disease 2019 (COVID-19) (Mizumoto *et al.*, 2020).

Nevertheless, human coronaviruses have caused 15-30% mild upper respiratory tract infections, at times linked with bronchiolitis and pneumonia, up to date no any antiviral drugs to treat human coronaviruses infections, but rather demonstrated chloroquine to be widely used antimalarial drug and also inhibits the HCoV-OC43 replication as carried out by (Keyaerts *et al.*, 2009).

Moreover, traditionally, there was no available drugs for SARS-CoV be it conventional antiviral agents or non- antivirals with some mode of actions, but efforts have been made with a novel compounds to target the precise pathways against the virus (Wong & Yuen, 2008). Indian medicinal plants have been used traditionally against many multi-drug resistant bacteria and reported a wide spectrum potencies which is in line with some viruses (Sawadogo *et al.*, 2018). About 15 medicinal plants were used traditionally and tested against drug resistant isolates, among the plants; *Acorus calamus*, *Camellia sinensis*, *Cichorium intybus*, *Delonix regia*, *Hemidesmus indicus*, *Lowsonia inermis*, *Mangifera indica*,

Terminalia spp among others, were active against the multi-drug resistant isolates (Sawadogo *et al.*, 2018).

More so, *Radix isatidis* which belongs to the family Brassicaceae and used traditionally to cure diabetes and treat encephalitis B and viral infections as well, this came to the notice that, it has a pharmacological values while using methanol as the solvents (Muluye, Bian & Alemu, 2014). It also addressed some skin diseases; eczema, impetigo, acne, pruritus and also for upper respiratory tract infections with high fever (Muluye, Bian & Alemu, 2014).

Nevertheless, the use of Sage EO extracts has been used as herbal medicine time immemorial (Muluye, Bian & Alemu, 2014). Its raw materials and extracts have sanitization and antimicrobial actions against SARS-CoV (RNA virus), *Escherichia coli*, *Bacillus subtilis*, *Salmonella typhi*, *S. enteritidis*, *Shigella sonnei*, *Staphylococcus aureus*, *S. epidermidis* and *S. mutans* (Wińska *et al.*, 2019). The activity of such plant was due to the fact that, its secondary metabolites happened to be camphor, thujone and 1,8-cineole which served as preservatives as well as give enjoyable odour to the herbal formulation for the plant extract (Wińska *et al.*, 2019). Subsequently, Dandelion extracts have confirmed to be therapeutic against the viral cells after being exposed at different concentrations, where by morphological changes were recorded in some viruses while in some were not active in killing some them (Keyaerts *et al.*, 2009). Lastly, herbal formulation of medicinal plants is in line with synergistic effect of phytochemicals. Rural and urban people made use of medicinal plants as their curative measures as well as raw materials for their day to day activities, more importantly, combat various microbial and other disorders for their well-being. From one of the surveyed carried out, certain number of medicinal plants have been certified for the cure of gastrointestinal ailments, the major family among the surveyed plants were; Fabaceae (dominant), followed by Anacardiaceae and Combretaceae, while the rest of the families appeared once. The families were: Anacardiaceae, Apocyanaceae, Combretaceae, Cucurbitaceae, Fabaceae, Fabales, Malvaceae, Myrtaceae, Moringaceae, Nymphaeaceae, Rutaceae, Rhamnaceae and Zygophyllaceae as shown in table 1. (Per. Comm.).

Traditional Chinese formulations

Many plants extracts have been evaluated from Chinese medicinal herbs accessed to be the most potent plants in killing the viruses due to their valuable therapeutic agents more especially, the SAR-CoV. The plants used include: *Gentianae radix*, *Gentiana scabra*, *Dioscorea rhizome*, *Dioscorea batatas*, *Cassia tora*, *Loranthi ramus*, *Taxillus chinensis*, *Cinnamomi cortex* etc., these were in conjunction with one another among the listed plants extracts with their different valuable parts; leaves, rhizome, semen, latex, roots and stem (He *et al.*, 2011). However, most of the Chinese herbal plants were taken orally after boiling with water for anti- coronavirus (2019-nCoV), so as to have complete ingredients after boiling, so also, the knowing specific type of the plants taken is of paramount importance (Zhang *et al.*, 2020). The principle of molecular docking, network pharmacological analysis and others were employed in searching for a suitable compounds containing anti-coronavirus and other viruses that contributed to the pneumonia like infections (Zhang *et al.*, 2020).

However, some of the natural compounds have been reported and compared with some Chinese herbal formulation ingredients to be anti-coronavirus, which dealt with the virus replication as recently discovered (Mizumoto *et al.*, 2020). Chloroquine has become an inhibitory agent against the human coronavirus infection, this came up after being exposed to the chloroquine at different concentrations to attack the viral RNA (Keyaerts *et al.*, 2009). Lastly, an overall medicinal plants actions in relation to drug production, has revealed that, almost 30% botanical data was recorded, where by signifying that, traditional medicine is only limited to locals (Abdallah *et al.*, 2019). Some compounds like Oleanane-type triterpenes (1-15) were extracted from the following plants: *Camellia japonica*, *Saposhnikovia divaricata* and *Dryopteris crassirhizoma* happened to be very active in inhibiting the PEDV replications and also concluded to share similar replications pattern with Coronaviridae family like MERS (Yang, Ha & Oh, 2016). Nevertheless, PEDV theory of vaccine often shared same with MERS, which also be applied to curtail the mortality rate of the human Coronaviruses (Yang, Ha & Oh, 2016).

Subsequently, liquorice roots possessed a very good bioactive compound called Glycyrrhizin, Baicalin another flavonoids contents extracted from a Chinese herb called *Radix scutellaria* and Ginseng stem and leaf extracts have the ability to inhibit the SARS-associated viral infections, Newcastle disease virus and infectious bronchitis virus. Moreover, were recommended by the Chinese medicine as remedy as well as enhanced the immune system of the COVID -19 patients (Zhang & Liu, 2020). However, Herbacetin, quercetin 3-β- d- glycosides, iso-bavachalcone, helichrysetin and bioflavonoids from *Torreya nucifera* block the enzymatic activity of both SARS-Co and MERS-Co (Zhang & Liu, 2020). More so, antivirals, broad- spectrum antibiotics and convalescent plasma with supportive care often applied for the management of COVID-19 due to the dearth of an exact antiviral drugs (Yang, 2020). Some TCM herbal formulations; *Chinese Rhubarb* extracts, *Houttuynia cordata* water extracts, Litchi seeds flavonoid contents and beta- sitosterol of *Isatis indigotica* root extracts have been reported to inhibit enzymatic actions of SARS-CoV and SARS-CoV-2 (Yang, 2020). Moreover, some plants extracts have been identified to have anti SARS-CoV and also anti- HCoV which include: *Calophyllum blancoi*, *Euphorbia neriifolia*, *Lycoris radiata*, *Artemisia annua* and *Pyrrosia lingua* (Zhang & Liu, 2020). TCM has been a reliable system of medicine in conjunction with orthodox as declared by the China government so as to curtail the menace of COVID-19. In line with the latter, 85.20% of 60,107 confirmed COVID-19 cases have been cured using TCM, as for March 1, 2020 (Yang, 2020).

Drug discovery from plants

Some plants have been reported to be effective in curing many infectious diseases, which served as biopharmaceuticals potential in the production of orthodox. These plants include: Tobacco, duckweed, moss, alfalfa and others. It has also been recommended to utilize them in the COVID-19 vaccine development too (Shanmugaraj, Malla & Phoolcharoen, 2020).

Moreover, Drugs and vaccines developments will be the only way to eliminate the world disaster (Corona viral disease) which lead to high mortality rate, economic instability and lack of security worldwide (Rao *et al.*, 2020). In line with the latter, Medicago came up with the idea of providing COVID-19 vaccine from plants. By using virus -like particle (VLP) grown in *Nicotiana benthamiana* being a tobacco plant relative, to come up with probable vaccine against the tragic Coronavirus disease worldwide (<https://www.pmi.com/media-center/news/medicago-develops-a-plant-based-vaccine-for-coronavirus>).

Conclusion

Coronavirus has declared an international recommendations as a public emergency, in searching an alternative to curtail the menace of its fatal actions. So many environmental factors have contributed towards its emergence, where by serious actions need to be taken to eliminate it. Lastly, some compounds have been found to be active in killing the viral replications. Further pharmacological researches need to be conducted so as to develop a promising drug for the novel-coronavirus with its families.

Conflict of Interest

The authors declare that they have no competing interests.

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List of abbreviation of terms

COVID-19: Coronavirus infectious disease-2019

PEDV: Porcine epidemic diarrhoea virus

RNA: Ribonucleic acid

SARS: Severe acute respiratory tract syndromes

SARS-CoV: Severe acute respiratory tract syndromes Coronavirus

TGEV: Transmissible gastroenteritis virus of swine

TCM: China traditional medicine

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