ORIGINAL ARTICLE

What is the efficacy of herbal medicine in the treatment of COVID-19 infection?

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ABSTRACT

Currently, the cases continue to develop due to the rapid spread of COVID-19 via human-to-human transmission. Because there are no definitive anti COVID-19 drugs or vaccines available to treat this fatal infection, supporting medication to relieve the patient's manifestations is generally the only choice. Because of the homology of COVID-19 pandemic and the previous SARS coronavirus outbreak in epidemiology, genomics, pathogenesis, and the widespread use of herbal medicine for the previous SARS outbreak, clinical data suggesting the beneficial impact of herbal medicine in the treatment of COVID-19 infections is discussed. 3-Chymotrypsin-protease inhibition, blocking RNA-dependent RNA polymerase activity, inhibition of helicase protein, inhibition of replication, inhibition of viral cell entry and immunomodulatory effect are the scientific reported anti-coronavirus effects of herb-derived compounds. The findings of a number of clinical experiences have shown that herbal medicine plays an important role in the treatment of COVID-19, giving new hope for COVID-19 prevention and control.

KEYWORDS: herbal medicine, COVID-19, treatment.

INTRODUCTION

The cases currently continue to grow because of the rapid spread of COVID-19 via human-to-human transmission. Needless to say, there are currently no anti-COVID-19 pharmaceutical products or vaccines eligible for care[1]. In accordance with the current clinical recommendations and the experience in the treatment of patients with Severe Acute Respiratory Syndrome (SARS) or Middle East Respiratory Syndrome (MERS), both traditional medicine and herbal therapy are used to treat patients with COVID-19 infection, particularly in China. Because of the homology of COVID-19 and SARS coronavirus in epidemiology, genomics and pathogenesis[1,2] and the widespread usage of herbal remedies in the therapy of cases with SARS coronavirus in 2002-2003 outbreak[3,4], the clinical data suggesting the adequacy and protection of herbal remedies in the therapy of cases with emerging COVID-19 will be analysed and summarized.

ANTI-CORONAVIRUS ACTIVITY MECHANISM OF HERBS

It has been performed and reported from randomized and controlled trials, case reports or series, aimed at investigating the impact of herbal remedies on SARS coronavirus in the late of 2002 outbreak. The clinical beneficial effects of many of them were supported by clinical studies and published in the high-profile journals[5,6]. Throughout the last decade, researchers have made significant efforts to classify the substances with anti-coronavirus activity in numerous herbal formulae. And, further ingredients need to be found in herbals responsible for these effects[7,8].

3-Chymotrypsin-like protease inhibition

3-Chymotrypsin-like protease is essential for viral replication and, therefore, represents an encouraging drug goal for the production of SARS coronavirus therapeutic agents in addition to other

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human coronaviruses, such as COVID-19. It was confirmed that the Houttuynia cordata water extract, Chinese rhubarb extract, litchi seeds flavonoid extract and Isatis indigotica root extract were capable of inhibiting the enzymatic activity of 3-Chymotrypsin-like protease. Houttuynia cordata water extract also blocks the activity of viral RNA-dependent RNA polymerase. Furthermore, natural extracts including sinigrin, indigo, rhoifolin, aloe-emodin, hesperetin, quercetin, epigallocatechin gallate, gallocatechin gallate, herbacetin and pectolinarin were reported to inhibit the 3-Chymotrypsin-like protease[9-13].

Blocking viral RNA-dependent RNA polymerase action

Another possible druggable target is also represented by the RNA-dependent RNA polymerase, a main important enzyme for positive and negative-strand RNA synthesis. It was shown that RNA-dependent RNA polymerase was inhibited by the extracts of Sinomenium acutum, Coriolus versicolor and Ganoderma lucidum in a dose-dependent manner[8,14].

Inhibition of helicase protein

Helicases are important targets for antiviral drugs, as their enzymatic activities are necessary for replication, transcription and translation of the anti-coronavirus genome. It was described that scutellarein and myricetin inhibited potent in vitro SARS coronavirus helicase protein by affecting the function of ATPase[15].

Inhibition of replication

It was conducted a wide-ranging review of natural products to analyse successful anti-SARS coronavirus agents through Vero E6 cells and a cell-based SARS test. Wu et al. found that Panax ginseng extract ginsenoside-Rb1, horse chestnut tree extract aescin, Rauwolfia genus extract, eucalyptus extracts and Lonicera japonica inhibited the replication of SARS coronavirus at non-toxic levels[16].

Inhibition of viral cell entry

COVID-19, similar to other human coronaviruses, uses the ACE2 host receptor for cellular entry. Theoretically, ACE2 blockage could prevent COVID-19 infection. Hence, a herbal compound with ACE2 targeting capability retains the promise to avoid COVID-19 infection. Emodin (prepared from the genus Rheum and Polygonum), baicalin (prepared from Scutellaria baicalensis), nicotianamine (prepared from soybean), tetragalloylglucose (prepared from Galla chinensis), scutellarin and luteolin from Veronica lina riifolia significantly suppressed the interaction between COVID-19 and ACE2 host receptors. Moreover, Emodin blocks the 3a ion channel of SARS coronavirus and Human coronavirus OC43. Glycyrrhizin, saikosaponins, quercetin and Toona sinensis Roem leaf water possibly had potent anti-coronavirus action through inhibition of viral cell penetration and entry[17-23].

Immunomodulatory effect

Deaths in patients with SARS coronavirus infection, or MERS coronavirus, or COVID-19 are due to excessive inflammatory responses. Therefore, anti-inflammatory agents could potentially minimize frequency and mortality rates. Indirubin is the most frequently developed as a by-product of bacterial metabolism. This compound had significant immunomodulatory and antiviral effects, as reported by a study based on the observation of human macrophages infected with the influenza H5N1 virus and alveolar Type I cells[24]. A self-control research showed that herbal formula administration can have favourable immunomodulatory protective effects against a viral infection like SARS coronavirus[8,25,26].

Others

The clinical effectiveness of an herbal formula composed of *Glycyrrhizae, Lonicera japonica, Forsythia suspensa, Gypsum Fibrosum, Ephedra sinica, Isatis indigotica, Rheum palmatum, Mentha haplocalyx, Dryopteris crassirhizoma, Pogostemon cablin, Houttuynia cordata, Rhodiola rosea, uralensis, and Armeniaca sibirican* in treating confirmed COVID-19 cases was retrospectively evaluated. The findings suggested that this herbal formula could substantially relieve fever and cough, and was able to improve recovery[8,26].

CONCLUSIONS

Effective and supplementary therapies for the administration of cases with COVID-19 are still urgently needed. Nevertheless, most of the studies have been found to not be adequately designed and the results might lead to serious biases in evaluating the efficacy of the therapy in the COVID-19 infection.

Hopefully, the contemporary studies to assess the action of herbal medicine on COVID-19 will use more stringent protocols, with acceptable international standards. Standardized herbal products should be used in clinical trials, rather than self-prepared formulations.

The best way to supply the most credible evidence for a treatment, like a generally accepted treatment, is through randomized, placebo-controlled and double-blind trials. It is promising that

the controlled clinical trials have been performed and published to assess the efficacy of herbal medicine in the treatment of the COVID-19 infection.

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