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Chinese herbal medicine for SARS and SARS-CoV-2 treatment and prevention, encouraging using herbal medicine for COVID-19 outbreak

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ABSTRACT

Chinese herbs and plants have been used as traditional medicine, immune system booster for human being for thousands of years in China and other parts of Asia. Seven coronaviruses are known to infect humans, three of them are serious which are SARS (severe acute respiratory syndrome), MERS (Middle East respiratory syndrome), and SARS-CoV-2 (Covid-19). In this mini-review article, we have mentioned the key role some of the most important plants with antiviral activities and herbs against SARS and SARS-CoV-2 on the basis of traditional Chinese medicine.

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KEYWORDS
SARS; SARS-CoV-2; Licorice; traditional herbal plants

Introduction

Medicinal plants application dates back to the origin of human civilisation (Soleymani and Shahrajabian 2012; Lin et al. 2014; Shahrajabian et al. 2020). Traditional Chinese Medicine includes herbal medicine and acupuncture, works to prevent and treatment of disease by boosting the immune system (Shahrajabian et al. 2019a, 2019b). If Chinese herbs use correctly, there will be no adverse reactions (Shahrajabian et al. 2019c; Sun et al. 2019a, 2019b). Seven coronaviruses are known to infect humans, three of them are serious, namely, SARS (severe acute respiratory syndrome, China, 2002), MERS (Middle East respiratory syndrome, Saudi Arabia, 2012), and SARS-CoV-2 (2019–2020). Their family is *Coronaviridae*, and its genus is *Coronavirus*. Its genome sequence analysis has shown that SARS-CoV-2 belons to betacoronavirus genus, which includes Bat SARS-like coronavirus, SARS-CoV and MERS-CoV. On the basis of nucleic acid sequence similarity, the newly identified 2019-nCoV is a betacoronavirus. The aim of this mini-review article is survey and introduce important medicinal herbs and plants with antiviral activities against SARS and Covid-19.

Plants with antiviral activities, and anti-SARS plants

Zhang and Chen (2008) found that 15 compounds namely, chrlorogenic acid, rutin, hyperoside, *p*-hydroxyacephenone, scopoletin, quercetin, (3*R*,4*R*,6*S*)-3,6-dihydroxy-1-menthene, acaciin, scoparone, luteolin, quercetin, apigenin, acacetin, artistolactam, and apigenin-7,4′-dimethyl ether are notable compounds used for treatment and prevention of SARS. It has been reported *Houttuynia cordata* (HC) extract may activate the cell-mediated immunity to prevent viral infection to combat SARS (Lau et al. 2008). Several studies introduced quercetin, as an antioxidant flavonoids in both fruits and vegetables with tremendous antiviral activities which may influence SARS-CoV when cultured with target cells and causal agents of URT1 (Chiang et al. 2003; Chen et al. 2006; Heinz et al. 2010). Wen et al. (2011) also suggested herbal extracts of *Cibotium Barometz*, *Gentiana Scabra*, *Dioscorea Batatas*, *Cassia Tora*, and *Taxillus Chinese* to inhibit SARS-CoV replication. Licorice is a common herb with more than 20 triterpenoids and around 300 flavonoids which has great potential therapeutic effects as an antiviral or an antimicrobial agent (Li and Peng 2013; Wang et al. 2015). Cheng et al. (2006) reported that saikosaponings (A, B2, C, D) can be used against HCoV-22E9 because saikosaponin B_2 inhibits viral attachment and penetration stages. Lin et al. (2005) found that amentoflavone isolated from Torreya nucifera can be used against SARS-CoV. Also, Yu et al. (2012) introduced myricetin and scutellarein as helicase inhibitor against SARS-CoV. Ho et al. also found that Emodin in *Radix et Rhizoma Rhei* and *Radix*

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Table 1. Plants with antiviral activities.

Plant name	Mechanism	Reference
Maca (*Lepidium meyenii*)	It has antiviral activities against both Flu-A and Flu-B viruses	Dell Valle Mendoza et al. (2014)
Eucalyptus camaldulensis Dehn.	It has considerable antimicrobial activity, and its increase in combinations with antivirals and extracts of *Annona senegalensis* and *Psidium guajava*	Sabo and Knezevic (2019)
Betula papyrifera	Metahnolic plant extract of *Betula papyrifera* was proved for antiviral activity against coronavirus (BCV, Coronaviridae). The 80% methanolic extract fraction showed significant antimicrobial activity.	Rastogi et al. (2015)
Zanthoxylum piperitum	Its leaf extract has antiviral activities against influenza A/WS/33, A/PR/8, and B/Lee/40 viruses	Choi et al. (2008)
Sunflower (*Helianthus annuus L.*)	Flowers and seeds extracts of sunflower at various concentrations may treat different human infectious diseases	Al-Shukaili and Hossain (2019)
Codonopis lanceolata	The most important phytochemical in the leaves are chlorogenic acid, luteolin, benzoic acid and apigenin which may be helpful against infectious diseases.	Ghimire et al. (2017)
Verbascum pterocalycinum var. mutense Hub.-Mor.	The isolated saponins can be considered as potential drug in treatment of infected diseases.	Yagmur Diker et al. (2019)
Limonium densiflorum	Flavonoids and saponins are the major classes of natural products in shoot extracts which may have antiviral activities.	Medini et al. (2014)
Robinia pseudoacacia cv. idaho	Its natural compounds in traditional Chinese medicince can be considered as antiviral therapeutics	Guo et al. (2019)
Isatidis Radix	Its derived glucosinolate isomers and components like progoitrin, goitrin, epigotrin and epiprogoitrin have antiviral potency and may contribute for influence virus infection	Nie et al. (2020)
Licorice (*Glycyrrhiza uralensis* Fisch.)	It inhibits pathogenic H5N1 influenza through its antioxidant activities. It has several antiviral components against infections. It is also against and SARS coronavirus.	(Lin 2003; Chen et al. 2004; Hoever et al. 2005; Sui et al. 2010; Michaelis et al. 2010, 2011; Wang et al. 2013)
Houttuynia cordata Thunb.	Its antiviral activities extract such as quercetin, quercetrin and cinanserin has antiviral activities and effects on murine coronavirus and dengue virus infection	Chiow et al. (2016)
Isatis indigotica Fort.	Isatindigoticamides A and B exhibited antiviral activities	Liu et al. (2017)
Toona sinensis Roem	TSL-1 which is an extract from its tender leaf has an evident effect against SARS-CoV	Chen et al. (2008)
Compounds of *A. annua*, *L. radiate*, *P. lingua*, and *L. aggregata*	Herbal extracts and the compound lycorine can be use as a treatment of SARS-CoV	Li et al. (2005)
Fructus arctii	Arctigenin inhibits viral replication. Arctigenin also exhibit hemagglutination inhibition	Gao et al. (2002); Yang et al. (2005a, 2005b)
Sinupret, a herbal medicinal product made from Gentian root, Primula flower, Elder flower, Sorrel herb and Verbena hers	Concentration-dependent antiviral activity (EC_{50} between 13.8 and 124.8 μg/ml) is against RNA and DNA viruses independent of a viral envelope, so it is a good treatment of acute and chronic rhiosinusitis and respiratory viral infections	Glatthaar-Saalmuller et al. (2011)
Bioaron C, an herbal medicinal product consisting of an aqueous extract of *Aloe arborescence* Mill, vitamin C, and *Aronia melanocarpa* Elliot	Its aqueous extract has been proved as a selective antiviral treatment against influenza viruses	Glatthaar-Saalmuller et al. (2015)
Plant kingdoms like *Clusiaceae*, *Umbelliferae* and *Rutaceae*	They contain coumarin which has antiviral activity against a wide range of viruses, especially influenza viruses	Mishra et al. (2020)

Polygoni Multiflori may block the S protein and ACE2 interaction and glycyrrhizin in *Radix glycyrrhizae* can inhibit viral attachment and penetration in fight against SARS-CoV. The most important plant species as treatment remedies for respiratory diseases are *Acasia polyacantha* Willd., *Andira inermis*, *Asparagus africanus* Lam., *Cussonia arborea* Hochst, *Entada Africana* Guill and Perr., *Euphorbia hirta* L., *Keetia hispida*, *Phyllanthus muellerianus*, *Terminalia schimperiana* Hochst, *Sophora flaescens* Ait., *Scutellaria baicalensis* Georgi, *Artemisia* afra, *Sambucus nigra* L., *Anchusa italic* Retz., *Cynodon dactylon* (L.) Pers., *Thymus kotschyanus* Boiss. et Hoh., *Glycyrrhiza echinata* L., *Trigonella foenum-graceum* L., *Althaea officinalis* L., *Malva sylvestris* L., *Prunus mahaleb* L., *Adiantum capillus-veneris* L., *Ferula oopoda* (Boiss. & Buhse.) Boiss., *Stachys turcomica* Trautv, *Acacia kempeana* F. Muell., *Acacia ligulata* Cunn. Ex Benth, *Eremophia alternifolia* R. Br., *Cymbopogon ambiguous* (Steudel) A. Camus. Plants with antiviral activities are shown in Table 1. The most important herbal plants for preventing SARS are shown in Table 2.

Conclusion

Traditional Chinese medicine (TCM) has a long history which is formed by summarising the precious experience of understanding life, maintaining health and fighting diseases accumulated in daily life, production and

Table 2. The most important herbal plants for preventing SARS (Lau et al. 2005; Zhang et al. 2005).

Folium mori
Flos chrysanthemi
Semen armeniacae amarum
Fructus forsythia
Herba menthae
Radix menthae
Radix platycodonis
Radix glycyrrhizae
Rhizoma phragmitis
Radix saposhnikoviae
Folium isatidis
Radix scutellariae
Lonicerae Japonicae Flos
Radix astragali
Rhizoma Atractylodis Macrocephalae
Radix saposhnikoviae
Glehniae Radix
Crystal sugar
Radix astragali
Rhizoma Atractylodis Macrocephalae
Radix saposhnikoviae
Cyrtomium fortune J. Sm.
Isatidis Folium
Radix Scutellariae
Talcum
Radix glycyrrhizae

Notes: *Plants for treatment and prevention of Covid-19*. TCM is highly valued by both government of people of China in their efforts to prevent and eradicate SARS-CoV-2 (Yang et al. 2020). Qingfei paidu decoction (QPD) consists of *Ephedrae Herba*, *Glycyrrhizae Radix et Rhizoma Praeprata cum Melle*, *Armeniacae Semen Amarum*, *Gypsum Fibrosum*, *Cinnamomi Ramulus*, *Alismatis Rhizoma*, *Polyporus, Atractylodis Macrocephalae Rhizoma*, *Poria*, *Bupleuri Radix*, *Scutellariae Radix*, *Pinelliae Rhizoma Praepratum cum Zingibere et Alumine*, *Zingiberis Rhizoma Recens*, *Asteris Radix et Rhizoma*, *Farfarae Flos*, *Belamcandae Rhizoma*, *Asari Radix et Ehizoma*, *Dioscoreae Rhizoma*, *Aurantii Fructus Immaturus*, *Citri Reticulatae Pericarpium*, and *Pogostemonia Hebra* has been suggested in treatment of COVID-19 in China (National Health Commission of the People's Republic of China 2020). Xu and Zhang (2020) suggested that Yupingfeng San, which consists of three herbs, namely Astragalus, Fangfeng and Atractylodes is a king of preventive treatment, and regulate the body's immune function. In this medicine, Astragalus may improve lung Qi and reduce phlegm; Fangfeng may relieve the pathogenic Qi and remove dampness and pain, and Atractylodes increases the spleen Qi which may influence digestion and absorption. They have also proposed prescriptions for mild and severe patients which are shown in Table 3.

medical practices. Extracts from *Artemisia annua*, *Lycoris radiate*, *Lidera aggregate*, *Isatis indigotica*, *Torreya nucifera* and *Houttuynia cordata* showed anti-SARS effects. Extract of *Pelargonium sidoides* root and dandelion also have anti-influenza activities and they can inhibit virus entry and key viral enzyme activities. Licorice root has been in used in both traditional Chinese and Indian medicine for eons especially for respiratory ailments and diseases including pneumonia. Some other suggested herbs from TCM which use to treat and prevent coronavirus are *Radix astragali* (Huangqi), *Radix glycyrrhizae* (Ganacao), *Radix saposhnikoviae* (Fangfeng), *Rhizoma*

Table 3. Different types of prescriptions for mild and severe patients (Xu and Zhang 2020).

Mild patients				
Sangjuyin	Mulberry leaf 15 g Mint 6 g	Chrysanthemum 10 g Chinese bellflower 6 g	Forsythia 10 g Reed root 15 g	Almond 9 g Licorice 3 g
Yinqiaosan	Forsythia 15 g Bamboo leaves 6 g Burdock 6 g	Chinese bellflower 6 g Licorice 3 g	Honeysuckle 15 g Nepeta 6 g	Mint 6 g Light tempeh 5 g
Severe patients				
Maxinshigan Tang	Ephedra 15 g	Almond 10 g	Plaster 20 g	Licorice 9 g
Baihegujin Tang	Shudihuang 15 g Xuanshen 10 g Beimu 6 g	Dihuang 15 g Chinese bellflower 6 g Licorice 3 g	Angelica 15 g Ophiopogon 6 g	White peony 6 g Lily 6 g

Notes: Luo et al. (2020) introduced *Astragalus membranaceus*, *Glycyrrhizae uralensis*, *Saposhnikoviae divaricata*, *Rhizoma Atractylodis Macrocephalae*, *Lonicerae Japonicae Flos*, *Fructus Forsythiae*, *Atractylodis Rhizoma*, *Radix platycodonis*, *Agastache rugosa*, *Cyrtomium fortune J. Sm*., for prevention of Covid-19 infection, while Xu and Zhang (2020) recommended Astragalus *membranaceus*, *Atractylodis Rhizoma*, *Eupatorii Herba*, *Agastache rugosa*, *Ophiopogon japonicas*, *Scrophularia ningpoensis*, *Rhizoma phragmitis*, *Adeinophora stricta Miq*, and *Dendrobium nobile Lindl*. for the prevention of Covid-19 infection. Zhang et al. (2020) reported the network pharmacology analysis predicted that the general in vivo roles of 25 herbal plants were related to regulating viral infection, immune inflammation reactions and hypoxia response. The 26 Chinese herbals screened and classic catalogue is shown in Table 4. Composition of Huo-Gu formula is indicated in Table 5. Traditional Chinese medicine treatments for different COVID-19 cases are presented in Table 6. Some important chemical constituents in traditional herbs which can consider them in fight against COVID-10 are Betulinic acid, Coumaroyltyramine, Cryptotanshinone, Desmethoxyreserpine, Dihomo-γ-linolenic acid, Dihydrotanshinone I, Kaempferol, Lignan, Moupinamide, N-cis-feruloyltyramine, Quercetin, Sugiol and Tanshinone IIa.

Table 4. The 26 Chinese herbals screened and classic catalogue (Zhang et al. 2020).

Herbal name (Latin)	The number of antiviral natural compounds contained in the plant	Classic catalogue (Latin/English)
Forsythiae fructus	3	Antipyretic detoxifying
Licorice	3	Qi-reinforcing
Mori cortex	3	Antitussive antiasthmatics
Chrysanthemi flos	2	Pungent cool diaphoretics
Farfarae flos	2	Antitussive antiasthmatics
Lonicerae japonicae flos	2	Antipyretic-detoxifying drugs
Mori follum	2	Pungent cool diaphoretics
Peucedani radix	2	Phlegm-resolving medicine
Rhizoma fagopyri cymosti	2	Antipyretic detoxifying
Tamaricis cacumen	3	Pungent-warm exterior-releasing medicine
Erigeron breviscapus	2	Pungent-warm exterior-releasing medicine
Radix bupleuri	2	Pungent cool diaphoretics
Coptidis rhizome	2	Heat-clearing and dampness drying medicine
Houttuyniae herba	2	Antipyretic-detoxifying
Hoveniae dulcis semen	2	Antipyretic-detoxifying
Inulae flos	2	Phlegm-resolving medicine
Eriobotryae folium	3	Antitussive antiasthmatics
Hedysarum multijugum maxim.	3	Qi-reinforcing
Lepidii semen descurainiae semen	3	Antitussive antiasthmatics
Ardisiae japonicae herba	2	Antitussive antiasthmatics
Asteris radix et rhizome	2	Antitussive antiasthmatics
Euphorbiae helioscopiae herba	2	Diuretic dampness-excreting
Gikgo semen	2	Antitussive antiasthmatics
Anemarrhenae rhizome	3	Fire-purging
Epimrdii herba	2	Yang-reinforcing
Fortunes bossfern rhizome	2	Warming interior

Atractylodis Macrocephalae (Baizhu), *Fructus forsythia* (Lianqiao). Qingfei Paidu decoction (QPD) is considered because of high efficacy contain *Ephedrae Herba*, *Glycyrrhizae Radix et Rhizoma Praeprata cum Melle*, *Armeniacae Semen Amarum*, *Gypsum Fibrosum*, *Cinnamomi Ramulus*, *Alismatis Rhizoma*, *Polyporus*, *Astractylodis Macrocephalae Rhizoma*, *Poria*, *Bupleuri Radix*, *Scutellariae Radix*, *Pinelliae Rhizoma Praepratum cum Zingibere et Alumine*, *Zingiberis Rhizoma Recens*, *Asteris Radix et Rhizoma*, *Farfarae Flos*, *Belamcandae Rhizoma*, *Asari Radix et Rhizoma*, *Dioscoreae Rhizoma*, *Aurantii Fructus Immaturus*, *Citri Reticulatae Pericarpium* and *Pogostemonis Herbal*. Combining traditional Chinese medicine andchemical medicines may give better results, but it is better pharmacologists separate active pharmaceutical ingredients and identify explicit targets. The compounds extracted from *A. annua*, *L. radiate*, *P. lingua*, and *L aggregate* have been identified to show antiviral against SARS-CoV which; but it may need to be tested for SARS-Covid-2. The compounds of *Houttuynia cordata* contribute to the superior antiviral efficacy of EA fraction which lacked cytotoxicity in vitro and acute toxicity *in vivo*, and it has great potential for the development of antiviral agents against coronavirus infection; furthermore, three of its constituent flavonoids against murine coronavirus are quercetin, auercitrin and ruitn. *Radix astragali* (Huangqi), *Glycrrihizae Radix Et Rhizoma* (Ganacao), *Radix saposhnikoviae* (Fangfen), *Rhizoma Atractylodis Macrocephalae* (Baizhu), *Lonicerae Japonicae Flos* (Jinyinhua), *Fructus forsythia* (Lianqiao), *Atractylodis Rhizoma* (Cangzhu), *Radix platycodonis* (Jiegeng), *Pogostemonis Herba* (Huoxiang), *Cyrtomium fortune J. Sm*. (Guanzhong), *Perillae Folium* (Zisuye), *Rhizoma phragmitis* (Lugen), *Glehniae Radix* (Shashen), *Citri Reticulatae Pericarpium* (Chenpi), *Ophiopogonis Radix* (Maidong), *Eupatorii Herba* (Peilan), *Folium isatidis* (Banlangen), *Coicis Semen* (Yiyiren), and *Folium mori* (Sangye) are the most common herbs in preventive formulae for COVID-19. Some important chemical constituents in traditional herbs which can consider them in fight against COVID-10 are Betulinic acid, Coumaroyltyramine, Cryptotanshinone, Desmethoxyreserpine, Dihomo-γ-linolenic acid, Dihydrotanshinone I, Kaempferol, Lignan, Moupinamide, N-cis-feruloyltyramine, Quercetin, Sugiol and Tanshinone IIa. The most important herbal formulae for COVID-19 were herbal formula of Shen Fu Tang with Su He Xiang Pill or Angong Niuhuang Pill in the severe stage and the combined formula of Xiang Sha Liu Junzi Tang and Li Zhong Pill in the recovery stage; furthermore, Angong Niuhuang Pill, Zhi Bao Dan, Zi Xue San, and Su He Xiang Pill were the only

Table 5. Composition of Huo-Gu formula (Huang et al. 2020).

Pharmaceutical name of herbal compounds	Chinese name	Dosage (g)
Poria	Fuling	12
Cinnamomi ramulus	Guizhi	10
Atractylodis macrocephalae rhizoma	Baizhu	12
Glycyrrhizae radix et rhizome	Ganacao	3
Pinelliae rhizome praeparatum	Fabanxia	9
Radix salvia miltiorrhizae	Dangshen	12
Angelicae sinensis radix	Danggui	9
Chuanxiong rhizome	Chuanxiong	10
Rehmanniae radix praeparatum	Shudihuand	12
Paeonia radix rubra	Chisaho	9
Eupolyphaga steleophaga	Tubiechong	9
Cervicornuscolla	Lujiaojiao	12

Table 6. Traditional Chinese medicine treatments for different COVID-19 cases (Ho et al. 2020).

Clinical feature	Recommended Chinese patent medicine	Ingredients
	Suspected COVID-19 case	
Muscle fatigue accompanied with gastrointestinal discomfort	Huoxiang Zhengqi capsules	*Pogostemonis Herba*, *Glycyrrhizae Radix et Rhizoma*, *Praeparata cum Melle*, *Atractylodis Macrocephalae Rhizoma*, *Pinelliae Rhizoma*, *Citri Reticulatae Pericarpium*, *Magnoliae Officinalis Cortex*, *Platycodonis Radix*, *Perillae Folium*, *Arecae Pericarpium*, *Poria*, *Angelicae Dahuricae Radix*, *Zingiberis Rhizoma Recens*, and *Jujubae Fructus*
Muscle fatigue accompanied with fever	Jinhua Qinggan granules	*Lonicerae Japonicae Flos, Gypsum Fibrosum, Ephedrae Herba Praeparata cum Melle, Armeniacae Semen Amarum, Scutellariae Radix, Forsythiae Fructus, Fritillariae Thunbergii Bulbus, Anemarrhenae Rhizoma, Arctii Fructus, Artemisiae Annuae Herba, Menthae Haplocalycis Herba, and Glycyrrhizae Radix et Rhizoma*
	Lianhua Qingwen capsules	*Forsythiae Fructus, Lonicerae Japonicae Flos, Ephedrae Herba Praeparata cum Melle, Armeniacae Semen Amarum, Gypsum Fibrosum, Isatidis Radix, Dryopteridis Crassirhizomatis Rhizoma, Houttuyniae Herba, Pogostemonis Herba, Rhei Radix et Rhizoma, Rhodiolae Crenulatae Radix et Rhizoma, Menthae Haplocalycis Herba, and Glycyrrhizae Radix et Rhizoma.*
	Shufeng Jiedu capsules	*Polygoni Cuspidati Rhizoma et Radix, Forsythiae Fructus, Isatidis Radix, Bupleuri Radix, Patriniae Herba, Verbenae Herba, Phragmitis Rhizoma, and Glycyrrhizae Radix et Rhizoma.*
	Confirmed COVID-19 case	
Qingfei Paidu Decoction	Application: ased on the clinical observations made by clinicians across different regions, this is a basic Chinese herbal medicine formula applies to mild cases, moderate cases, and severe cases. It may also apply to critical cases, depending on the condition of individual patients. Where appropriate, medical professionals may choose to prescribe other formulae introduced in the subsequent sections of this article, based on the TCM diagnosis of patients.	Basic formula: *Ephedrae Herba* 9 g, *Glycyrrhizae Radix et Rhizoma Praeparata cum Melle* 6 g, *Armeniacae Semen Amarum* 9 g, *Gypsum Fibrosum* 15–30 g (decoct first), *Cinnamomi Ramulus* 9 g, *Alismatis Rhizoma* 9 g, *Polyporus* 9 g, *Atractylodis Macrocephalae Rhizoma* 9 g, *Poria* 15 g, *Bupleuri Radix*16 g, *Scutellariae Radix* 6 g, *Pinelliae Rhizoma Praeparatum cum Zingibere et Alumine* 9 g, *Zingiberis Rhizoma Recens* 9 g, *Asteris Radix et Rhizoma* 9 g, *Farfarae Flos* 9 g, *Belamcandae Rhizoma* 9 g, *Asari Radix et Rhizoma* 6 g, *Dioscoreae Rhizoma* 12 g, *Aurantii Fructus Immaturus* 6 g, *Citri Reticulatae Pericarpium* 6 g, and *Pogostemonis Herba* 9 g.

prescription that were not required in the form of decoction and only prescribed in the severe stage. Traditional Chinese herbal medicines can consider as an important key in the management of new and emerging infectious disease.

Authors' contribution

All authors contributed equally to literature research, writing manuscript, etc.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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