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PERSPECTIVA

The trends on plants in the prevention and treatment of the COVID-19

DOI 10.32712/2446-4775.2021.1026

Porto, Polliana Fernandes[1]; Bragança, Maylla Luanna Barbosa Martins[1]*; Oliveira, Bianca Rodrigues de[1]; Coelho, Carla Cristine Nascimento da Silva[1]; Serra, Hellen Cristina Oliveira Amorim[1]; Muniz, Alessandra Karla Oliveira Amorim[1]; Santana, Karen das Graças Ferreira Passos[1].

[1]Universidade Federal do Maranhão, Restaurante Universitário. Avenida dos Portugueses, Vila Bacanga, CEP 65080-805, São Luís, MA, Brasil.

*Correspondência: mayllabmartins@gmail.com.

The use of natural products is growing everyday around the world. Herbal phytoconstituents have been effective in the past reducing infectious conditions for many years, before antibiotics were introduced. Herbal medicinal products appear to be an alternative for the manufacturing of novel antivirals, antibodies, vaccines, growth factors and cytokines[1].

Identifying the antiviral mechanisms, of these herbal medicinal products has elucidated on how and where they interact or interrupt with the viral life cycle. This includes viral input, replication, assembly and release, as well as virus-specific interactions[1,2].

The greatest advantage of using products that originate from plants to produce vaccines is the inability they have to replicate human pathogens, because these products can diminishing the risk of contamination and making the purification process less strident. In otherwise they can be produced in massive quantities by molecular farming in plants, reducing the cust of production[2,3].

Phytonutrients in the diet (originating from fruits and vegetables) generally promote immune responses, due to the presence of antioxidants and anti-inflammatory compounds. These include phenolic compounds, flavonoids, carotenoids and vitamins of complex B, C, D and E, in addition to iron, selenium and zinc. The strategy of providing a diet with anti-inflammatory compounds has proven to be a viable option for managing COVID-19. The insufficiency of micronutrients and others nutritional aspects, have been shown to affect the clinical course of the disease[4].

Flavonoids belong to a group of secondary metabolites by plants with a polyphenolic structure, which is widely found in fruits and vegetables. They have a biochemical and antioxidant effect in some diseases. The effects are as antioxidants, anti-inflammatory, anti-mutagens, anti-cancer-causing and antiviral activity, associated with the ability to control major cell enzyme functions. Specifically, apigenin, luteolin, quercetin, amentoflavone, puerarin, epigallocatechin, epigallocatechin gallate, gallocatechin gallate and kaempferol, these show the ability to inhibit the proteolytic activity of SARS-CoV 3CLpro[5].

Ocasionally Chinese medicinal herbs have been used in the treatment of viral epidemics in some countries. China and South Korea have produced a protocol that considers the use of these components in the treatment of COVID-19. The SARS-CoV2 (similar to SARS-CoV) uses the ACE-2 receiver as the gateway to the cell. Some compounds can inhibit infection because they have the same virus receptor, so the compound blocks the receptor and blocks the virus from accessing the cell. Thus, herbal compounds that have this binding capability with the ACE-2 receptor have been used in China and Korea in the treatment of COVID-19, such as, *Glycyrrhiza uralensis*[6].

Furthermore, some herbal products of Traditional Chinese Medicine, may have potentially immunosuppressive effect, this can reduce inflammatory markers (TNF-α, IL-1β, IL-6, IL-8, IL-10), resulting in decreased lung inflammation or acute lung disease. Other formulas showed significant inhibition of SARS-CoV-2 replication and reduced pro inflammatory cytokines (TNF-α, IL-6, CCL2/MCP-1, and CXCL10/IP-10) produced at the mRNA level[6].

Considering the evidence, there are many studies being produced, these aim to focus on the use of plant products in the treatment and prevention of viral infections, especially COVID-19. Find on the **TABLE 1** some species that have shown promising results in several studies.

TABLE 1: Potential antiviral strategies from plants against Coronavirus.

Plant specie Autor Família	Biological action	Active compound	EC50 or IC50 (SD)
Allium porrum J. Gay Alliaceae	Action of lecithins in inhibition of viral action	Agglutinin	0.45 (0.00) µg[7,8]
Allium sativum	Secondary metabolites that inhibit the action of the virus	Quercetin	ND[7,9,10]
Angelica keiskei (Ashitaba)	3CLpro inhibitor	Chalcones	11.40-129.80 µg[7,11]
Camellia sinensis	3CLpro Inhibitor	Tannic acid	3.00 µg[7,8]
		3- isotheaflavin urtiga3-gallate	7.00 µg[7,8]
	Binding to RNA-dependent RNA polymerase	Theaflavin	ND[7,8]
	Replication & 3CLpro	Betulinic acid	ND[7,8]
	PLpro & 3CLpro	Coumaroyltyramine	ND[7,8]
	PLpro & 3CLpro	Cryptotanshinone	ND[7,8]
	Replication, 3CLpro & entry	Desmethoxyreserpine	ND[7,8]
	Entry & spike protein	Dihydrotanshinone	ND[7,8]
	PLpro & 3CLpro	Kaempferol	ND[7,8]
	Replication & 3CLpro	Lignan	ND[7,8]
	PLpro	Moupinamide	ND[7,8]
	PLpro & 3CLpro	N-cis-feruloyltyramine	ND[7,8]
	PLpro & 3CLpro	Quercetin	ND[7,8]
	Replication & 3CLpro	Sugiol	ND[7,8]
	PLpro & 3CLpro	Tanshinone IIa	ND[7,8]
Cinnamomi sp.	Early stage inhibition of viral entry (clathrin-dependent endocytosis pathway)	Procyanidin A2	10.70 (0.40) µg/mL (EtOH fraction) - Water extraction followed by phase extraction[8,11]

Dioscoreae Rhizoma	Viral growth inhibitor	Plant extract	200.00 µg/ml[7,11]
Galla chinensis	ACE2 receptor inhibitor	Tetra-O-galloylβ-d-glucose	4.50-240.00 µg (from 85 % ethanol extract) 1.70 (0.30) µg (Isolated compounds)[7,11]
Galla chinensis	ACE2 receptor inhibitor	Tetra-O-galloylβ-d-glucose	4.50-240.00 µg (from 85 % ethanol extract) 1.70 (0.3) (Isolated compounds)[7,11]
Glycyrrhiza glabra and Glycyrrhiza uralensis (Licorice)	Viral growth inhibitor of SARS - CoV	Glicirrizina	30.00 ug/ml[10,11]
		Glycyrrhizin	365.00 (12.00) ug/ml (Chemical standards)[8]
		18β-glycyrrhetinic acid	> 20.00 ug/ml[8]
Houttuynia cordata (Fish leaf)	3CLpro Inhibitor and RNAdependent RNA polymerase (RdRp) Inhibitor. May inhibit pivotal enzymes and trigger negative feedback control in immune systems.	Plant extract	>200.00 µg/ml[7,11]
		Boiled water extract	50.00 µg/ml ~1000.00 µg/mL[8,11]
		Boiled water extract	
Isatis indigotica	3CLpro inhibitor	Hesperetin	8.30 µg[1,7]
		Sinigrin	2170.00 µg[1,7]
Laurus nobilis	Viral Growth inhibitor	Plant Extract	120.00 µg/ml[7]
	Inhibition of viral replication	L. nobilis: β-ocimene, 1,8-cineole, αpinene, β-pinene	120.00 (1.20) µg/mL (Essential oil)[8]
Nicotiana tabacum	Plant bioreactors that can be used in the development of oral vaccines	Antígeno Viral S1 Antígeno Viral N	1.60 (0.50) µg[3,7,11]
Nicotiana benthamiana	Viral growth inhibitor. Studying its use for creating a vaccin.	NICTABA Lectin	ND[3]
Psoralea corylifolia	Mixed inhibitor of SARS-CoV PLpro (isobavachalcone and psoralidin also reversible)	Ethanol extract of seeds	15.00 µg/ml[7,8]
		Bavachinin	38.40 (2.40) µg[7,8]
		Neobavaisoflavone	18.30 (1.10) µg[7,8]
		Isobavachalcone	7.30 (0.80) µg[7,8]
		4′-O-methylbavachalcone	10.10 (1.20) µg[7,8]
		Psoralidin	4.20 (1.00) µg[7,8]
		Corylifol A	32.30 (3.20) (rest in µM)[7,8]
Rheum palmatum	Inhibition of 3CLpro	Plant extract in 75 % etanol. Possibly anthraquinones	13.76 (0.03) µg/ml[7,11]
Rheum officinale	Viral spike protein and human ACE2 receptors inhibitor	Emodin	1.00-10.00 µg/ml[7,8]
	Inhibited binding of S protein to ACE2	Emodin Water extracts (at 40°C) of roots	~5.00 µg/mL[7,8]
Salvia miltiorrhiza	Non-competitive enzyme isomerization inhibitor of protease (except for rosmariquinone which exhibits simple reversible slow-binding inhibition). Isolated compounds from ethanol extract	Tanshinones	0.80-30.00 µg[7]
		Tanshinone IIA	89.10 (5.20) µg[8]
		Tanshinone IIB	24.80 (0.80) µg[8]
		Methyl tanshinonate	21.10 (0.80) µg[8]
		Cryptotanshinone	226.70 (6.20) µg[8]
		Tanshinone I	38.70 (8.20) µg[8]
		Dihydrotanshinone I	14.40 (0.70) µg[8]
		Rosmariquinone	21.10 (0.80) µg[8]
		Tingenone	9.90 µg[8]
		Iguesterin	9.90 µg[8]

Toona sinensis Roem	Inhibit the cellular entry of SARS-CoV	Quercetin	30.00−43.00 µg/mL Boiled water extract of leaves[7,8]

Legend: CLpro = chymotrypsin-like protease; n/a = not applicable to this study; ND = no data; PLpro = papain-like proteas; RNA = ribonucleic acid; EC50 = effective concentration, IC50 = inhibitory concentration, ACE2 = angiotensin-converting enzyme; SARS –CoV = Severe Acute Respiratory Syndrome CoV.

The species of *Camellia sinensis*, *Glycyrrhiza glabra, Glycyrrhiza uralensis, Nicotiana tabacum* and *Nicotiana benthamiana* are being widely studied and have brought great promises to the prevention and treatment of the coronavirus, especially COVID-19 kind. The use of isolated plants or compounds has shown the ability to act from the moment the virus enters the cell, until the inhibition of its replication. Thus, the development of a plant-based vaccine is a real possibility and it is already in testing phase. However, further studies are needed to establish how effective, safe to use, individual dose and possible side effects expected from these compounds.

References

1. Ahmad A, Rehman UM, Alkharfy KM. An alternative approach to minimize the risk of coronavirus (Covid-19) and similar infections COVID-19 Overview. **Eur Rev Med Pharmacol Sci**. 2020; 24(7): 4030-4034. ISSN 1128-3602. [CrossRef].

2. Rosales-Mendoza S, Márquez-Escobar VA, González-Ortega O, Nieto-Gomez R, Arevalo-Villalobos JI. What does plant-based vaccine technology offer to the fight against COVID-19? **Vaccines.** 2020; 8(2): 1-19. ISSN 2076-393X. [CrossRef]

3. Capell T, Twyman RM, Armario-Najera V, Ma JKC, Schillberg S, Christou P. Potential applications of plant biotechnology against SARS-CoV-2. **J T Plants Sci**. 2020; 25(7): 1-9. ISSN 1878-4372. [CrossRef].

4. Gasmi A, Noor S, Tippairote T, Dadare M, Menzel A, Bjørklundg G. Individual risk management strategy and potential therapeutic options for the COVID-19 pandemic. **Clin Immunol**. 2020; 215: 108409. ISSN 1521-6616. [CrossRef].

5. Jo S, Kim S, Shin DH, Shin DH, Kim MS. Inhibition of SARS-CoV 3CL protease by flavonoids. **J Enzyme Inhib Med Chem**. 2020; 35(1): 145–151. ISSN 1475-6374. [CrossRef].

6. Wu R, Wang L, Kuo H-CD, Shannar A, Peter R, Chouet PJ et al. An Update on Current Therapeutic Drugs Treating COVID-19. **Curr Pharmacol Rep**. 2020; 6: 56-70. ISSN 2198-641X. [CrossRef].

7. Yonesi M, Rezazadeh A. Plants as a prospective source of natural anti-viral compounds and oral vaccines against COVID-19 coronavirus. **Preprints** 2020; [CrossRef].

8. Mani JS, Johnson JB, Steel JC, Broszczak DA, Neilsena PN, Walsha KB et al. Natural product-derived phytochemicals as potential agents against coronaviruses: a review. **Virus Res**. 2020; 284: 197989. ISSN 1872-7492. [CrossRef].

9. Vellingiri B, Jayaramayya K, Iyer M, Narayanasamy A, Govindasamy V, Giridharan B, et al. COVID-19: A promising cure for the global panic. **Sci Total Environ**. 2020; 725: 138277. ISSN 0048-9697. [CrossRef].

10. ul Qamar MT, Alqahtani SM, Alamri MA, Chein LL. Structural basis of SARSCoV-2 3CLpro and anti-COVID-19 drug discovery from medicinal plants. **J Pharm Anal**. 2020; 10(4): 313-319. ISSN 2095-1779. [CrossRef].

11. Ho LTF, Chan KKH, Chung VCH, Leung TH. Highlights of traditional Chinese medicine frontline expert advice in the China national guideline for COVID-19. **Eur J Integr Med**. 2020; 36: 101116. ISSN 1876-3839. [CrossRef] [PubMed].

Histórico do artigo | Submissão: 10/06/2020 | **Aceite:** 08/10/2020 | **Publicação:** 31/03/2021
Conflito de interesses: O presente artigo não apresenta conflitos de interesse.
Como citar este artigo: Porto PF, Bragança MLBM, Oliveira BR, Coelho CCNS et al. The trends on plants in the prevention and treatment of the COVID-19. **Rev Fitos**. Rio de Janeiro. 2021; 15(1): 115-119. e-ISSN 2446.4775. Disponível em: <http://revistafitos.far.fiocruz.br/index.php/revista-fitos/article/view/1026>. Acesso em: dd/mm/aaaa.