



Research article

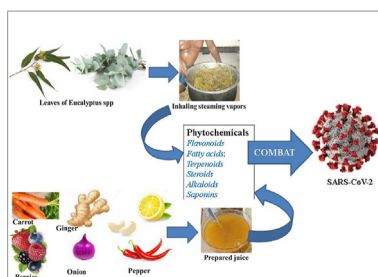
The role of natural products from medicinal plants against COVID-19: traditional medicine practice in Tanzania



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GRAPHICAL ABSTRACT



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ABSTRACT

Background: Pandemic COVID-19 is a dangerous disease caused by a new coronavirus known as severe acute respiratory syndrome (SARS-CoV-2). There is non-reliable drug or vaccine available to combat for SARS-CoV-2. More efforts to search for antiviral agents against COVID-19 are obligatory, whereas phytochemicals are potent solution. Thus, this study involved phytochemical screening and examining medicinal plants used to combat COVID-19 in Tanzania.

Methods: The plant materials were collected from practitioners. The plant extracts were then subjected for qualitative phytochemical screening so as to identify the nature of secondary metabolites.

Results: Eucalyptus species, pepper, berries, ginger, garlic, onions and lemon were identified as commonly plants used. The flavonoids, tannins, fatty acids, steroids, terpenoids, and saponins were identified through phytochemical screening. Identified natural phytocompounds revealed to be potential in exhibiting antiviral activities by disrupting the viral life cycle including viral entrance, replication, assembly, and discharge, as well as virus-specific host targets. Thus, this prompt increasing of pharmaceutical industry focused on phytochemical extracts from medicinal plants, and aromatic herbs in the hopes of discovering lead compounds, with purposeful to antiviral medications.

Conclusion: The medicinal plants and phytocompounds revealed to have significant role due to their substantial antiviral activity against SARS-CoV-2 and other coronaviruses. The noted natural products inspire collective efforts in determination and gathering funds to support scientific researchers to investigate more phytochemicals from medicinal plants for development of antiviral drug against COVID-19.

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1. Introduction

COVID-19 is one of current global pandemic disease as it was declared by World Health Organization since early March 2020 [1]. The disease has affected billions of people and caused multitudes of deaths globally. People with immuno-compromised are the even mostly vulnerable. The COVID-19 is triggered by a new coronavirus known as severe acute respiratory syndrome (SARS-CoV-2), which belong in family Coronaviridae of coronaviruses [2, 3]. Studies have disclosed that there is a kind of relationships of SARS-CoV-2 with SARS-CoV, the virus that reported to cause severe acute respiratory syndrome (SARS) in 2002 and Middle East respiratory disease (MERS) in 2012 [3]. On the other hand, possession of the biggest RNA genome and the positive-sense single-stranded RNA in SARS-CoV-2 is a major reported genetic difference from other virus [2, 3]. Indeed, SARS-CoV-2 is a 2019 novel coronavirus (2019-nCoV) that spread quickly since its discovery in patients with serious pneumonia in Wuhan in China [1, 3]. Individual people, group of people, and institutions have been working day and night searching medication drug against COVID-19. Regardless of the efforts to this prevailing situation, there is non-reliable drug or vaccine available currently for treatment of human infection with SARS-CoV-2.

Nevertheless, in most cases the antiviral medications used to treat SARS and MERS are currently being commonly used to treat COVID-19 because their genomic sequence is strikingly similar to that of SARS-CoV-2. A number of antiviral drugs that show promising results and which are on-going examined in mass clinical trials on the patients of COVID-19 as recommended by WHO are Remdesivir, Lopinavir, Hydroxychloroquine, and Dexamethasone [4, 5, 6, 7, 8]. The dexamethasone has been mostly recommended to severely patients while hydroxychloroquine has been recommended commonly in case of asymptomatic patients especially those involved to care of suspected or confirmed cases of COVID-19 [6]. Furthermore, the viral resistance and side effects, as well as viral re-emergence and latency on majority of currently available antiviral medications are concerned challenge. This situation prompts for several institutions, scientists, researchers, and practitioners get not settled as they daily search for solution of COVID-19. As a result, a lot of medication and vaccine research studies at the experimental and clinical levels are now being done worldwide in focus to tackle SARS-CoV-2 [6, 9]. Certainly, vaccines, interferon treatments, and small-molecule medicines are likely to be among the choices for controlling or preventing developing 2019-nCoV infections. What is important here? The world need drugs which can either kill the SARS-CoV-2 or interferes its replication or make human body immunity strong to fight against COVID-19 for sustainable global and environmental health.

Nature through natural products is a potential source for the solution to out-weigh the pandemic COVID-19 [10]. Yes, for instance, small-molecules drugs can be synthesised in the laboratory or can be obtained as biosynthesised secondary metabolites (natural products) from living things such as medicinal plants or microorganisms. Medicinal plants have been used since medieval time of human life for treatment of numerous diseases, communicable and non-communicable diseases as they can biosynthesize voluminous of bioactive phytochemicals [11, 12, 13, 14]. The exhaustive medicinal properties of medicinal plants based on their origin native region, used plant parts, and their antiviral promises have been conducted [15]. Understanding the action mechanisms of complex plant extracts and isolated plant-derived compounds are needed as may help to pave the way towards combating of this life-threatening disease. Traditional practitioners have been caretakers of this medicinal plants and herbal drugs in traditional medicine health settings. Medicinal plants used to cure viral diseases are potential to coronavirus as well as SARS-CoV-2 [16, 17]. For instance, the African, Indian, and Chinese traditional medication systems have practiced in this era to fight against COVID-19 [9, 14]. Cocktail of extracts and distilled herbals rich of natural products have been reported in several countries such as India in Asia continent [9, 16, 18]. Tanzania and Mozambique are

among African countries that employed natural products to fight against SARS-CoV-2. For this reason, there are many potential antiviral drug lead compounds that can be derived from the traditional medicines hence used for treating influenza, SAR-CoV or similar to SAR-CoV-2 as for comparison symptoms.

The natural products (secondary metabolites or phytochemicals) from medicinal plants are therefore bringing hope to contain phytocompounds which can either kill the SARS-CoV-2 or interferes its replication or make human body immunity strong to fight against. Hypericin is among of the recently reported natural products with antiviral activities against SARS-CoV-2 [19]. Thus, this paper does not only highlights important medicinal plants used by traditional medication healing but also unveil potential phytochemicals for drug discovery and development as efforts to fight against COVID-19.

2. Material and methods

2.1. Plant materials

The medicinal plants used by traditional practitioners to combat COVID-19 in Tanzania were identified and their extracts of collected from Iringa district in Iringa region. The plant materials were leaves of *Eucalyptus globulus*, fruits of lemon and pepper, as well as tubers of ginger, garlic, onion, and carrot. The first category of materials collected from practitioners was leaves extracts before heating; those were used up by patients through inhalation as hot gases. The second category of materials was extract from lemon fruits, pepper fruits, ginger, garlic, onion, and carrot; and patients consumed all those as a mixture (cocktail) of warm juices. Both categories of plant materials were extracted using distilled water. Collected extracts were then subjected for phytochemical screening so as to identify the nature of secondary metabolite content in such plants used to combat SARS-CoV-2. Finally, the bioassay reference was carried to pinpoint pharmacological activities of the identified phytochemicals against coronavirus as well as SARS-CoV-2 with the inspiration to put extra effort in phytochemistry and bioprospecting on the identified medicinal plants.

2.2. Phytochemical screening

Qualitative phytochemical screening of steroids, alkaloids, terpenoids, flavonoids, glycosides, tannins, and saponins was conducted according to standard procedures as previously described [20, 21, 22, 23, 24].

2.3. Test for steroids

Mixture was made by adding 1 mL of chloroform into 0.1 g of the extract. Then 1 mL of acetic anhydride was added to the mixture. This was followed by two drops of concentrated sulfuric acid which were added gently to the mixture alongside the test tube. Changes of colour from violet to blue/green indicated the presence of steroids.

2.4. Test for alkaloids

About 0.5 g of the extract was added to 3 mL of 1% aqueous hydrochloric acid and stirred in a steam bath. The mixture was then filtered, and 1 mL of the filtrate was poured into two test tubes, each containing 0.5 mL. Finally, 3 drops of Mayer's reagent were added to one of the test tubes, and 3 drops of 1% picric acid were added to another test tube. The formation of precipitates with any of the final added two reagents confirmed the presence of alkaloids.

2.5. Test for glycosides

Mixture of made by adding 1 mL of glacial acetic acid containing one drop of ferric chloride solution into 0.1 g of extract. Then 1 mL of

concentrated sulphuric acid was added to the mixture by pouring alongside the test tube. The brown ring formation indicated the presence of glycosides.

2.6. Test for saponins

About 0.5 g of extract was added to 5 mL of distilled water and shaken well. Then the mixture was gently warmed. Persistent frothing even after warming indicated the presence of saponins.

2.7. Test for tannins

Mixture of made by adding 1 mL distilled water into 0.5 g of extract. Then the mixture was stirred, filtered and few drops of ferric chloride were added to the filtrate. The formation of blue-black precipitates indicated the presence of tannins.

2.8. Test for flavonoids

Mixture of made by adding 15 mL of distilled water into 0.25 g of plant extracts, and then mixture was filtered. The filtrate, about 10 mL were collected which then divided into two test tubes each containing 5 mL. Then 5 mL of 20% sodium hydroxide was added to 5 mL of the filtrate. In another tube of 5 mL of the filtrate 5 mL of lead acetic solution was added. Formations of yellow colour with either of the reagents added to the filtrate confirmed the presence of flavonoids.

2.9. Test for terpenoid

About 0.1 g of the extract was dissolved in 1 mL of chloroform. Then 1 mL of acetic anhydride was added to the mixture. Finally, two drops of concentrated sulfuric acid were added gently to the mixture alongside the test tube. Changes of colour from violet to pink-red indicated the presence of terpenes.

3. Results and discussion

It is undoubtedly that medicinal plants and their therapeutic properties have been useful worldwide as primary health care for a variety of disorders. In this study, medicinal plants used to combat against COVID-19 in Tanzania, and their respective phytochemicals compositions were determined. The medicinal plants identified were in two categories based on how they applied for treatments. Leaves of eucalyptus *spp* were boiled and inhaled as steam vapour, while mixture of lemon, ginger, garlic, pepper, onion, and carrot were boiled to make juice as summarized in Figure 1. According to ethnomedicine report, leaves of Eucalyptus *spp* have aromatic oil with antibacterial, antiseptic, and expectorant qualities. The practitioners recommended hanging a mesh bag filled with eucalyptus leaves under the hot tap while taking a bath, or pouring boiling water over the leaves and hanging your head, covered in a towel, over the steaming vapours to relieve congestion, asthma, and other breathing disorders including COVID-19. This is supported with pharmacological studies that reported Cineole as one of these components, and it loosens phlegm, relieves coughs, and helps with other common respiratory disorders [25]. Similarly, the other mixtures to make a juice are considered as food ingredients for boosting body immunity and treatment of several diseases including COVID-19. At least three anti-COVID-19 drugs formulated from medicinal plants in Tanzania, and they are in the various stages for clinical trials and verification. These formulated drugs are Covidol, Udanol, and Uzima. Furthermore, the secondary metabolites such steroids, fatty acids, flavonoids, saponins, and alkaloids were identified through phytochemical screening from the plants extracts (Table 1).

While searching for reliable medicine or vaccine is on-going worldwide, the preventive measures such as use of soap water, use of hand sanitizer, and disinfectants are the commonly chemical available options in the stocks to fight against COVID-19. Dressing face masks and social distances are also among many preventive measures to community given by WHO and healthcare workers. On the other hand, many medication

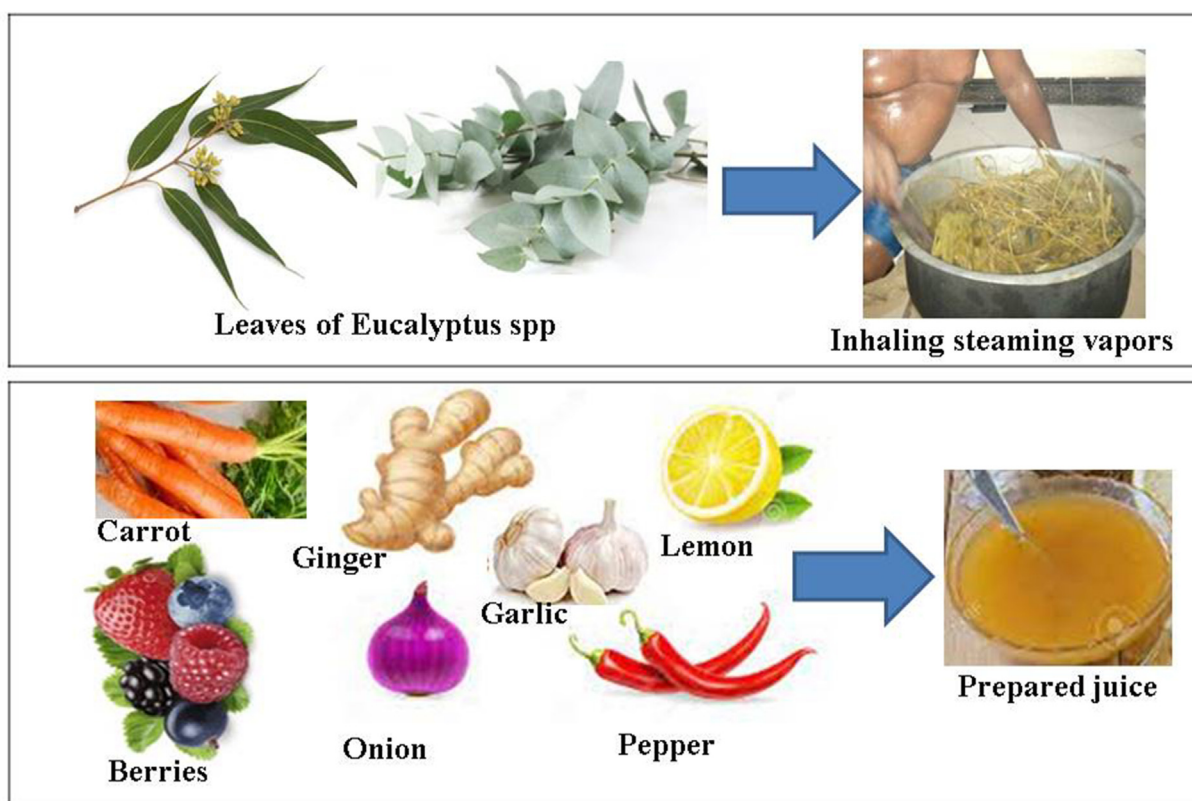


Figure 1. Identified plants and formulations used to fight against COVID-19.

Table 1. Results of qualitative phytochemical screening of the collected extracts.

Nature of tested phytochemicals	Phytochemical test of screened extracts	
	Plant extracts taken as juice	Plant extracts inhaled as hot vapour
Flavonoids	+	+
Terpenes	+	+
Saponins	+	+
Tannins	+	+
Alkaloids	+	+
Glycosides	+	+
Fatty acids	+	+
Steroids	+	+

Key: (+) = present; (-) = absent

and vaccine research studies of medicinal plants at the experimental and clinical levels are now being done worldwide to tackle SARS-CoV-2 [11, 18]. Various places apply spices and herbs in the strategic to fight against COVID-19 [26]. In fact, SAR-CoV-2 is comprised of three basic structure components that is surface proteins, membrane composed of lipid-bilayer, and a single-stranded RNA genome [4]. Equally, chemicals for prevention or medication depend on the interactions with the viral building structure. Accordingly, functional groups in chemicals play a purposeful role on the interference of biochemical reactions to SARS-CoV-2. This means that, chemical drugs for medication against SARS-CoV-2 are needed either to disrupt lipid layer, or to bind with protein to cause biochemistry malfunctions leading to interfere targeted viral metabolisms or viral RNA components to inhibit genetic replication [27]. The recognized nature of secondary metabolites in this study bear a resemblance to combat the COVID-19 as compared with other studies [11, 18, 28]. Fatty acids, flavonoids, and steroids are commonly important potential with respect to COVID-19 fighting.

Fatty acids, particularly essential oil such oleic, linoleic, and linolenic acids (Figure 2) are biosynthesized phytochemicals with various anti-microbial activities, antioxidant activities, and anti-inflammatory activities [29, 30, 31, 32]. Studies have shown that small molecules, such as fatty acids, disclosed many hydrophobic and hydrogen bond interactions with the interface's major residues due to the hydrogen bonding. In fact, commonly all phytochemicals attach securely to the binding pocket of the spike protein (S protein) through strong hydrogen bond interactions, according to docked complex analysis [28, 33]. Nevertheless, all of the Fatty acids appear to be potential *in vivo* inhibitors of the SARS-CoV-2 S protein [25, 28, 34]. Essential oils reported to be the top-ranked compounds among the chemicals investigated in terms of binding affinity [33]. Essential oil from garlic acid and Eucalyptus spp [25, 34, 35], due to high binding to viral protein [28] might be potent with high contribution to such evidenced traditional treatments in Tanzania. With regards to this study and other reported pharmacological activities of the medicinal plants, they inspire more determination of such potential bioactive phytochemicals from plants for drug discovery and development to combat SARS-CoV-2.

Steroids such as androsteroids and progesterone have been found in plants, in addition to a preliminary examination in animals [36, 37]. Phytosterols, which are sterols biosynthesized in plants, are used as low-cost substrates for the manufacture of steroid derivatives. Phytosterols are of various structures with different health benefits [38]. For decades, the steroids as termed as corticosteroids drugs have been available as generic and reliable drugs. They are used to treat a variety of ailments such as rheumatism, asthma, allergies, skin infection, inflammations, and even to help cancer patients cope with nausea caused by chemotherapy [8, 39, 40, 41]. for instance, dexamethasone is among important of synthetic generic steroid that is commonly used to treat inflammation in different conditions even those related with COVID-19 [8, 42]. This medicine protects the body from some of the damage that can occur when the immune system goes into overdrive in the fight against coronavirus. Technically, steroids (dexamethasone) are used to

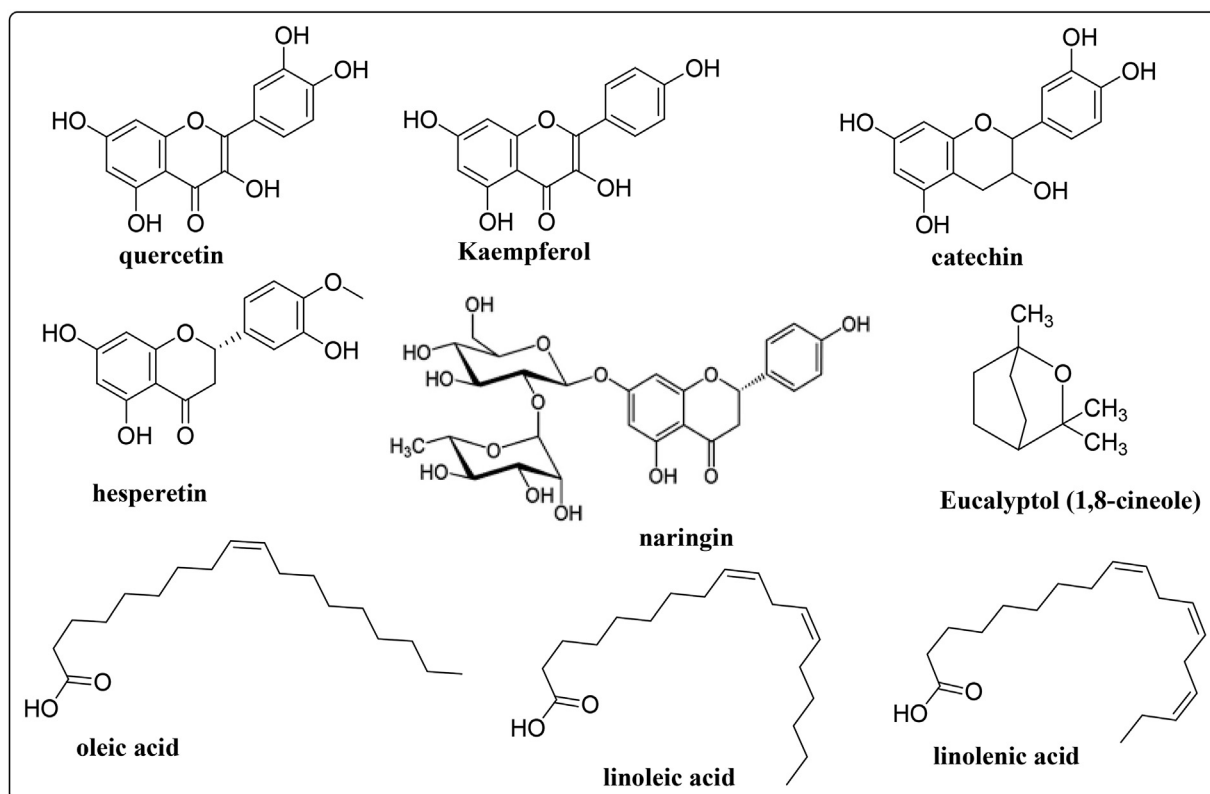


Figure 2. Apparent potential phytochemicals present in the medicinal plants used to fight against COVID-19 in Tanzania.

treat inflammation, which can occur in Covid-19 patients when the immune system overreacts to the infection. It works by suppressing the migration of neutrophils and decreasing lymphocyte colony proliferation [40]. Scientists in the United Kingdom claim that the generic steroid medicine dexamethasone reduced fatalities in very ill hospitalized patients by up to one-third in a major breakthrough in COVID-19 treatment [8]. The presence of steroids in the medicinal plants extracts used traditionally in fighting against COVID-19 as per this study entails that such traditional approach is in correct. However, there is a need to perform scientific approach to come up with appropriate dose, evaluate toxicity for largest randomized trials of medications to treat COVID-19 patients in the globe.

Flavonoids are secondary metabolites that belong to among large class with versatile phytochemicals of various functional groups. They are potent phytochemicals because of possessing various medicinal properties including antioxidant activities, anti-inflammatory activities, and antimicrobial activities [13, 43, 44]. Of course, reported antiviral activities among some of flavonoids; quercetin, naringin, hesperetin, Kaempferol, and catechin (Figure 2) are likely being present in the extracts studied with prominent exhibited antiviral activities against SARS-CoV-2 too [44, 45, 46]. For instance, studies reported that the *in vitro* antiviral activities of these flavonoids evidenced against polio-virus type 1, para-influenza virus type 3 (Pf-3), and respiratory syncytial virus (RSV) [45, 47]. In addition, *in vivo* studies signpost that quercetin was the most effective against tested virus as compared to other flavonoids [45]. The straw berries, grapes (used to make red wines), seeds of pepper (*Capsicum annuum*) and leaves of radish (*Raphanus raphanistrum*) are examples of sources of quercetin. This means all these can be used to fight against COVID-19 [48] as traditionally practiced in Tanzania. These medicinal properties enlighten an avenue on medicinal plants for more extensive research to find out the possibility of reconciling flavonoids resembling quercetin with antiviral activities to fight against SARS-CoV-2.

4. Conclusion

Flavonoids, alkaloids, phenolics, fatty acids, steroids, and terpenoids are among the biosynthesised chemical compounds by plants characterizing potentiality of medicinal plants. The phytochemicals with antiviral activities are potential powerful to fight against SAR-CoV-2 as they can disrupt the viral life cycle including viral entrance, replication, assembly, and virus-specific host targets. Evidently, this trend geared to increasing of pharmaceutical industry focused on phytochemical extracts from medicinal plants, and aromatic herbs in the hopes of discovering lead compounds, with a particular emphasis on purposeful to antiviral medications. As a result, the spices, herbal medicines, and essential oils, have a wealth of chemicals that can be used to develop new antiviral treatments. In this regard, identified medicinal plants and bioactive phytochemicals have significant role to play due to their substantial antiviral activity against SARS-CoV-2 and other coronaviruses. On the other hand, flavonoids, steroids, free fatty acids such linoleic acid or/and their derivatives may conquer a central part and lead role in the antiviral drug discovery process against COVID-19. Such natural products (plant extracts and phytochemicals) inspire collective efforts in gathering funds to support researchers to investigate more phytochemicals for antiviral drug development against COVID-19.

Declarations

Author contribution statement

Stephano Hanolo Mlozi: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

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Data availability statement

Data will be made available on request.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

References

- [1] WHO, WHO Director-General's Opening Remarks at the Media Briefing on COVID-19 - 11 March 2020, WHO, 2020. <https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19-11-march-2020>.
- [2] A. Wu, Y. Peng, B. Huang, X. Ding, X. Wang, P. Niu, J. Meng, Z. Zhu, Z. Zhang, J. Wang, J. Sheng, L. Quan, Z. Xia, W. Tan, Commentary genome composition and divergence of the novel coronavirus (2019-nCoV) originating in China, *Cell Host Microbe* 27 (2020) 325–328.
- [3] A.E. Gorbalenya, S.C. Baker, R.S. Baric, R.J. de Groot, D. Christian, A.A. Gulyaeva, B.I. Haagmans, C. Lauber, A.M. Leontovich, Benjamin W. Neuman, D. Penzar, S. Perlman, L.I.M. Poon, D.V. Samborskiy, I.A. Sidorov, I. Sola, J. Ziebuhr, The Species Severe Acute Respiratory Syndrome-Related Coronavirus: Classifying 2019-nCoV and Naming it SARS-CoV-2, 2019.
- [4] B. Adhikari, N. Sahu, COVID-19 into chemical science perspective: chemical preventive measures and drug development, *Biol Chem Chem Biol* 6 (2021) 2010–2028.
- [5] A.A. Balkhair, COVID-19 pandemic: a new chapter in the history of infectious diseases, *Oman Med. J.* 35 (2020) 2–3.
- [6] F. Lamontagne, T. Agoritsas, H. Macdonald, Y. Leo, J. Diaz, A. Agarwal, J.A. Appiah, Y. Arabi, L. Blumberg, C.S. Calfee, A Living WHO Guideline on Drugs for Covid-19, 2020.
- [7] WHO, Therapeutics and COVID-19: Living Guideline, 2020.
- [8] WHO, Corticosteroids for COVID-19: Living Guidance, 2020.
- [9] S. Alam, M.R. Sarker, S. Afrin, F.T. Richi, Traditional herbal medicines , bioactive metabolites, and plant products against COVID-19 : update on clinical trials and mechanism of actions, *Front. Pharmacol.* 12 (2021) 1–20.
- [10] O. Tanyi, E. Smith, B.B. Fidele, N. Kang, Natural products as potential lead compounds for drug discovery against SARS- CoV-2, *Nat Products Bioprospect* 11 (2021) 611–628.
- [11] S. Li, C. Cheng, C. Zhang, G. Tang, H. Tan, H. Chen, Edible and herbal plants for the prevention and management of, *Front. Pharmacol.* 12 (2021) 1–13.
- [12] B. Adhikari, G. Lamichhane, Potential roles of medicinal plants for the treatment of viral diseases focusing on COVID-19: a review, *Phyther. Res.* (2020) 1–15.
- [13] T. Wang, Q. Li, K. Bi, Bioactive flavonoids in medicinal plants: structure , activity and biological fate, *Asian J. Pharm. Sci.* 13 (2018) 12–23.
- [14] Redeploying plant defences, *Native Plants* 6 (2020) 177.
- [15] O. Sytar, M. Brestic, S. Hajjhashemi, M. Skalicky, J. Kubeš, L. Lamilla-Tamayo, U. Ibrahimova, S. Ibadullayeva, M. Landi, Covid-19 prophylaxis efforts based on natural antiviral plant extracts and their compounds, *Molecules* 26 (2021) 1–19.
- [16] R. Kumar, G. Piya, P. Mudgal, H. Maity, D. Dowarha, Herbal plants and plant preparations as remedial approach for viral diseases, *Virus Dis.* (2015).
- [17] T. Bich, N. Trinh, D. Hong, L. Thanh, T. Kim, In vitro antiviral activities of ethanol and aqueous extracts of Vietnamese traditional medicinal plants against Porcine Epidemic Diarrhea virus: a coronavirus family member, *Virus Dis.* 32 (2021) 797–803.
- [18] N. Yashvardhini, D.K. Jha, Pharmacological intervention of various Indian medicinal plants in combating COVID-19 infection, *Biomed. Res. Ther.* 8 (2021) 4461–4475.
- [19] A. da R. Matos, B.C. Caetano, J.L. de Almeida Filho, J.S.C. de C. Martins, M.G.P. de Oliveira, T. das C. Sousa, M.A.P. Horta, M.M. Siqueira, J.H. Fernandez, Identification of hypericin as a candidate repurposed therapeutic agent for COVID-19 and its potential anti-SARS-CoV-2 activity, *Front. Microbiol.* 13 (2022) 1–11.
- [20] R.S. Kujur, V. Singh, M. Ram, H.N. Yadava, K.K. Singh, S. Kumari, B.K. Roy, Antidiabetic activity and phytochemical screening of crude extract of *Stevia rebaudiana* in alloxan-induced diabetic rats, *Pharmacogn. Res.* 2 (2010) 258–263.
- [21] M. Dube, Sushma, Phytochemical status of some selected medicinal plants (*Eclipta alba*, *Catharanthus roseus* and *Swertia chirata*), *Asian J. Plant Sci. Res.* 4 (2014) 28–34.

- [22] P. Tiwari, Bimlesh Kumar, M. Kaur, G. Kaur, H. Kaur, Phytochemical screening and extraction: a review, *Int. Pharm. Sci.* 1 (2011) 98–106.
- [23] D.N. Onwukaeme, T.B. Ikuogbvweha, C.C. Asonye, Evaluation of phytochemical constituents, antibacterial activities and effect of exudate of *pycanthus angolensis* weld warb (myristicaceae) on corneal ulcers in rabbits, *Trop. J. Pharmaceut. Res.* 6 (2007) 725–730.
- [24] A.M. Khan, R.A. Qureshi, F. Ullah, S.A. Gilani, A. Nosheen, S. Sahreen, M.K. Laghari, M.Y. Laghari, I. Hussain, W. Murad, Phytochemical analysis of selected medicinal plants of Margalla Hills and surroundings, *J. Med. Plants Res.* 5 (2011) 6017–6023.
- [25] D.M. Galan, N.E. Ezeudu, J. Garcia, C.A. Geronimo, N.M. Berry, B.J. Malcolm, Respiratory disorders ? *J. Essent. Oil Res.* 32 (2020) 103–110.
- [26] N.A. Singh, N. Kumar, Spices and herbs: potential antiviral preventives and immunity boosters during COVID-19, *Phyther. Res.* (2021) 1–13.
- [27] S.A. Ayatollahi, J. Shari, P. Valere, T. Fokou, Naturally occurring bioactives as antivirals: emphasis on coronavirus infection, *Front. Pharmacol.* 12 (2021) 1–19.
- [28] C. Toelzer, K. Gupta, S.K.N. Yadav, U. Borucu, A.D. Davidson, R. Milligan, J. Capin, A.J. Mulholland, J. Spatz, D. Fitzgerald, Free Fatty Acid Binding Pocket in the Locked Structure of SARS-CoV-2 Spike Protein, 2020.
- [29] M.L. Cartron, S.R. England, A.I. Chiriac, M. Josten, R. Turner, Y. Rauter, A. Hurd, H.G. Sahl, S. Jones, S.J. Foster, Bactericidal activity of the human skin fatty acid cis-6-hexadecanoic acid on *Staphylococcus aureus*, *Antimicrob. Agents Chemother.* 58 (2014) 3599–3609.
- [30] J.J. Kabara, D.M. Swieczkowski, A.J. Conley, J.P. Truant, Fatty acids and derivatives as antimicrobial agents, *Antimicrob. Agents Chemother.* 2 (1972) 23–28.
- [31] S.M. Méndez-Zúñiga, J.E. Corrales-García, E.P. Gutiérrez-Grijalva, R. García-Mateos, V. Pérez-Rubio, J.B. Heredia, Fatty acid profile, total carotenoids, and free radical-scavenging from the lipophilic fractions of 12 native Mexican avocado accessions, *Plant Foods Hum. Nutr.* 74 (2019) 501–507.
- [32] M. Chandrasekaran, K. Kannathasan, V. Venkatesalu, Antimicrobial activity of fatty acid methyl esters of some members of chenopodiaceae, *J. Biosci.* 63 (2008) 331–336.
- [33] D. Sourav, S. Sharat, L. Sona, S.R. Atanu, An investigation into the identification of potential inhibitors of SARS-CoV-2 main protease using molecular docking study, *J. Biomol. Struct. Dyn.* (2020).
- [34] B. Thi, P. Thuy, T. Thi, A. My, N. Thi, T. Hai, L.T. Hieu, T.T. Hoa, H. Thi, P. Loan, N.T. Triet, T.T. Van Anh, P.T. Quy, P. Van Tat, N. Van Hue, D.T. Quang, N.T. Trung, V.T. Tung, L.K. Huynh, N. Thi, A. Nhung, Investigation into SARS-CoV - 2 resistance of compounds in garlic essential oil, *ACS Omega* (2020).
- [35] Z. Cai, J. Peng, Y. Chen, L. Tao, Y. Zhang, L. Fu, Q. Long, X. Shen, 1, 8-Cineole: a review of source, biological activities, and application, *J. Asian Nat. Prod. Res.* (2020) 1–17.
- [36] R. Yang, L. Xue, L. Zhang, X. Wang, X. Qi, J. Jiang, Phytosterol contents of edible oils and their contributions to estimated phytosterol intake in the Chinese diet, *Food* 8 (2019) 1–12.
- [37] M. Ta, B. Bilgin, Ü. Geçgel, A.Ş. Demirci, Phytosterols as functional food ingredients chemical structures of phytosterols, *J. Tekirdag Agric. Fac.* 3 (2006) 153–159.
- [38] E. Trautwein, I. Demonty, Phytosterols: natural compounds with established and emerging health benefits, *OCL* 14 (2007) 259–266.
- [39] C. Colitis, STEROIDS (ORTICOSTEROIDS), 2019. www.crohnsandcolitis.org.uk.
- [40] D.M. Williams, Clinical pharmacology of corticosteroids, *Respir. Care* 63 (2018) 655–670.
- [41] S. Samuel, T. Nguyen, H.A. Choi, Pharmacologic characteristics of corticosteroids, *J. Neurocritical Care* 10 (2017) 53–59.
- [42] O.R. Ciobotaru, M.-N. Lupu, L. Rebegea, O.C. Ciobotaru, O.M. Duca, A. Laurentiu, C.D. Voinescu, Dexamethasone - chemical structure and mechanisms of action in prophylaxis of postoperative side effects, *Rev.Chim.* 70 (2019) 843–847.
- [43] U. Maheswari, K.S. Sridevi Sangeetha, S. Umamaheswari, C. Uma, M. Reddy, S.N. Kalkura, Flavonoids: therapeutic potential of natural pharmacological agents, *Int. J. Pharma Sci. Res.* 7 (2016) 3924–3930.
- [44] L.H. Yao, Y.M. Jiang, J. Shi, F.A. Thomas-barberan, A. Datta, S. Chen, R. Singanusong, Flavonoids in food and their health benefits, *Plant Foods Hum. Nutr.* 59 (2004) 113–122.
- [45] T.N. Kaul, E. Middleton, P.L. Ogra, Antiviral effect of flavonoids on human viruses, *J. Med. Virol.* 15 (1985) 71–79.
- [46] T. Takahashi, R. Kokubo, M. Sakaino, Antimicrobial activities of eucalyptus leaf extracts and flavonoids from *Eucalyptus maculata*, *Lett. Appl. Microbiol.* 39 (2004) 60–64.
- [47] H. Zakaryan, E. Arabyan, A. Oo, K. Zandi, Flavonoids: promising natural compounds against viral infections, *Arch. Virol.* 162 (2017) 2539–2551.
- [48] R. Manuel, L. Colunga, M. Berrill, J.D. Catravas, P.E. Marik, Quercetin and vitamin C: an experimental, synergistic therapy for the prevention and treatment of SARS-CoV-2 related disease (COVID-19), *Front. Immunol.* 11 (2020) 1–11.