RESEARCH
www.commprac.com
ISSN 1462 2815

EFFICACY OF NATURAL PRODUCTS FOR PREVENTION OF COVID-19-A CRITICAL REVIEW

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DOI: 10.5281/zenodo.10991234

Abstract

COVID-19 is the infectious dreadful disease caused by the new Coronavirus started in Wuhan China December 2019. Entire world is suffering from this disease on earth till today. The death rate status increasing day by day unexpectedly. Many strains developed and people still suffering even though many countries are vaccinated. we cannot take back the pain that happened in the last two years. Many synthetic drugs were used by people for treatment and troubled with side effects. To eradicate this type of horrible incident in the future plant-based products can be used. Natural products show inhibitory effect on COVID-19 or at least they reduce the rate of infections. This paper reviews on current status of COVID-19, drugs used by COVID-19 patients, symptoms and diagnosis. It highlights the importance and mechanism of plant-based products that improve the immune system and throws light on treatment and future prevention of COVID-19.

Keywords: Current Status of COVID-19; Symptoms And Diagnosis; Side Effects of Synthetic Drugs; Natural Products and its Role, Risk Ratio, Odds Ratio, Hazard Ratio.

INTRODUCTION

Many viruses come under Coronaviridae family and Nidovirales order that affect mammals, fishes and birds. Many published papers reveal that coronavirus can also spread through animals and birds. In the 1960s human coronavirus was first established and caused serious respiratory problems in adults and children [1, 2]. Several studies reported that transmission from human to human takes place through direct contact or droplets [3,4]. First the virus attacked China and infected other twenty-three countries through travelers. Typical symptoms include fever, Pneumonia and shortness of breath [3,5,6]. Several precautionary measures like isolation of patients, travel limitations and many more had controlled this infection. Many synthetic drugs like Methyl Prednisolone, Lopinavir combined with Ritonavir and Moxifloxacin, Chloroquine Phosphate, acetaminophen, hydroxychloroquine, remdesivir, tenofovir, disoproxil lamivudine, Nelfinavir, Pitavastatin, Perampanel, Praziquantel, Baricitinib, Fedratinib, Ruxolitinib, Arbidol (Umifinover), IFN-α, favipiravir, penciclovir, paracetamol, griffithsin, nafamostat were used to treat the infections caused by

COVID-19. This treatment is not so successful and given temporary relaxation for few days. Many of these drugs lead to side effects and even today people are suffering. So, to avoid these kind of side effects and develop immunity products extracted from nature can be used. These products from nature are ecofriendly and never cause side effects. This review helps people to identify the drugs that can be derived from nature and encourages to concentrate further and discover vaccines or curable drugs.

Current status of COVID-19

632 million confirmed cases and 6.5 million deaths were reported by the end of November 2022.The COVID-19 remains an acute global emergency today and government of many countries face uncertainties to deal with new risks of variants. WHO prepare global preparedness, readiness and response plan in 2022 to reduce the circulation of virus and treat the virus to control death rate. Sixty percent of population got vaccinated in every country it led to the development of immunity. Omicron variant of SARSCOV was reported in the month of December 2021 and it came into predominant circulation in the United States. COVID NET (Corona diseases 19 hospitalization surveillance network children with 0-11 years and adolescents with 12-17 years were affected with Delta July 1st to December 2021 and Omicron from December 19, 2021 to January 22 2022. COVID -19 variants affected different people in different ways. The symptom is less severe in non-vaccinated people than vaccinated people. The COVID -19 has created hell in the last two years many of the people lost their lives and suffered a lot.

Symptoms and Diagnosis

Symptoms of COVID-19 include respiratory infection, acute lung injury or respiratory distress syndrome, and death, however, it can be prevented by the detection of antibodies against the virus. Many studies have shown that S protein from SARS-CoV gives rise to neutralizing antibodies [7]. These neutralizing antibodies will block the membrane fusion of coronavirus [8] by directing against S1 or S2 fragments. In laboratory tests like viral nucleic acid test, serological test, hematological test, chest CT scan test and saturation test were done to detect the virus. Patients in clinical manifestation laboratory, chest CT examination were infected with pneumonia. Some corona-infected patients also complained of cardiovascular damage and respiratory issues that lead to their death [5]. MERS-COV also leads to myocarditis and heart failure [9] and these symptoms are similar to SARS-COV2 occurred in Wuhan, China. A study was conducted to understand the pathogenesis of COVID-19 by Xu, Zhe, et al 2020. Investigations of pathological characteristics of COVID-19 patients has shown the symptoms of fever, chills, cough, fatigue and shortness of breath. Chest X ray detected multiple patchy shadows on lungs. To treat this patient, they were given lopinavir combined with ritonavir (550 mg twice daily and moxifloxacin 0.4mg once daily to curb secondary infections). To prevent lung inflammation patients were given 80mg of methyl prednisolone twice daily, but even that led to no control over cough and fatigue. Finally, on day 12, chest X ray detected infiltrate and diffuse gridding shown in both lungs that became severe and required high flow nasal cannula and oxygen therapy. The condition became very critical on day13 and shortens of breath resulted to cardiac arrest and death on day-14 [10]. Acetaminophen is a drug that helps to regulate fever. COVID-19 can be prevented by early detection of virus, diagnosis, blocking transmission and close contacts, secondary infections. State council of China in the year 2020 found that chloroquine phosphate is the drug that

treats malaria can control pneumonia caused by COVID-19 [11, 45]. Drugs like chloroquine and Hydroxy chloroquine can reduce SARS-COV2and it was found in recent surveys that Chloroquine has a significant effect on treating SARS-COV1D19 [12, 13]. Hydroxychloroquine is effective in reducing the viral load of COVID-19 in corona patients and its effect strengthened by Azithromycin drug. A recent study from Wang et al reveals that remdesivir and chloroquine are responsible for treating SARS-COV-2. Some of the drugs like Lopinavir/ritonavir, nucleoside analogs, neuraminidase inhibitors, DNA synthesis inhibitors like tenofovir disoproxil and lamivudine can treat COVID-19, Chinese traditional medicine like ShuFeng JieDu or Lianhua Qingwen capsules are used to treat this infection [45, 47]. Chloroquine phosphate 2times/day (500mg) to treat COVID -19 [14]. IFN-α prevent the viral RNA synthesis and controls viral replication. In China this IFN-α can be used to treat Bronchiolitis in children and it can be available in the form of injection, spray and gels [15, 16 50, 51]. Xu et al investigated the drug called Nelfinavir that inhibits COVID19 Mpro. Another drug called Teicoplanin prevents the cell entry of COVID-19. It also treats ebola virus, influenza, HIV virus, flavivirus, Hepatitis C virus including SARS-CoV and MERS-CoV [17]. Arbidol (umifenovir) is an antiviral compound used in China and Russia for the treatment of Influenza. It also treats SARS-CoV in vitro [11]. All the drugs to treat SARS- CoV, MERS-CoV, SARS-CoV 19 and its mechanism against COVID-19 explained in Table-1. All these drugs given temporary relaxation for the people and leads to many side effects.

According to the research papers to reduce symptoms or get relaxation some treatment methods are adopted. Antibiotics cannot kill virus and it treat only bacteria. It is very difficult to cure SARS-COV-2 so we our self should take responsibility to treat it. This can be possible by spreading awareness through internet, television, media. Safety measures are required and used by everyone to avoid contamination. Researchers should work hard and develop proper vaccines and drugs to cure this microbial disaster. Many countries working on these serious issues to reduce the spread of infection and to discover vaccines and treatment measures for SARS-COV19 [18].

Table 1: Drugs to treat Coronavirus (SARS- CoV, MERS-CoV, SARS-CoV 19)

S.NO	Name of the drugs	Control	Mechanism
1	Lopinavir Combined with Ritonavir and Moxifloxacin	Fever, Chills, Cough, Fatigue and Shortness of breath. Chest X-Ray detected Multiple Patchy Shadow on the lungs can be treated [19]	800-200mg was the dose given daily. It inhibits 3CLpro [20] and blocks the post-entry replication of MERS-CoV [21]. Lopinavir controls SARS-CoV-2 replication in Vero E6 cells [22]. Treatment with 0.1gm Moxi floxacin each time once after one week decreased IL-6 [23].
2	Methyl Prednisolone	To prevent lung infection. Controls fever improved respiratory function [19]	40mg daily for three days later reduced to 20 mg.
3	Acetaminophen	Regulate Fever	It is antipyretic and analgesic so most of critically ill patients use frequently
4	Chloroquine Phosphate	Control Pneumonia caused By COVID19.	It changes the PH of endosomes. Prevents viral entry transport and post transport [24, 25]

5	Hydroxychloroquine	Prevent Pneumonia and also effective in reducing the viral load of COVID19.	Its mechanism of action (MOA) includes the interference in the endocytic pathway, blockade of sialic acid receptors, restriction of pH mediated spike (S) protein cleavage at the angiotensin-converting enzyme 2 (ACE2) binding site and prevention of cytokine storm. Unfortunately, its adverse effects like gastrointestinal complications, retinopathy and QT interval prolongation are evident in treated COVID-19 patients [26]
6	Remdesivir	Treats Covid-19 [Wang 2020]	It inhibits RNA polymerase and controls viral replication. RDV binds RdRp and terminates RNA chain. Remdesivir shows resistance in coronavirus and consists of extended intracellular half-life that permits for once daily dosing [27]
7	Tenofovir, Disoproxil and Lamivudine	DNA Synthesis Inhibitors	Inhibits RNA polymerase virus in COVID-19 patients. Tenofovir, disoproxil and lamivudine can control SARS–CoV-2 by viral RNA [28]
8	Angiotensin Receptor	Prevents Lung injury Allow the blood to flow	Blood Pressure Drug that blocks Angiostensin11 effect which will narrow blood vessels and by using this medication It will allow the blood to flow. Angiotensin Receptor Blockers (ARBs) play a vital role in protecting multiple organs including the brain and the lung of COVID19 patients [29]
9	Nelfinavir, Pitavastatin, Perampanel and Praziquantel	Potential inhibitor again st COVID19	Based on the binding free energy calculations Nelfinavir is regarded as potential inhibitor against COVID-19Mpro
10	Azithromycin	Prevent infection and control virus transmission [30]	The intracellular accumulation of Azithromycin led to increase in PH that impairs trans-Golgi network and lysosome functions [31]
11	Baricitinib, Fedratinib and Ruxolitinib	Prevents COVID -19[32]	These are powerful anti-inflammatory as JAK-STAT signaling inhibitors and are effective against the consequences of elevated levels of Cytokines (including interferon-ɣ). seen in COVID -19people
12	Tocilizumab	It is used as adjunctive therapy. This therapy treated 21 patients by improving C reactive protein levels, CT Opacity changes, percentage of lymphocytes [33]	Tocilizumab recombinant humanized anti-human-IL -6R receptor monoclonal antibody can be used alone or combined with different drugs and can show improvement against SARS-CoV [34]
13	Methylprednisolone	Control shortness of breath in COVID19 patients	Methylprednisolone are the traditional immunosuppressive drugs.

			They are important and effective to delay the pneumonia progression and treating the ARDS (Acute respiratory disease syndrome).
14	Three potential drug combinations (sirolimus plus dactinomycin, mercaptopurine plus melatonin, and toremifene plusemodin) are candidate repurposable drugs [35]. Convalescent sera [79].	antiviral properties	Sirolimus is an inhibitor of mTOR. mTOR play a vital role in MERS-CoV infection [36] and it shows antiviral and antineoplastic properties and improves the condition of patients with H1N1 Pneumonia and respiratory failure [37]. Dactinomycin can control the growth of feline enteric cov [38]. Toremifene plus emodin can control SARS-CoV-2. The toremifene control growth of MERS-CoV [39] and SARS- CoV Emodin extracted from Rheumtangutium has anti-viral properties and cure SARS-CoV [40] Convalescent sera from SARS-CoV-2–recovered patient treatment plays a vital role in the significant reduction of the mortality rate. So, it is useful for SARS-CoV-2-infection [41]
15	Paracetamol	Fever and sore throat	Usage: Tablet form lps to reduce fever, body aches.
17	IFN-α	Used to treat COVID-19 in children [42].	Reduce viral RNA synthesis and control replication of virus
18	Arbidol (Umifinover)	Recovery of body temperature Reduce cough and Pyrexia	Antiviral drugs treat SARS-CoV in vitro [11]. It's not used for children. Umifinover results in membrane fusion of viral envelop and S protein/ACE2
19	Favipiravir and Penciclovir.	Reduce cough and Pyrexia Antiviral	Antiviral drug it controls RNA dependent RNA polymerase treats COVID -19 [27].
20	Galidesivir	Prevents viral RNA polymerase function (prevents infections of SARS-CoV-2, MERS-CoV [43]	Galidesivir tightly attached to the catalytic centre of RdRp and other SARS-CoV proteins to control the virus replication [44]
21	Imatinib mesylate	Blocks viral stages of entry (prevents infections of SARS-CoV, MERS-CoV [45, 46].	Control early stage of corona virus. It is arthritis suppressor and inhibits IL-6 and pro inflammatory cytokines [47]
22	Griffithsin	Stops viral entry (prevents SARS- CoV [48].	Inhibition of spike protein function entry as these spike proteins binds to the host cells and its fusion with viral envelop with host cell membrane [49]
23	Nafamostat	Antiviral properties Prevents the virus entry [50]	It blocks the viral entry process and Stops spike mediated membrane Fusion (COVID-19, MERS-CoV)

Side effects

Many people face side effects due to many drugs during and after treatment. Side effects of Ribavirin include ate acneiform eruptions, skin rashes, eczematous lesions, scleroderma, alopecia. Side effects of interferons are psoriasis, eczematous drug reactions, lupus. Baricitinib causes melanoma and skin rashes [51, 52]. Tocilizumab causes skin infections and hypersensitivity reactions [53, 54]. Hydroxychloroquine or Chloroquine QT reactions are capable of triggering drug-induced sudden cardiac death especially if used in combination with azithromycin [55]. Lopinivir and Ritonavir results in headache, anxiety, weakness, myalgia, Administration of corticosteroids caused seizures, anxiety, insomnia [56]. Hydroxychloroquine leads to neurosis and loss of hearing. Drugs like Thyroxin, Bupropion, and Nicotinic Acid with Azithromycin causes bone marrow failure, cardiac failure, loss of neutrophils in blood, and loss of blood platelets [57]. Many adverse reactions were noticed in the research survey by using hydroxychloroquine or chloroquine, azithromycin, Lopinivir and Ritonavir, Thyroxin, Bupropion, Nicotinic Acid, Tocilizumab and interferons. Many measures need to be taken to control these effects. On the contrary adopting eco-friendly products or drugs made from nature is better and no side effects occur in the future. Homeopathy drugs give relaxation from pain and help to treat infection but may lead to many side infections as well. So, it is better to use natural products from home which can develop immunity and prevent from infections. Research can be done on the natural products to prevent infection or to get relaxation from the symptoms. Hot steam bath, fruits consumption, drinking hot water, Vitamin-c and flavonoids with moderate exercises give relaxation and prevent infection

Plant products/extracts/parts and their role

Some of the traditional plants can treat COVID19 patients [58, 59, 60]. Herbaceous plants like thyme, hillyhock, marjoram can help COVID patients when consumed. Birds soup like Perdicinae, Streptopelia and Phasianus develop resistance for COVID-19 (Table-2). This develops resistance against coronavirus as the human antibodies against microbe disease have protein structure similar to bird's proteins might be human antibody function and hence it increases resistance power [61]. Such resistance is built on the principle that human antibodies fighting against microbes have similar infection protein structure. Fruits like lemon, pear, strawberry, milk, honey, carrot can be consumed by COVID-19 patients. Watermelon and Pear have antipyretic properties. Some of the drugs that shows antipyretic properties are acetaminophen, Diuretics, Antiasthma drugs however these require continues supervision of the involved physician. Multivitamin tablets and immune syrups are also prescribed as add ones [62, 63, 64]. The leaves of Ocimum are edible and cure pain, fever, cough, diarrhoea among COVID19 infected people [65]. Cow ghee plus ocimum helps to control Pneumonia1[66, 67]. Ocimum also protect the cells from being damaged [70 68]. Terpenoids are the major secondary plant constituents and have 36,000species [71 69]. Terpenoids show properties like anticancer [70] Being antioxidants they also project anti-inflammatory, anti-viral and anti-bacterial properties. Antioxidant [73 71] anti-inflammatory, antiviral [72] and antibacterial [73]. *Ocimum sanctum* has immune modulating features and ACE2 (Angiotensin-converting enzyme 2 gene) blocking properties and it can prevent replication of CoV [74]. Some of the plants extracted drugs that are less risky can prevent COVID19 protease.

For example, Thymoquinone compound extracted from *Nigellasativa,* SalvinorinA from *Salviadivinorum,* Betaseliene from *Apium graveolens*, Menthol from mentha, Citral from *Backhousiacitriodora,* Bilobalide from *Ginkogobiloba*. The crystal structure of proteinase and low risk herbal medicine are used for docking analysis and the results have revealed that terpenoids can control virus protease [75]. Plants like *Clerodendrum* and plant based organic compounds like resveratrol, Glycyrrhizin and medicine from plants like phytomedicine, phytochemicals and phytoconstituents have important pharmaceutical properties and prevent COVID-19. Phytopharmaceuticals like flavonoids, lycopene's, terpenoids, Omega 3 fatty acids, resveratrol, limonoids, carotenoids, phytosterols shows antibacterial and antimicrobial activities that can be used to treat infections (88).

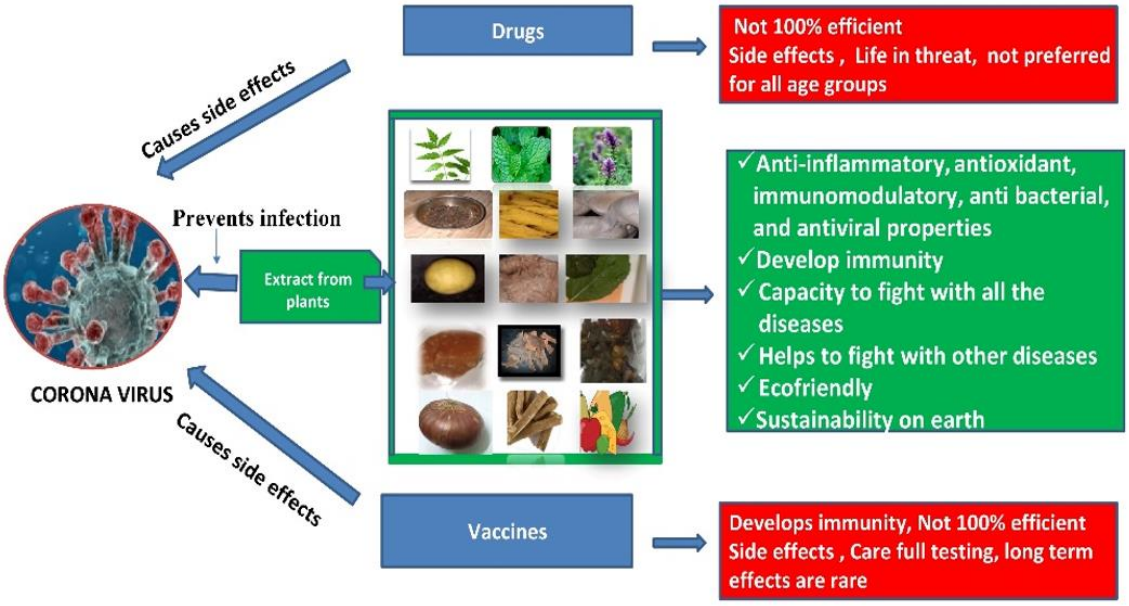

Figure 1: Plants extract and its benefits to prevent COVID-19

According to Dr. Sunil Kumar Verma used plant-based inhibitors of CD13 can be used to treat COVID. Quaternary Benzo (c) phenanthridine alkaloids from *Macleaya cordata* can be used as potent inhibitor of CD13 [76]. From Curcumalona L. (turmeric) a yellow phenolic compound called (E, E1,7-bis-(4-hydroxy-3-methoxyphenyl)-16-heptadiene-3,5-dione) can be obtained that treat Corona by irreversibly inhibiting Aminopeptidase N/CD13 [77]. Turmeric has antiviral activities and it can prevent SARS-CoV entry into the host cells and even replication of the virus can be controlled [78, 79]. From plants like birch trees, Arbutus sp, *Diospyros sp, Ancistrocladus sp, Picramnia sps, Syzygium sps,* Betulinic acid can be extracted that help to prevent COVID-19. Dr. Sunil Verma also said that plants like *Pterocarpus marsupium, Eugenia jambolana, Gymnema sylvestre* consists of antiDPP-4activity which can treat several corona viruses [80]. Astragalus is another herb it has antiviral property [81] that increases the immune system and controls the respiratory diseases. Both Astragalus and Lycorice prevent COVID-19 [82]. Some plant extracts like *Cerasusavium, Alcea digitata, Rubia tinctorium,Citrus aurantium, Allium sativum, Peganum harmala* shown inhibitory effect on Angiotensin converting enzyme(ACE) [83]. So, it is better to suggest herbal products to treat COVID-19. High dosage of intravenous vitamin C helps to treat COVID-19 in early stage

The Beijing Health commission in China revealed that treating of COVID patients with Acupuncture and Herbal medicine reduced fever and cough. Report from National Administration of Chinese Medicine stated that by using herbal formula called Qing Fei Pai Du Tang to treat COVID patients effected with Pneumonia [84]. shown 90% response. Recent study suggested that citrus peels can be used to treat COVID19. Citrus consists of flavonoids called hesperidin which binds receptors of SARS CoV and control the proteins that cause viral infection [85]. All citrus fruits like lemon and orange can bind the receptors causing infection. Many vegetables and herbs have health benefits that can be consumed for resistance. Dietary molecules present in vegetables and herbs help to produce medicine for the prevention of COVID19 [86]. Khaerunnisa Siti investigated Kaempferol, quercetin, luteolin-7-glucoside, desmethoxycurcumin, naringenin, apigenin-7-glucoside, oleuropein, curcumin, catechin, Zingerol, Gingerol, Allium are used as a potential inhibitor for COVID-19 [87]. Ashwagandha prevents the entry of COVID-19 in to human beings. According to Indian tradition Ayurvedic treatment regime like natural phytochemicals extracted from Ashwagandha, gilloy and Tulsi can curb COVID- 19. They also said that herbs in combination with hydroxychloroquine can treat COVID-19. Eucalyptus oil 1,8-cineole gives muscle relaxation and inhibits viral reproduction. Cinnamaldehyde has very good binding properties. It reduces lung problems and pulmonary edema. Presence of prenylated flavonoids from *Paulownia tomentosa* exhibit antioxidant, antibacterial and antiphlogistic properties that Prevents PL pro that controls SARSCOV. Phytopharmaceuticals also play a significant role in improving the health. So, the pharmaceutical professionals should take up the responsibility in improving herbal drugs that can treat infections (88). The mechanism and the protection against COVID-19 mentioned in Table-2.

Figure 2: ***Saccharum officinararum***

Figure 3: ***Ocimum sanctum***

Figure 4: ***Curcuma longa***

Figure 5: ***Cinnamomum vernum***

Figure 6: ***Piper nigrum***

Figure 7: ***Syzygium aromaticum***

Figure 8: ***Zingiber officinale***

Figure 9: ***Citrus limon***

Figure 10: extract with all the ingredients

Some of the natural products used in home has phenomenally developed the resistance power of people during lockdown period. Some of the important products from nature like *Saccharum officinanarum, Ocimum sanctum, Curcuma longa, Cinnamomum vernum, Piper nigrum, Syzygium aromaticum, Zingiberofficinale, Citruslimon,* available everywhere on earth which have antibacterial, antiviral and antifungal properties and can be used to develop resistance and immunity in man.

All these ingredients shown in the figure 2, 3, 4, 5, 6, 8, 9 that are powdered and water and Jagerry (figure-10) is added to prepare decoction (Figure-10). Consumption of these extract is useful to fight against the diseases including COVID-19. COVID-19 vaccine develop immunity in our body to fight against virus. Applications of these vaccines are not so successful and cases of severe complications Many vaccines discovered to fight against COVID-19 is not 100% effective and many side effects occurred so product from nature is preferred. To control infections and attain sustainability in and around individual sanitary practices and natural substances are preferred (113).

Practical applications in Statistical Theory:

general statistical examples related to the efficacy of natural products for preventing COVID-19, drawing from common themes and trends in research.

Effectiveness Rate: Suppose a study examines the effectiveness of a natural product, such as vitamin C or zinc, in preventing COVID-19. The study might report the percentage of participants who remained uninfected despite exposure to the virus while using the natural product compared to those who did not use it.

Relative Rate Reduction (RRR): If a study compares the risk of contracting COVID-19 between individuals using a specific natural product and those who are not, the relative risk reduction can be calculated. For instance, if the risk of infection among non-users is 10% and among users is 5%, the RRR would be 50%.

Numbered Needed to Treat (NNT): This statistic represents the number of people who need to be treated with a natural product to prevent one additional case of COVID-19. For example, if the NNT for a particular natural product is 20, it means that for every 20 people treated, one additional case of COVID-19 would be prevented.

Numerical Example:

Certainly, let's create a hypothetical numerical example to illustrate the efficacy of a natural product for preventing COVID-19.

Suppose a randomized controlled trial (RCT) is conducted to investigate the efficacy of consuming a specific herbal supplement in reducing the risk of COVID-19 infection among healthcare workers. In this trial:

500 healthcare workers are randomly assigned to two groups: **Group A:** Receives the herbal supplement daily for three months. **Group B:** Does not receive the herbal supplement and serves as the control group. After the three-month intervention period, the researchers observe the following: In Group A (supplement group), 5 healthcare workers out of 500 contract COVID-19.

In Group B (control group), 20 healthcare workers out of 500 contracted COVID-19. Now, let's calculate some statistical measures based on this hypothetical data:

Effectiveness Rate: Effectiveness Rate = (Number of COVID-19 cases in control group - Number of COVID-19 cases in supplement group) / Number of COVID-19 cases in control group. Effectiveness Rate = (20 - 5) / 20 = 0.75 or 75%. This means the herbal supplement reduced the incidence of COVID-19 by 75% compared to not taking the supplement.

Table 2: Natural Products,Properties and their mechanism against to treat Covid-19

Name of the plant	Drugs	properties	Mechanism
Herbaceous plants like *Origanummajorana* (Marjoram)	Plant extract	Antibacterial	Drinking this Marjoram extract reduces cough, headache, running nose
Feeding soup of birds like Perdicinae, *Streptopelia* and *Phasianus*	Soup of birds	Develops resistance against corona virus.	Feeding of fish meat, broth and soup from the birds like perdicinae, Streptopelia, pasianus increases the immunity against COVID-19in human beings. Birds show resistance to COVID-19 patients The antibodies function of human beings against corona infection is similar to that of bird's protein and prevents infection [61]
Citrulluslanatus (Watermelon) and *Pyrus communis* (Pear)	Fruits	Antipyretic and diuretic properties	Drinking juice helps to increase the immunity and resistance of the patients
Ocimum sanctum (Holy basil)	leaves	Manage pain, fever, cough, diarrhoea in COVID-19 infected people [65]. Repair cell damage, control Pneumonia [66, 67, 68]. Immunomodulating features and ACE2 (Angiotensin-converting enzyme 2 gene) blocking properties and it can prevent replication of CoV	Drinking extraction of compound from plant in water and alcohol reduce cough and cold
Nigellasativa (black cumin)	Thymoquinone	Control viral protease	Thymoquinone treats the virus by killing it, inhibiting its proliferation, kills bacteria causing Pneumonia. It kills SARS COV infection by anti-

			inflammatory and immunomodulatory effects. The antiviral action of Thymoquinone is similar to that of chloroquine and hydro chloroquine and it neutralizes the new virus and effective in treating COVID-19 [79].
Curcuma Longa	Cyclocurcumin and Curcumin	Control viral teprotease	The chemical compounds from *Curcuma longa* called cyclo curcumin and curcumin bind with the active site of COVID-19 main protease with a Glide score of more than -6 compared to hydroxy chloroquine (G score -5.47) control COV2 protease and active against COVID-19 [89].
Mentha	Menthol	Control viral protease	Menthol major component of essential oils has binding affinities towards SARA COV2 spike protein, main protease (Mpro), RNA-dependent RNA polymerase binding affinity and human ACE 2 proteins [90].
Citrus medica and *Zingiber officinale*	Nasal rinse	Helps in controlling viral load and shedding of SARS Co2 in the nasal passage Nasal cleaning and treats fever.	The nasal rinse manufactured from *Citrusmedica* and *Zingiber officinale* makes the virus inefficient to host cells
Grapes, blue berries, peanuts extract Licorice root extracts Glycyrrhizin	Resveratrol, Glycyrrhizin Roots of *Glycyrrhiza glabra* (plant extract)	Pharmaceutical properties and prevent COVID19 This plant extract with other plants control COVID 19	Resveratrol (3,4,5-trihydroxy-trans-stilbene, RES) from Grapes, and peanuts extract can stop MERS COV infection and increases the viability of cells infected by the virus [91]. Glycyrrhizin is anti-inflammatory and shows protective effects on ALI in mice by inhibiting pro inflammatory cytokines. It also inhibits the TLR4/NF-K B signal and play an important role in the

			inflammatory response of pulmonary inflammation [92].
Macleaya cordata	Phenanthridine	Potent inhibitor of CD13	Quaternary benzo(c) phenan tridine extract from *Macleayacordata* which is five seeded plume poppy inhibits CD13. Blokage of CD13 treats COVID-19 [69].
Birch trees, *Arbutus* sp, *Diospyros* sp, Ancistrocladus sp, *Picramnia* sps, *Syzygium* sps	Betulinic acid	prevent COVID-19 antiviral properties	Betulinic acid is the natural substance which play an important inhibiting viral proteases role in elaboration of new anti-COVID-19 formulations [93].
Astragalus [83 80]	antiviral properties	antiviral properties. Increases the immune system and controls the respiratory diseases and prevent COVID-19. It improves lung QI and reduce phlegm.	Astragalus should be mixed and boiled with 100ml pure water for 15minutesand after boiling to get 6ml tincture that can take 200ml orally three times a day [94].
Cerasusavium Alcea digitata, Rubiatinctorium, Citrusaurantium, Aliumsativum, Peganum harmala	Extracts from plants	Treat COVID-19 patients	Inhibitory effect on Angiotensin converting enzyme (ACE) [83].
Ephedra stem, Chinese licoroot, Apricot seed, Gypsum, Cassia twig, Asian water plantain rhizome, Ahu ling sclerotium, Bai-Zhu atractylodes rhizome, Poria sclerotium, Bupleurum Barbed skullcap root, Pinilla rhizome cured with ginger, Tartarian aster root, Fresh ginger rhizome, Colt's foot flower bud, Belamcanda rhizome, Chinese wild ginger root and rhizome, Chinese yam rhizome, Bitter orange immature fruit, Tangerine dried rind, Chinese giant hyssop aerial part	Qing Fei Pai Du Tang	Treats COVID-19 patients effected with Pneumonia [84]. Treats lungs and spleen Increase immunity and reduces inflammation	Qing Fei Pai Du Tang treats lungs and spleen. It targets the ribosomal proteins necessary for viral replication, controls mRNA transmission and controls the proteins that interact with virus proteins [95].

Spinacia oleracea (Spinach), (*Brassica oleracea* (Cabbage), *Anethumgraveolens* (Dill), Brassicarapa (Chinese cabbage). [97 96].	Kaempferol	Inhibitors of COVID19 Mpro	Kaempferol formsydrogen bonds with the 6LU7 aminoacid Tyr54, His164, Glu166, Apr187, Thr190 and these hydrogen bonds interacts with aminoacids of COVID-19 Mpro active site. Mpro in CoV results in proteolytic maturation of virus and it's the target protein to control infection by inhibiting the cleavage of viral Poly protein [97].
Allium sativum (Garlic) *Camellia sinensis* (Green tea)	Allicin [98, 99]. Catechin [100, 101].	*Allium sativum* has anti modulatory, antimicrobial, anti-mutagenic, antitumor properties Controls immune system dysfunctions Decreases pro inflammatory adipose tissue concentrations and reduces symptoms in COVID infected patients	Compounds from *Allium sativum* decreases the pro inflammatory cytokines and controls immunological abnormalities
Alliumsepa (onion), *Capsicum frutescens* (chillis), *Piper nigrum* (pepper), *Foeniculum vulgare* (fennel leaves), *Anethumgraveolens* (Dill)	Quercetin [102].	Inhibitors of COVID19 Mpro	Quercetin is the prevents the development of COVID -19 inducing virus. Plant derived propenol's can be used in pharmaceutical preparations as raw materials from herbs and consumable plants easy to consume by human beings
Withania Somnifera (Ashwagandha)	Phytochemical	Controls the COVID19 entry in to host cells and helps in COVID19 management. It has antiviral properties [103]. It's an anti-viral agent and immune booster [104].	It has major components like with anilides which manage COVID -19 infection. It acts as immune booster in COVID -19 infection and binding affinity to three three reported targets 3CLpro, PLpro and spike protein in COVID 19 infection.
Citrus limon (Citrus)	flavonoids called hesperidin	It has antihyper lipidemic emic, antiatherogenic, venotonic, antidiabetic, cardioprotective, antihypersensitive Properties.	Binds receptors of SARS CoV and control the proteins that cause viral infection [86]. It attributes antioxidant defense mechanism and suppression pro-inflammatory cytokine

			production. It reduces viral replication and fight against virus [105, 106].
Eucalyptus globulus (eucalyptus)	1,8-cineole Eucalyptus oil	Treat pharyngitis, bronchitis and sinusitis. Muscle relaxation by decreasing smooth muscle contractions [107]. Muscle relaxation by decreasing smooth muscle contractions [107].	1,8-cineole will bind with Mpro and inhibits viral reproduction. Mpro/eucalyptol complexes produce hydrophobic, hydrogen bond and strong ionic interactions [108].
Cinnamum cassia	cinnamaldehyde	cinnamaldehyde has more favorable binding properties [109].	Blocks the attachment of SARS-CoV-2. Treatment with cinnamaldehyde reduce lung wet or dry ratio and pulmonary oedema in mice and decrease the levels of inflammatory cytokines such as TNF-α, IL-6, IL-13, IL-1β [110].
Azadirachta indica (Neem)		Antimicrobial Antiviral activity	Neem compounds may prevent assembly SARS-CoV particles and reduce viral propagation. Viral replication and assembly inhibitors combination are effective for therapeutic intervention [111].
Paulowniatomentosa (Empress tree)	Tomentin A	Prenylated flavonoids shows antioxidant, antibacterial and antiphlogistic properties [112].	Prevents PL pro that controls SARA Cov

Confidence Intervals (CI): Statistical analyses often include confidence intervals to express the precision of estimates. For instance, a study might report that the use of a natural product resulted in a 95% confidence interval of 0.70 to 0.90 for preventing COVID-19, indicating the range within which the true effect is likely to fall.

P-Values: Researchers use p-values to determine the statistical significance of their findings. A p-value less than 0.05 is commonly considered statistically significant, suggesting that the observed effect (e.g., reduced risk of COVID-19 with natural product use) is unlikely to be due to chance.

Meta Analysis Findings: If the critical review includes a meta-analysis of multiple studies, statistical techniques such as pooling effect sizes can be used to provide a more comprehensive assessment of the overall efficacy of natural products for preventing COVID-19.

Publications Bias Assessment: Statistical methods such as funnel plots or Egger's regression can be employed to assess whether there is a bias in the literature towards

publishing studies that report positive results regarding the efficacy of natural products for COVID-19 prevention.

These statistical examples provide a framework for evaluating the efficacy of natural products for preventing COVID-19 based on the critical review you mentioned. However, it's essential to consider the specifics of each study and the overall body of evidence when drawing conclusions about the effectiveness of natural products for COVID-19 prevention.

Relative Risk Reduction (RRR): RRR = (Risk in control group - Risk in supplement group) / Risk in control group. Risk in control group = 20 / 500 = 0.04 or 4%. Risk in supplement group = 5 / 500 = 0.01 or 1%. RRR = (0.04 - 0.01) / 0.04 = 0.75 or 75%. This indicates a 75% reduction in the relative risk of COVID-19 among those taking the herbal supplement compared to the control group.

Numbered Needed to Treat (NNT): NNT = 1 / (Risk in control group - Risk in supplement group). NNT = 1 / (0.04 - 0.01) = 33.33. This means that approximately 33 healthcare workers need to consume the herbal supplement to prevent one additional case of COVID-19 compared to not taking the supplement.

Confidence Intervals (CI): Assuming the study provides confidence intervals, these would indicate the range within which the true effect size lies with a certain level of confidence (e.g., 95%).

P-values: A statistical test, such as a chi-square test, could be used to determine if the observed difference in COVID-19 incidence between the two groups is statistically significant (e.g., $p < 0.05$). These numerical examples demonstrate how statistical measures can be used to assess the efficacy of a natural product for preventing COVID-19 based on hypothetical trial data.

CONCLUSION

Recently vaccines for COVID-19 were discovered but administration of vaccine effected some people and lead to side effects. But there is no end for diseases like this again. New strains of Delta and Omicron came in to the earth symptoms reappear or become critical and same measures of COVID-19 should be taken by the people to save their lives. In 2022 another variant called XBB. It is the recombinant of two variants BA.2.10.1 and BA.2.7.5 that infects human by swapping their genes to form new variant XBB that is highly contagious. So, it is better to adopt ecofriendly measures to treat infection. Increase of immunity and development of resistance is required and the special focus on further research should be done. Many herbaceous plants have medicinal properties they can play a better role to treat COVID-19 and its variants. It was noticed that some of the countries did not take proper action against COVID so it became panic and spread across the world. Lack of awareness about the disease, lack of test kits availability, and overcrowding increased the risk. Rest of the people should take proper diet to develop resistance across infection. Many natural products like ocimum, Mentha, camphor, ginger, turmeric, lemon, garlic, aloe vera, ashwagandha, Jagerry, eucalyptus, cinnamon can be used as they were easily available in their houses. Natural drugs from plants, animals and birds are ecofriendly and helps to control dreadful diseases through further research. Essential oils from plant extract have anti-inflammatory, antioxidant, immunomodulatory and antiviral properties and can work against COVID-19. These products from nature not only helps to prevent dreadful diseases like COVID-19 but also improves immunity and develop

resistance across many infections in the coming future. Maintenance of hygiene in and around. Allocation of budget for supporting infected people treatment, awareness and health education for the people is required. Product from nature is endless and won't create any side effects even though many drugs discovered in future.

Conflicts of interest

Author declares no conflicts of interest

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