Original article

Previously published ethno-pharmacological reports reveal the potentiality of plants and plant-derived products used as traditional home remedies by Bangladeshi COVID-19 patients to combat SARS-CoV-2

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ABSTRACT

Several plants have traditionally been used since antiquity to treat various gastroenteritis and respiratory symptoms similar to COVID-19 outcomes. The common symptoms of COVID-19 include fever or chills, cold, cough, flu, headache, diarrhoea, tiredness/fatigue, sore throat, loss of taste or smell, asthma, shortness of breath, or difficulty breathing, etc. This study aims to find out the plants and plant-derived products which are being used by the COVID-19 infected patients in Bangladesh and how those plants are being used for the management of COVID-19 symptoms. In this study, online and partially in-person survey interviews were carried out among Bangladeshi respondents. We selected Bangladeshi COVID-19 patients who were detected Coronavirus positive (+) by RT-PCR nucleic acid test and later recovered. Furthermore, identified plant species from the surveys were thoroughly investigated for safety and efficacy based on the previous ethnomedicinal usage reports. Based on the published data, they were also reviewed for their significant potentialities as antiviral, anti-inflammatory, and immunomodulatory agents. We explored comprehensive information about a total of 26 plant species, belonging to 23 genera and 17 different botanical families, used in COVID-19 treatment as home remedies by the respondents. Most of the plants and plant-derived products were collected directly from the local marketplace. According to our survey results, greatly top 5 cited plant species measured as per the highest RFC value are *Camellia sinensis* (1.0) > *Allium sativum* (0.984) > *Azadirachta indica* (0.966) > *Zingiber officinale* (0.966) > *Syzygium aromaticum* (0.943). Previously published ethnomedicinal usage reports, antiviral, anti-inflammatory, and immunomodulatory activity of the concerned plant species also support our results. Thus, the survey and review analysis simultaneously reveals that these reported plants and

plant-derived products might be promising candidates for the treatment of COVID-19. Moreover, this study clarifies the reported plants for their safety during COVID-19 management and thereby supporting them to include in any future pre-clinical and clinical investigation for developing herbal COVID-19 therapeutics.

1. Introduction

COVID-19 is a viral disease caused by SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2); also known as a novel coronavirus that was firstly originated in Wuhan City, Hubei, China in late December 2019 (Rahman et al., 2020; Sharma et al., 2021). This contiguous disease has now become a global concern causing serious economic and health crises all over the world. Coronavirus (CoVs) is a positive (+) sense single-stranded RNA virus which affects the epithelial cells of the respiratory tract and causes inflammation of the mucosal membrane that damages the alveoli and eventually leads to pneumonia (Mhatre et al., 2020). COVID-19 was reported to cause SARS and is closely linked to Middle East respiratory syndrome (MERS) found in the past (Wu et al., 2020; Xie and Chen, 2020). According to World Health Organization (WHO) (https://www.who.int), as of July 03, 2021, there were already 1, 82,319,261 confirmed cases of which 3,954,324 were confirmed deaths in approximately 223 countries. In Bangladesh, there were already 9, 44,917 confirmed cases, 15,065 confirmed deaths, and 8, 33,897 recovery cases reported (https://corona.gov.bd).

Pandemics are not a new phenomenon in the history of human civilization but rather an old phenomenon and since ancient times humans relied on plants to solve other health-related problems including pandemics. The pandemics have wreaked havoc in the history of human civilization (Rosenwald, 2020). Several pandemics include Death or Black Plague caused by the bacterium *Yersinia pestis* in the Middle Ages (1347–1351) in Eurasia (Haensch et al., 2010), Smallpox caused by the Variola virus in the 18th century (Behbehani, 1983), Tuberculosis caused by the *Mycobacterium tuberculosis* in Europe and North America during the 18th and 19th centuries (Daniel, 2006), Malaria caused by the *Plasmodium* group (Medicine, 2004), Spanish flu caused by Hemagglutinin Type 1 and Neuraminidase Type 1 (H1N1) influenza virus in 1918 (Spreeuwenberg et al., 2018), and the swine flu pandemic caused by the same virus H1N1 influenza in 2009 (Jilani et al., 2020). Plant-based traditional herbal remedies have played a central role in all of the pandemics in human history. There is strong evidence of using traditional plant-based remedies to combat the outbreak of various pandemics caused at different times in human history (Garcia, 2020). An example of which is garlic was used as a remedy for various epidemics such as dysentery, cholera, typhus, influenza, and whenever an epidemic emerged, garlic was the first preventive and curing remedy (Petrovska and Cekovska, 2010).

Traditional medicines are mostly plant-based and the therapeutic options in many developing countries are still dependent on traditional medicine, but now the rich countries are also increasing their attention on plant-based herbal formulations for safe therapeutic purposes (Garcia, 2020). The WHO Africa (https://www.afro.who.int/news/who-supports-scientifically-proven-traditional-medicine) has already recognized and suggested the use of traditional, complementary, and alternative medicine in the treatment of COVID-19. However, these alternatives as still subject to safety maintenance and efficacy guideline. The Chinese government (http://en.nhc.gov.cn/) on the other hand, is heavily promoting and recommended traditional medicines as treatments for

COVID-19, which was proven effective in treating H1N1 diseases (Li et al., 2016). This strategy was significantly effective and played a vital role in treating SARS during the epidemic period in 2003 (Chen and Nakamura, 2004; Lau et al., 2005; Leung, 2006). Chinese traditional medicine was widely used singly or in combination with western medicine in most of the hospitals in China at the beginning of the COVID-19 outbreak, which played a very effective role in controlling symptoms (DU et al., 2020).

Bangladesh is a developing country with a high population density, where hospital scarcity exists due to not having adequate resources and facilities. According to a report (WHO, 2019) by DHTM (Director, Homeo & Traditional Medicine, 2007), about 20–39% of the population in Bangladesh seek medical treatment using indigenous traditional medicine. This country is rich in phytodiversity and here, more than 6000 plant species are found, of which about 450–500 plant species are known to have medicinal value (http://en.banglapedia.org/index.php/Flora). Since there was no effective treatment for COVID-19 and due to lack of adequate facilities for COVID-19 treatment in hospitals of Bangladesh, non-cooperative activities of health professionals and reluctance to treat, patients with COVID-19 are relying on traditional medicine at home. Treatment of COVID-19 using traditional medicine has been widely discussed on various online social media like Facebook©, Twitter©, Instagram©, and others in Bangladesh. In this context we, therefore, adopted research questions to investigate how patients infected with COVID-19 are recovering in Bangladesh; what methods they were employing for the COVID-19 treatment; what and how were their attitude and actual perception in the management of COVID-19.

A significant number of research articles including systematic reviews, *meta*-analysis, and *in silico* studies (Chowdhury and Barooah, 2020; Mhatre et al., 2020; Rahman et al., 2020; Rouf et al., 2020; Taghizadeh-Hesary and Akbari, 2020) on the potential use of traditional, complementary, and alternative medicine in the treatment of COVID-19 have already been published by several researchers in the scientific arena. They suggested that plant-based remedies such as various biologically active compounds derived from several medicinal plants can build resistance and might be a potential candidate to combat COVID-19 and could reduce the overall risks such as morbidity (cases) and mortality (deaths). However, almost all of these reviews and *in silico* studies have encompassed indirect evidence or partial studies. The practical application of these traditional medication systems and their effectiveness is not discussed yet sufficient. Limited ethnobotanical and cross-sectional studies (Chaachouay et al., 2021; Khadka et al., 2021; Nguyen et al., 2021) have yet been done to identify the medicinal plants and plant-derived products traditionally being used as home remedies in COVID-19 management and to investigate their efficacy against the SARS-CoV-2 virus and safety on the human body.

We assumed that majority of the COVID-19 infected patients in Bangladesh were receiving treatment with traditional home remedies based on plant and plant-derived products. To verify this hypothesis, we conducted a semi-online survey study on Bangladeshi COVID-19 patients. The persons who confirmed their COVID infection through RT-PCR nucleic acid test results and later recovered were selected. Furthermore, we also performed a sys-

tematic review analysis to comprehensively examine and interpret the efficacy, safety, and potentiality of the investigated plants. The review analysis was done in the light of literature references of past ethnomedicinal use reports of the studied plant species treated in other gastroenteritis and respiratory diseases similar to COVID-19 symptoms. Besides, we reviewed the studied plant species by their published data related to antiviral, anti-inflammatory, and immunomodulatory activities.

2. Methods

2.1. Study technique and sampling of the informants

Primary and secondary data were used and analyzed qualitatively and quantitatively to conduct the study. A survey was conducted throughout the country to collect the primary data from the participants being infected with COVID-19 and recovered eventually. A semi-structured and open-ended questionnaire was adopted for this survey, partially followed by Martin (1995) and Alexiades and Sheldon (1996). To facilitate a better understanding, the questionnaire was prepared in the Bengali language (see the English version in **Appendix A).** The participants were asked about what traditional home remedies based on plant and plant-derived products they used to recover from COVID-19. Questionnaires were converted to Google Docs form via Google service to make the online survey easier and faster. The Google Docs questionnaire form was shared among selective people using the snowball-sampling technique (Baltar and Brunet, 2012) through online-based various social media platforms such as Facebook©, Messenger©, WhatsApp©, email, and other online platforms. In addition to the online survey, the printed questionnaire form was supplied to a part number of participants who are less knowledgeable and uninterested in the online platform. After all, the necessary questionnaire data was collected by contacting them over the mobile phone. Initially, the questionnaire was sent to Facebook© friends and other personal acquaintances who were known and confirmed to be infected with COVID-19, and special requests were made for answering the questionnaire. They were later requested to send the questionnaire form to their acquaintances who had been infected and recovered from COVID-19.

The primary data obtained by the survey are further explained by the secondary data using literature references of past ethnomedicinal uses and pharmacological evidence relates to antiviral, anti-inflammatory, and immunomodulatory activities of the studied plant species in other diseases in the relationship of COVID-19 symptoms. This is done by analyzing various published research articles downloaded from the different bibliographic databases like Science-Direct®, PubMed®, Scopus®, Google Scholar®, etc.

2.2. Data collection

2.2.1. Ethical statement

The study was conducted following the ethical guidelines formulated by the American Anthropological Association (2012) and the Code of Ethics of the International Society of Ethnobiology (with 2008 additions). 2006; (http://www.ethnobiology.net/what-we-do/core-programs/ise-ethics-program/code-of-ethics/-code-in-English/). Ethical approval was taken from the Research and Ethics Committee, Department of Botany, University of Barishal, Bangladesh (approval number-BU/BOT/01/20). Before all interviews, we explained the aims and objectives of the study and obtained verbal informed consent from each respondent participating in the study. They have also been assured that their personal information would be kept confidential and obtained data will be used for research purposes only.

2.2.2. Primary data

To gather primary data, 436 respondents were interviewed from June to December 2020. It should be noted that in the case of respondent selection, only those were considered who were confirmed their infection and recovery with COVID-19 through RT-PCR nucleic acid test results. The data is collected and aggregated and sorted into different categories based on different titles in the Excel sheet. In the case of data on plants and plant-derived products used in the treatment of COVID-19 in the home-traditional method, the scientific names, family, and other botanical information of these plants were recorded with the help of standard literature books and the internet. All scientific names of plants were further reviewed and checked through the standardized database (http://www.theplantlist.org, Version 1.1). The herbarium voucher specimens were prepared and stored in the herbarium of the Department of Botany, University of Barishal, Bangladesh based on the availability of plant species found in the nearby area of our locations. Since most of the plants and plant-derived products used in COVID-19 treatment were collected from local marketplaces and some of the plants are not endemic in Bangladesh, therefore, herbarium sheets and/or voucher specimens of all their plants could not be prepared and stored except for a few.

2.2.3. Secondary data

The primary data obtained by the survey are further explained by the secondary data. Secondary data were generated from literature references of published articles on ethnomedicinal uses and pharmacological evidence related to antiviral, anti-inflammatory, and immunomodulatory activities of the studied plant species. To scientifically interpret the possible potentiality of the obtained primary data to fight against COVID-19, many published articles connected to the ethnobotanical study, antiviral activity, and bioactive compounds responsible for their antiviral properties were downloaded from various bibliographical databases such as ScienceDirect®, PubMed®, Scopus®, Google Scholar®, etc., and reviewed. The keywords used for searching the ethnobotanical use / antiviral activity and phytochemical compounds responsible for inhibiting the virus of the respective plant/anti-inflammatory and immunomodulatory activity were "ethnomedicinal use + scientific names of related plants, antiviral activity + scientific names of related plants, anti-inflammatory activity + scientific names of related plants and immunomodulatory activity + scientific names of related plants"; as - antiviral activity + *Allium cepa* L., " anti-inflammatory activity + scientific names of related plants", and/or "immunomodulatory activity + scientific names of related plants".

The previous ethnobotanical study, antiviral, anti-inflammatory, and immunomodulatory activity related published articles were studied as supporting evidence to explain the possible potentiality of the plant and plant-derived products obtained in the primary survey against coronavirus (SARS-CoV-2). Antiviral activity studies show a direct explanation for traditional uses of these plant and plant-derived products in favor of the treatment against Coronavirus (SARS-CoV-2) disease, whereas phytochemical studies provide indirect information and suggestions, these promising phytochemicals can be used for the development of future medicine and vaccines against SARS-CoV-2 infections. The anti-inflammatory and immunomodulatory reports provide evidence of a scientific explanation for the effective role of these studied plant species in reducing inflammation as well as immune stimulation.

2.2.4. Data analysis

Obtained primary and secondary data were systematically arranged in the tabulated form using Microsoft Excel spreadsheets. The data were then analyzed and computed to determine the val-

ues of different variables such as socio-demographics of the informants, quantitative ethnomedicinal data such as Frequency Citation (FC), Relative Frequency Citation (RCF), Use Reports (UR) and Use value (UV) for all plant species. Besides, all types of graphs, charts, and figures were prepared using statistical equations in Microsoft Excel 2013.

2.2.5. FC and RFC

The obtained ethnomedicinal information was quantitatively analyzed according to Tardío and Pardo-De-Santayana (2008) using an index of RFC. RFC displays the local importance of each species and it has been calculated as follows.

$$RFC = \frac{FC}{N} (0 < RCF < 1)$$

where FC denotes the number of informants mentioning the use of the species and N is the total number of informants participating in the survey. The RFC value ranges from 0 (when no one identifies a plant species as a useful one), to 1 (when entirely informants remark it as useful). RFC index does not consider the use category (UR or use-report is a single record for using a plant mentioned by an individual).

2.2.6. UV and UR

The UV demonstrates the relative importance of plants known locally. It was calculated using the following formula (Phillips et al., 1994);

$$UV = \frac{\Sigma UR}{n}$$

where UV is the use-value of a species, 'UR' is the number of use reports cited by each informant for a given plant species and 'n' is the total number of informants interviewed for a given plant species. The UV is applied in determining the plants with the highest use (most frequently indicated) in the treatment of an ailment, while UR is the use recorded for every species.

3. Results

3.1. Socio-demographic characteristics of the respondents

Of the 436 respondents asked in this present study, 392 were males, accounting for 90.14% of the total respondents, while female respondents were 44 (9.6%). Based on the age, people between 30 and 50 aged were the most affected, accounting for 84.63% of the total infected and which was the maximum. On the other hand, the number of infected people aged 50 and above was 11% and the number of infected people aged between 18 and 30 years was only 4.38% which was the lowest minimum (Fig. 1).

Most of the respondents who took part in our study were between 30 and 50 years of age and academically highly educated (75.46%). 94.26% of the total respondents were engaged in various occupations either job or business and a large part of them (98.39% of the total number) are from the urban areas (Town/city). All-female respondents (44; 9.86% of the total number) who participated in our study were engaged in employment and also lived
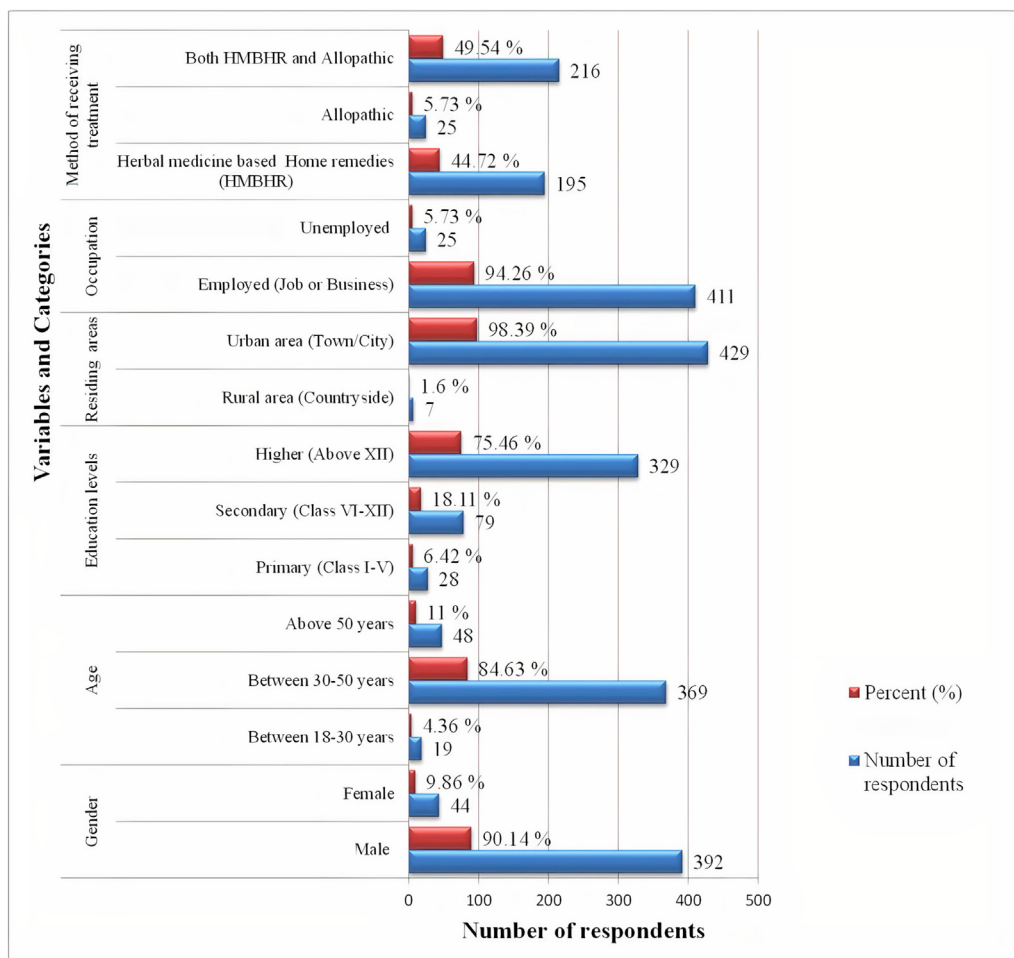

Fig. 1. Socio-demographic characteristics of the respondents (n = 436).

in the urban areas. These data suggest that the people who traveled outside the home for various purposes in urban areas were most affected by COVID-19. Most of the respondents who participated in this study relied on plants and plant-derived traditional home remedies for COVID-19 management. In this study, 44.72% of respondents received home remedies directly from plants and plant-derived products (Herbal Medicines Based Home Remedies; HMBHR) and 49.54% received both HMBHR and allopathic synthetic drugs. In this case, they have taken some fever and painkillers related to synthetic drugs like Paracetamol and/or Napa as per the physician's advice received over the phone. On the contrary, only 5.73% of the total surveyed respondents received allopathic treatment based on synthetic drugs.

3.2. Plants and plant-derived products reported in the study used for managing COVID-19 symptoms

We were able to uncover comprehensive information about a total of 26 plant species (in 23 genera) and traditional uses from 17 different families used in COVID-19 treatment as home remedies by the respondents participating in this study. The reported plant species were listed and arranged in alphabetical order of their scientific names in Table 1 and later their botanical family name, local name (Bengali name), common name (English name), habit, collection sources, used parts, mode of preparation, mode of administration, method of use recipe, number of citation, FC, RFC, etc., were sequentially included in the table. The habit-wise obtainability analysis of the 26 reported plant species categorized them as 42% herb, 39% tree, 15% shrub, and 4% are climber (Fig. 2).

The distribution of plant species among botanical families is illustrated in Fig. 3, where Lamiaceae and Rutaceae jointly ranked 1st position representing the largest number of plant species (3 species; which is 11.54% of the total number) in each family. And among other families, Amaryllidaceae, Apiaceae, Lauraceae, Myrtaceae, and Zingiberaceae achieved 2nd place by contributing with 2 species in each family. The remaining 10 families were placed in 3rd position contributing 1 species in each family. The majority of the plants and plant-derived products (23 plant species) used in COVID-19 treatment were collected directly from the market place and among them, 12 plant species were either collected from the marketplace or home garden which were cultivated domestically. Only 3 plant species were commonly available in the natural habitat.

3.3. Used parts, mode of preparation, and route of administration

The interview results in the present study revealed that various plant parts such as fruit (dried and fresh), flower bud, seed, leaf, bulb, rhizome, and bark were taken directly or mixed in combination with other supplementary products such as hot rice, honey, milk, tea, water, and vinegar, etc. The most frequently used plant parts were fruit and it accounted for 39% of the total use. The next most used plant part was leaves, which accounted for 29% of the total. Other plant parts used included seed (14%), bulb (7%), bark (4%), flower bud (4%), and rhizome (3%) (Fig. 4). Before using the above-mentioned plant parts, they were prepared through different preparation modes such as boiling, fresh, mashing, decoction, juice, raw, and powdering. Boiling and fresh form are the most notable modes of preparation in the present study and both of which accounted for 20% of the total. Other most common preparation methods include mashing and juice (16%), followed by raw and decoction (13%) and powdering (2%) (Fig. 5). These herbal remedies (HMBHR) prepared by different modes from various plant parts were either taken directly through the oral administration route (74%) or inhaled in vaporized form (26%) (Fig. 6). Detailed methods of "use/recipe" of herbal remedies used by the

respondents in the treatment of COVID-19 are described in the "Method of use/recipe" column in Table 1.

3.4. RFC

The RFC signifies the local importance of each species and its value depends on the frequency of citation. The RFC value of the studied plant species in the present study ranged from 0.305 to 1.0 (Table 1 & Fig. 7) for healing uses in the treatment of COVID-19 related symptoms. The maximum RFC value was recorded for *Camellia sinensis* (1.0) while the minimum RFC value was recorded for *Psidium guajava* (0.305). In addition, the others top 10 RFC value recorded plant species are *Allium sativum* (0.984), *Azadirachta indica* (0.966), *Zingiber officinale* (0.966), *Syzygium aromaticum* (0.943), *Ocimum tenuiflorum* (0.924), *Elettaria cardamomum* (0.911), *Mentha × piperita* (0.911), *Nigella sativa* (0.908), *Citrus aurantiifolia* (0.908), *Piper nigrum* (0.901) respectively (Fig. 8).

3.5. UV

The use-value signifies the relative importance of plants known locally. The UV of the studied plant species in the present study ranged from 0.009 to 0.038 (Table 1). The highest UV was found for *Cinnamomum tamala* (0.038) while the lowest UV was found for *Malus domestica* (0.009). In addition, the plant species with top 10 ranked UV are *Psidium guajava* (0.030), *Allium cepa* (0.028), *Camellia sinensis* (0.023), *Vitex negundo* (0.023), *Ocimum tenuiflorum* (0.022), *Phyllanthus emblica* (0.022), *Punica granatum* (0.022), *Citrus sinensis* (0.021), *Citrus aurantiifolia* (0.020), *Capsicum annuum* (0.019) and *Citrus reticulata* (0.019) respectively.

4. References for previous ethnomedicinal uses of the studied plant species

Generated data by reviewing the previously published ethnomedicinal use reports have been attached to **Appendix B** in the supplementary material. The review analysis shows that *Ocimum tenuiflorum* L. ranks 1st in the treatment with a maximum of 16 symptoms use reports, where *Citrus sinensis* and *Spondias mombin* are at the bottom with the lowest 1 use reports (Fig. 9). This is followed by *Allium cepa* L. ranked 2nd with 15 use reports. Moreover, *Allium sativum* L. and *Zingiber officinale* jointly ranked 3rd with 12 use reports. In addition, other plants including *Azadiracta indica*, *Cinamomum tamala,* and *Punica granatum* show 11 symptom use reports. This is followed by *Phyllanthus emblica* and *Vitex negundo* with 10 symptom use reports. Reports of the past ethnobotanical uses justify potential as in COVID-19 treatment.

4.1. Published pharmacological evidence supporting that studied plants could reduce overall risks related to COVID-19

There has now sufficient pharmacological evidence from *in vitro*, *in vivo*, and clinical trial reports related to anti-viral, anti-inflammatory, and immunomodulatory effects of the studied plant species. This pharmacological evidence favoring the ethnomedicinal usage claims in COVID-19 symptoms management.

4.1.1. Published reports on the antiviral activity of the studied plant species

Evaluating the published reports on *in vitro*, *in vivo*, and clinical antiviral activity of the studied plant species, we found that different extracts such as aqueous, ethanol, methanol, and other extracts from the various parts of these plant species exhibit inhibitory effects against a variety of RNA (ssRNA/dsRNA) and DNA (ssDNA/dsDNA) viruses. Data generated from the previously published

Table 1

List of plant species (Plants and plant-derived products) used in COVID-19 treatment mentioned by the participants in the study.

Serial No.	Scientific name / Family/Voucher No.	English name	Bengali name	Habit	Source of collection	Part Used	Preparation	Symptoms (COVID-19) treated	Administration	Method of use/Recipe	Side effects mentioned	FC	RFC	ΣUR	UV
	Allium cepa L. Amaryllidaceae BUH-CoV-01	Onion	Piyaz (পিয়াজ)	Herb	DC and/ M	Bulb, Leaf	Raw; Mashed	• Cold • Coughs • Flu • Fever • Headache • Sore throat • Body pain • Difficulty breathing	Oral and / steam inhalation	1/4 or 1/5 part of the onion is cut off into pieces and a large portion of the onion is placed under the patient's nose and inhaled volatile compounds through the nose, holding it for 1–2 s and exhaling naturally through the mouth and cutting pieces steamed in hot water and vapor is slowly breathed by nose and mouth. Moreover, onion leaves and bulbs were eaten as vegetables with hot rice.	NO	285	0.654	8	0.028
	Allium sativum L. Amaryllidaceae BUH-CoV-04	Garlic	Rosun (রসুন)	Herb	M	Bulb	Raw; Mashed	• Body pain • Sore throat • Diarrhoea • Cough • Cold • Fever • Difficulty breathing	Oral and / steam inhalation	About 5–6 raw garlic slices were eaten every morning with fried rice and mashed garlic was eaten with hot rice. Moreover, raw garlic slices are cut into pieces and steamed in hot water and vapor is slowly breathed by nose and mouth. Besides, the crushed bulb is boiled with tea and drunk.	NO	429	0.984	7	0.015
	Ananas comosus (L.) Merr. Bromeliaceae BUH-CoV-02	Pineapple	Anaras (আনারস)	Herb	M	Fruit	Fresh/ Juice	• Cough • Fever • Flu	Oral	Fresh Pineapple or Juice was eaten regularly.	NO	177	0.406	3	0.017
	Azadirachta indica A.Juss. Meliaceae BUH-CoV-03	Neem tree	Neem (নিম)	Tree	NH	Leaf sap	Juice	• Fever • Cough • Diarrhoea • Body pain • Fatigue • Thirsts • Loss of taste/ smell • Asthma	Oral	Juice made from neem leaf sap was eaten 3 times a day.	NO	421	0.966	8	0.019
	Camellia sinensis (L.) Kuntze Theaceae –	Green tea / Black tea	Cha pata (চা পাতা)	Shrub	M	Leaf	Boiling	• Fever • Dry cough • Diarrhoea • Muscle or body pain • Chest pain • Fatigue • Sore throat • Loss of smell	Oral	Green tea made with ginger, cinnamon, cloves, cardamom, bay leaves, and lemon juice was eaten 5–6 times a day.	NO	436	1.000	10	0.023

Table 1 (*continued*)

Serial No.	Scientific name / Family/Voucher No.	English name	Bengali name	Habit	Source of collection	Part Used	Preparation	Symptoms (COVID-19) treated	Administration	Method of use/Recipe	Side effects mentioned	FC	RFC	ΣUR	UV
	Capsicum annuum L. Solanaceae BUH-CoV-05	Chile pepper	Kaca morich (কাঁচা মরিচ)	Herb	DC and/M	Green fruit	Raw; Mashed	• Difficulty breath • Loss of speech • Asthma • Dry cough • Cold	Oral	Raw green Chile was eaten withhot rice. Besides, raw chili pastewas eaten with hot rice.	NO	155	0.356	3	0.019
	Cinnamomum tamala (Buch.-Ham.) T.Nees & Eberm. Lauraceae BUH-CoV-07	Indian bay leaf	Tejpata (তেজপাতা)	Tree	DC and/M	Leaf	Boiling/Decoction	• Headache • Diarrhoea • Dry cough • Fever • Body ache • Stimulant • Cold • Difficulty breathing	Steam inhalation and /oral	Bay leaves, Cardamom, cumin, black pepper, clove, and cinnamon were boiled altogether in water and its vapor was steam inhaled through the nose and mouth at 3–4 times a day. Some even mentioned that they drunk this mixed water directly in their mouths.	NO	211	0.484	8	0.038
	Cinnamomum verum J.Presl (Old botanical synonym *Cinnamomum zeylanicum*) Lauraceae -	Cinnamon	Darucini (দারুচিনি)	Tree	M	Bark	Boiling/Decoction	• Fever • Body ache • Chest pain • Dry cough • Diarrhoea • Difficulty breathing	Steam inhalation and / oral	Cinnamon, cumin, cardamom, black pepper, clove, and bay leaves were boiled altogether in water and its vapor was steam inhaled through the nose and mouth 3–4 times in a day. Some even mentioned that they drunk this mixed water directly in their mouths.	NO	369	0.846	6	0.016
	Citrus aurantiifolia (Christm.) Swingle Rutaceae BUH-CoV-06	Key lime	Kaghzilebu (কাগজিলেবু)	Shrub	DC and/M	Fruit	Juice/Boiling	• Loss of taste or smell • Vomiting • Sore throat • Headache • Cold • Fever • Flu • Fatigue/tiredness	Oral	The sherbet was made from a mixture of lemon juice and sugar and eaten 3 times a day. Moreover, Citrus skins were boiled with Ginger, Clove, Black pepper, Cardamom, Cumin, Cinnamon, and bay leaf, and the steam was inhaled 3–4 times a day.	NO	396	0.908	8	0.020
	Citrus reticulata Blanco Rutaceae -	Mandarin Orange	Komola (কমলা)	Tree	DC and/M	Fruit	Juice; Fresh	• Flu • Fever • Fatigue/tiredness • Sore throat • Loss of taste	Oral	About 2–3 orange were eaten daily.	NO	255	0.585	5	0.019
	Citrus sinensis (L.) Osbeck Rutaceae -	Sweet orange	Malta (মালটা)	Tree	M	Fruit	Juice; Fresh	• Flu • Fever • Cold	Oral	About 2–3 orange were eaten daily.	NO	286	0.656	6	0.021

Table 1 (continued)

Serial No.	Scientific name / Family/Voucher No.	English name	Bengali name	Habit	Source of collection	Part Used	Preparation	Symptoms (COVID-19) treated	Administration	Method of use/Recipe	Side effects mentioned	FC	RFC	ΣUR	UV
	Coriandrum sativum L. Apiaceae BUH-CoV-08	Coriander	Dhonia (ধনিয়া)	Herb	DC and/ M	Leaf; Dried seed	Mashed	• Fatigue/ tiredness • Sore throat • Loss of taste • Difficulty breathing • Cough • Sore throat • Loss of appetite • Loss of taste	Oral and / steam inhalation	Coriander leaf paste was madeand eaten with hot rice. Dried seeds were boiled with cumin, cinnamon, cardamom, black pepper, clove, and bay leaves in water and its vapor was steam inhaled through the nose and mouth 3–4 times a day.	NO	333	0.764	5	0.015
	Cuminum cyminum L. Apiaceae -	Cumin	Jira (জিরা)	Herb	M	Dried Seed	Boiling/ Decoction; Powder	• Dry cough • Cold • Flu • Difficulty breathing	Steam inhalation and /oral	Cumin, cinnamon, cardamom, black pepper, clove, and bay leaves were boiled together in water and its vapor was steam inhaled through the nose and mouth 3–4 times a day. Some even mentioned that they drunk this mixed water directly in their mouths.	NO	346	0.794	4	0.012
	Elettaria cardamomum (L.) Maton Zingiberaceae -	True cardamom	Elach (এলাচ)	Herb	M	Seed	Boiling/ Decoction	• Dry cough • Cold • Flu • Difficulty breathing	Steam inhalation and /oral	Cardamom, cumin, black pepper, clove, cinnamon, and bay leaves were boiled altogether in water and its vapor was steam inhaled through the nose and mouth 3–4 times a day. Some even mentioned that they drunk this mixed water directly in their mouths.	NO	397	0.911	4	0.011
	Malus domestica Borkh. Rosaceae -	Apple	Apple (আপেল)	Tree	M	Fruit	Fresh	• Fatigue/ tiredness • Fever • Loss of taste/ smell	Oral	About 2–3 apples were eaten daily.	NO	309	0.709	3	0.009
	Mentha × piperita L. Lamiaceae BUH-CoV-09	Peppermint	Pudina (পুদিনা)	Herb	DC and/ M	Leaf	Raw/Fresh; Mashed	• Cold • Dry cough • Flu • Difficulty breathing • Sore throat • Fever • Loss of taste/ smell	Oral	About 5–6 raw mint leaves were eaten directly every morning and the mint leaf paste was eaten with hot rice.	NO	397	0.911	7	0.017
	Nigella sativa L. Ranunculaceae	Black Cumin	Kalojira (কালোজিরা)	Herb	M	Seed	Raw; Mashed	• Dry coughs	Oral	Black Cumin seeds were eatenorally every morning.	NO	396	0.908	7	0.017

Table 1 (continued)

Serial No.	Scientific name / Family/Voucher No.	English name	Bengali name	Habit	Source of collection	Part Used	Preparation	Symptoms (COVID-19) treated	Administration	Method of use/Recipe	Side effects mentioned	FC	RFC	ΣUR	UV
	-							• Colds • Fever • Loss of appetite • Immune-system stimulant • Sore throat • Fatigue		Mash made from black cumin seeds was also eaten with hot rice and honey.					
	Ocimum tenuiflorum L. (Old botanical synonym *Ocimum sanctum*) Lamiaceae BUH-CoV-10	Holy basil	Tulsi (তুলসী)	Herb	DC and/ NH	Leaf	Raw/Fresh; Mashed	• Dry cough • Cold • Flu • Sore throat • Fever • Headache • Chest pain • Difficulty breathing • Diarrhoea	Oral	About 5–6 raw basil leaves were eaten directly every morning and the basil leaf paste was eaten with hot rice.	NO	403	0.924	9	0.022
	Phyllanthus emblica L. Phyllanthaceae BUH-CoV-11	Amla	Amloki (আমলকী)	Tree	DC and/ M	Fruit	Fresh	• Loss of taste or smell • Sore throat • Fever • Fatigue • Headache • Skin disease • Diarrhoea • Cough	Oral	Raw Amla was eaten regularly with salt.	NO	355	0.814	8	0.022
	Piper nigrum L. Piperaceae -	Black pepper	Gol morich (গোলমরিচ)	Climber	M	Dried Fruit	Boiling/ Decoction; Powder	• Difficulty breathing • Fever • Body ache • Dry cough • Cold	Steam inhalation and /oral	Black pepper, cumin, clove, cardamom, cinnamon, and bay leaves were boiled altogether in water and its vapor was steam inhaled through the nose and mouth 3–4 times in a day. Some even mentioned that they drank this mixed water directly in their mouths.	NO	393	0.901	5	0,013
	Psidium guajava L. Myrtaceae BUH-CoV-12	Guava	Peyara (পেয়ারা)	Tree	DC and/ M	Fruit	Fresh	• Diarrhoea • Fatigue • Loss of taste • Fever	Oral	About 2–3 fresh green guavas were eaten daily.	NO	133	0.305	6	0.030
	Punica granatum L. Lythraceae BUH-CoV-13	Pomegranate	Dalim (ডালিম)	Shrub	DC and/ M	Fruit	Fresh	• Loss of taste • Coughs • Diarrhoea	Oral	Fresh Pomegranate was eaten.	NO	361	0.828	8	0.022

6662

Table 1 (continued)

Serial No.	Scientific name / Family/Voucher No.	English name	Bengali name	Habit	Source of collection	Part Used	Preparation	Symptoms (COVID-19) treated	Administration	Method of use/Recipe	Side effects mentioned	FC	RFC	ΣUR	UV
	Spondias mombin L. Anacardiaceae BUH-CoV-14	Hog plum	Amra (আমড়া)	Tree	DC and/ M	Fruit	Fresh	• Cold • Flu • Thirst • Sore throat • Fever • Loss of taste or smell	Oral	Raw fresh Hog plum was eaten regularly.	NO	313	0.718	5	0.016
	Syzygium aromaticum (L.) Merr. & L.M.Perry Myrtaceae -	Clove	Lobongo (লবঙ্গ)	Tree	M	Dried Flower bud	Boiling / Decoction	• Sore throat • Fever • Cold • Flu • Difficulty breathing • Dry cough • Cold • Flu • Loss of speech • Chest pain	Steam inhalation and /oral	Clove, cumin, black pepper, cardamom, cinnamon, and bay leaves were boiled altogether in water and its vapor was steam inhaled through the nose and mouth 3–4 times a day. Some even mentioned that they drunk this mixed water directly in their mouths.	NO	411	0.943	6	0.015
	Vitex negundo L. Lamiaceae BUH-CoV-15	Chinese chaste tree	Nishinda (নিশিন্দা)	Shrub	NH	Leaf	Powder/ Juice	• Cold • Difficulty breath • Cough • Fever • Headache • Weakness • Joint pain or body pain	Oral	*Vitex negundo* L. leaves powder or leaf juice were taken orally or with green/ginger tea 2–3 times daily.	NO	297	0.681	7	0.023
	Zingiber officinale Roscoe Zingiberaceae BUH-CoV-16	Ginger	Ada (আদা)	Herb	DC and/ M	Rhizome	Boiling; Juice	• Voice loss • Headache • Sore throats • Dry cough • Loss of smell • Cold • Flue	Oral	Juice prepared from ginger rhizome was mixed with honey and taken 4 times a day. Besides, ginger rhizomes were sliced into pieces and mixed with boiled green tea, and taken 5–8 times a day.	NO	421	0.966	7	0.017

Collection source = DC (Domestically cultivated); M (Market); NH (Natural Habitat).
FC = Frequency Citation (Number of informants mentioning the use of the species).
FC = Relative Frequency Citation.
UR = Use Reports.
UV = Use Value.
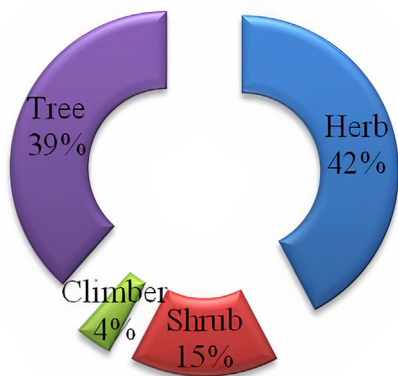
Habit wise analysis of plant species

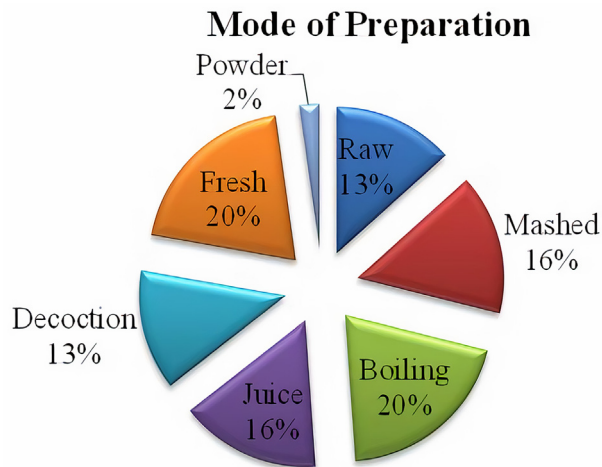**Fig. 2.** Habit-wise analysis of plant species.
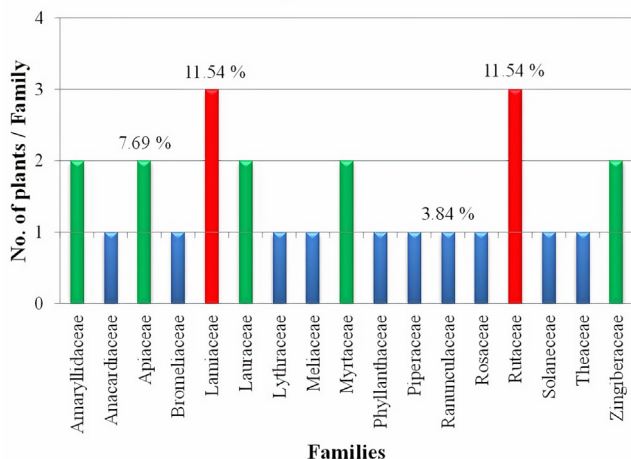
Fig. 3. Distribution of plant species per botanical family.
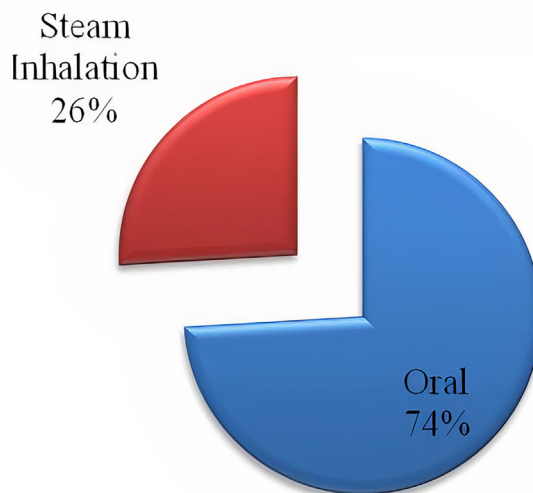
Used parts

Fig. 4. Percentage of plant parts used.

Mode of Preparation

Fig. 5. Mode of preparation.
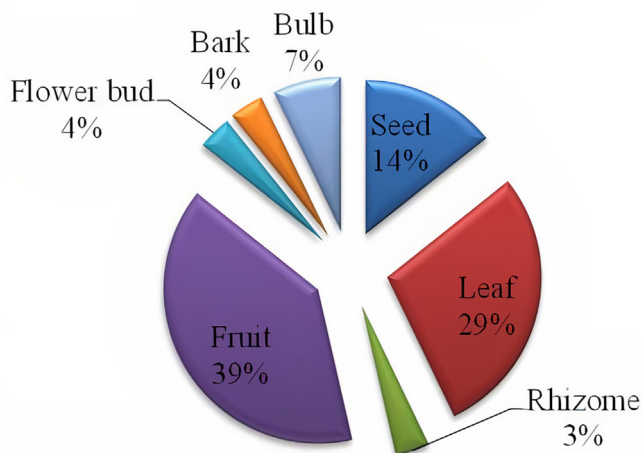
Mode of Administration

Fig. 6. Mode of administration.

in vitro, in vivo, and clinical trial reports (articles) on the antiviral activity of the studied plant species have been depicted in Fig. 10 and presented in a table attached to **Appendix C** as supplementary material.

Analyzing the published *in vitro, in vivo,* and clinical reports on the antiviral activity of the studied plant species used by the respondents in COVID-19 symptoms management, it has been observed that all plant species except 3 plants namely *Citrus aurantiaca, Cinnamomum tamala,* and *Elettaria cardamomum* exhibited antiviral activity against several RNA (ssRNA/dsRNA) and DNA (ssDNA/dsDNA) viruses (see **Appendix C and** Fig. 10). Analysis of the antiviral activity reports of the concerned plants shows that *Camellia sinensis* exhibits the highest number of antiviral activity against a variety of RNA (ssRNA/dsRNA) and DNA (ssDNA/dsDNA) viruses. Many *in vitro* and *in vivo* antiviral activities of the *Camellia sinensis* plant species revealed its potentiality to combat different viral diseases. Review analysis of the antiviral activity reports of *C. sinensis* shows that green and black tea derived from the leaves of *C. sinensis* are equally effective in showing inhibitory activity against different types of single-stranded RNA (ssRNA) viruses such as SARS-CoV-2, HIV, HAV, H1N1, H3N2, IBV, PRRSV, MNV,
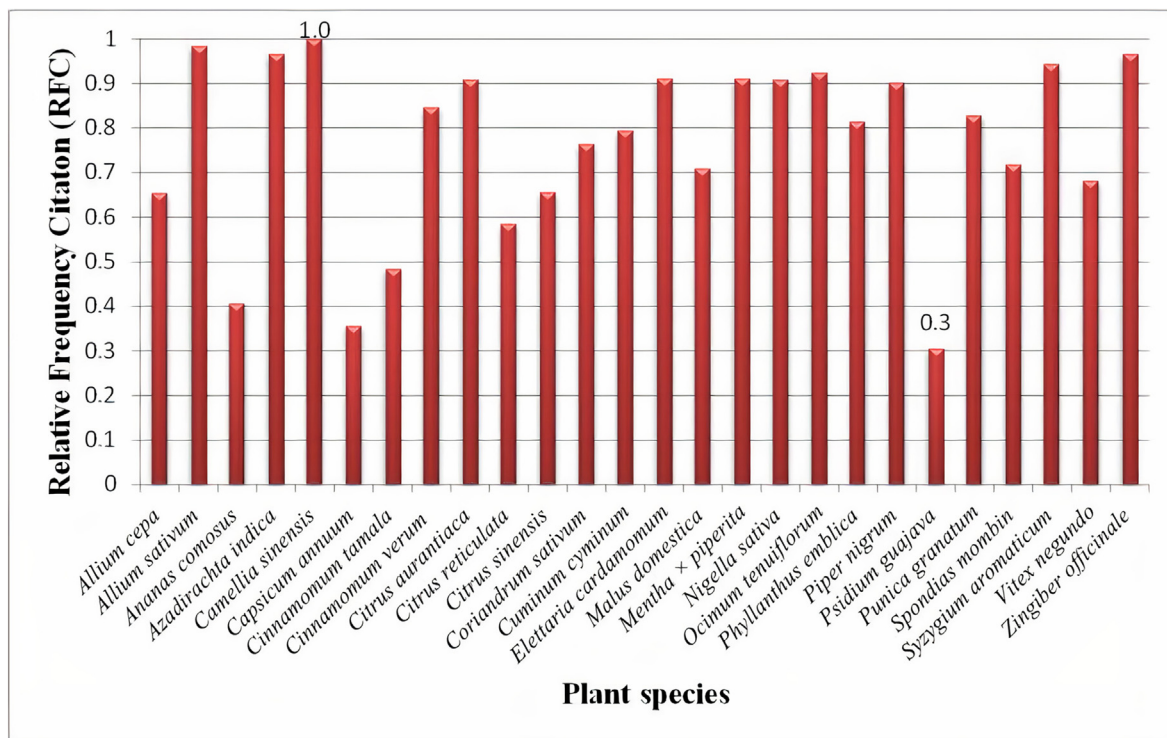
Fig. 7. Plant species with Relative Citation Frequency (RFC).
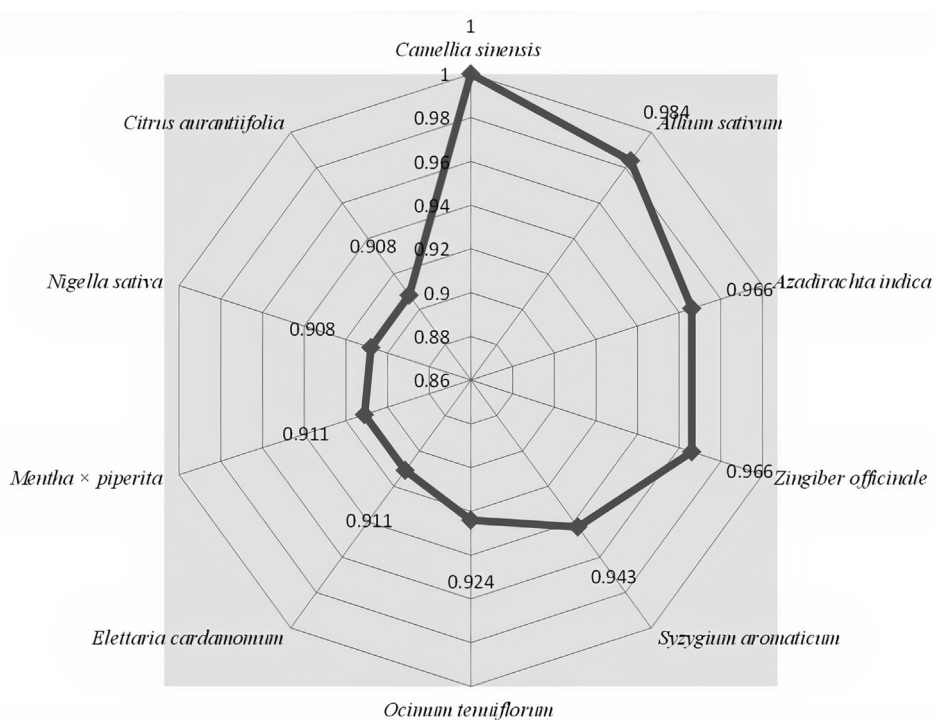
Fig. 8. Radar diagram showing the top10 ranked plant species according to RFC value.

FCV, HCV, DENV, CHIKV, IAV, VSV, etc. *Allium sativum* exhibits the 2nd highest number of antiviral activity against various RNA (ssRNA/dsRNA) and DNA (ssDNA/dsDNA) viruses among other plant species. *Punica granatum, Zingiber officinale,* and *Piper nigrum* jointly exhibit the 3rd highest number of antiviral activity against different RNA and DNA viruses among the remaining plant species.

Fig. 9. Past ethnomedicinal use reports of the studied plant species.

Fig. 10. Pyramidal peak diagram of the activity of plant species studied against different types of viruses (data generated from previously published articles).

4.1.2. Published reports on anti-inflammatory and immunomodulatory activities of the studied medicinal plant species

We evaluated the previous *in vitro*, *in vivo*, pre-clinical and clinical reports on anti-inflammatory and immunomodulatory activity of the studied plant species. Analyzing the published re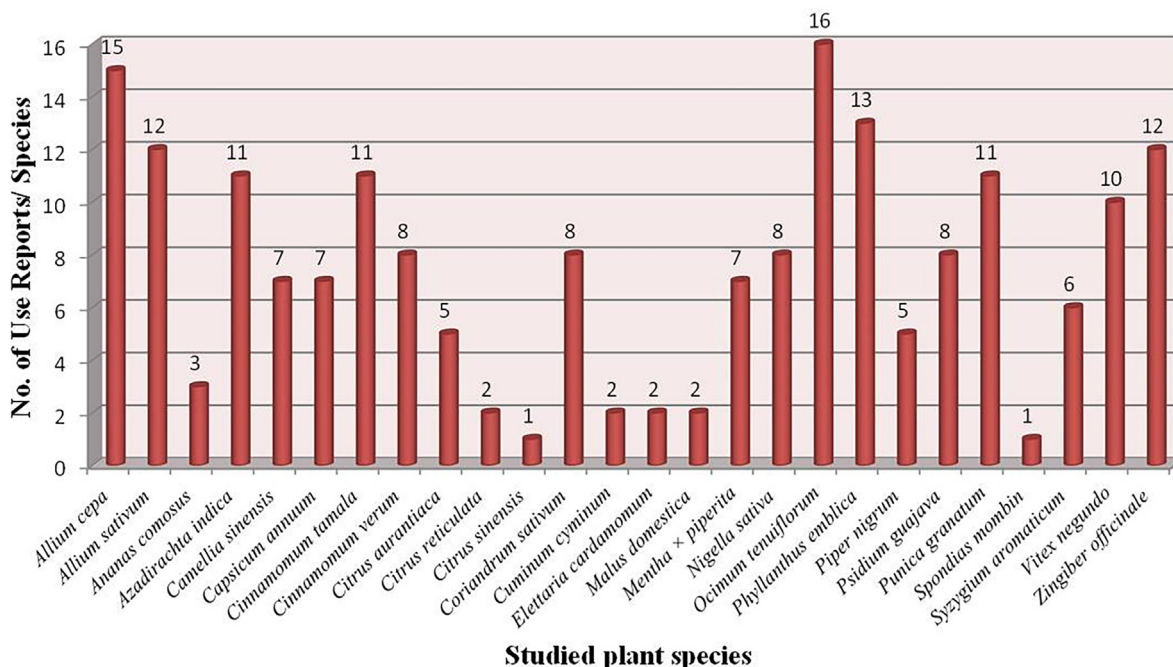port's references on anti-inflammatory and immunomodulatory activity, we observed that different extracts such as aqueous, ethanol, methanol, and other extracts from the various parts of these plant species have strong anti-inflammatory activity as well as significant immuno-stimulatory capabilities. The published *in vitro*, *in vivo*, pre-clinical, and clinical trial reports on anti-inflammatory and immunomodulatory activity of the studied plant species are attached to **Appendix D** in the supplementary section and illustrated in Fig. 11 as well. According to the published reports on

anti-inflammatory and immunomodulatory activity of the studied plant species (Fig. 11), *Nigella sativa* ranked the 1st position which showed the highest anti-inflammatory and immunomodulatory properties and it is therefore considered as the most promising and potent candidate. *Camellia sinensis* obtained the 2nd position followed by *Punica granatum*, *Allium sativum*, and *Zingiber officinale* which achieved the 3rd, 4th and 5th position, respectively. Apart from these, the top most plant species among the others showing the highest anti-inflammatory and immunomodulatory reports are *Allium cepa*, *Psidium guajava*, *Phyllanthus emblica*, *Azadirachta indica*, *Ocimum tenuiflorum*, *Vitex negundo*, *Syzygium aromaticum*, *Piper nigrum*, *Coriandrum sativum*, *Citrus sinensis*, and *Capsicum annuum*.
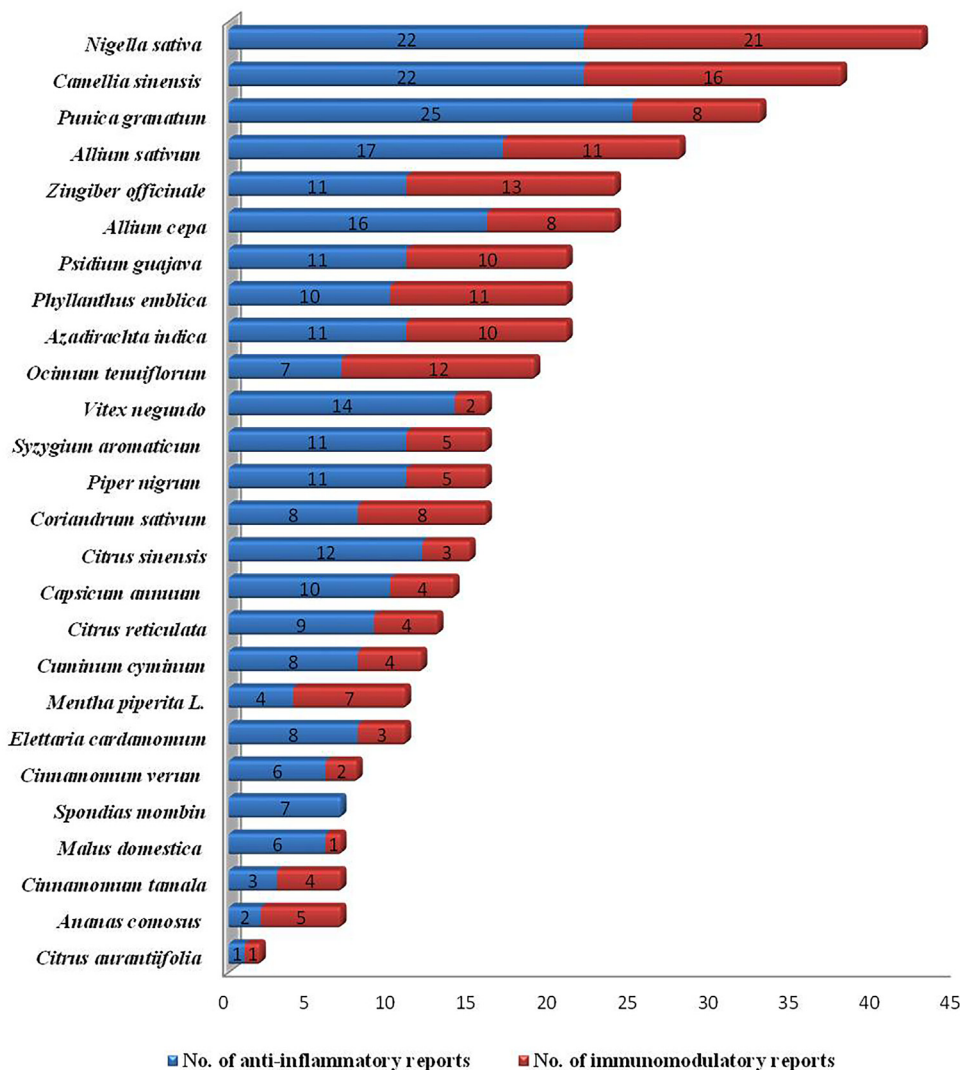
Fig. 11. Published pharmacological reports on the anti-inflammatory and immunomodulatory activities of the reported plant species.

5. Discussion

5.1. Socio-demographic characteristics of the respondents

From the mentioned data, it is understood that men are more affected comparatively than women with COVID-19. Several studies describe similar findings consistent with us (Bischof et al., 2020; Dehingia and Raj, 2021; Garima et al., 2020; Griffith et al., 2020; Ortiz-Prado et al., 2021; Richardson et al., 2020). These studies reported that men are at higher risk of infecting by COVID-19 than women. More men than women have died of COVID-19 (Chen et al., 2020; Gebhard et al., 2020; Li et al., 2020; Yang et al., 2020). The overall COVID-19 case-fatality ratio is approximately 1.0–3.5 times higher among men than women and this risk increases with age and the simultaneous presence of two or more complex diseases in a patient. Griffith et al., (2020) have explained the possible causes are biological (immune responses, hormones, and genes; Males and females differ in both innate and adaptive immunity, hormones and genes and women generally respond stronger innate and adaptive immunity than men), psychological, behavioral, and social factors (Men are involved in more high-risk behaviors that make COVID-19 more likely to be infected, Men also tend to be less likely than women to wash their hands,

social distance, wear masks, and seek medical help effectively and actively). Akiko Iwasaki, a professor of medicine, and associate research scientist Takehiro Takahashi at Yale University, USA (Takahashi et al., 2020) mentioned that sex biases in COVID-19 infection and women are generally respond with stronger innate and adaptive immunity than men. They explained that a larger volume of innate immune cytokines such as interleukin-8 (IL-8) and IL-18 and non-classical monocytes were found in infected male COVID-19 patients (which is blamed for worsening conditions in COVID-19) than females, while female patients had more robust T cell activation than male patients and acquired immunity worked more actively in women.

Through our investigation, it appears that middle-aged (between 30 and 50 years old) adults (84.63%) are more likely to be infected with COVID-19 than older (above 50 years) adults (11%); whereas, younger individuals (between 18 and 30 years old) are less affected (4.36%). These observations are consistent with and supported by others (Monod et al., 2021; O'Driscoll et al., 2021). Monod et al., (2021) stated that the majority of COVID-19 infection occurs in people between the ages of 20 and 49. O'Driscoll et al., (2021) said that "the infection fatality ratio is lowest among 5–9-year-old children, with a log-linear increase by age among individuals older than 30 years".

5.2. Diversity of plants and plant-derived products and method of use/Recipe

It was revealed in our study that a total of 26 medicinal plant species belonging to 23 genera and 17 different botanical families were traditionally used by the Bangladeshi people to prevent and manage the COVID-19 symptoms at home. A recent study (Khadka et al., 2021) found that a total of 60 plants belonging to 36 families were used by Nepali people to prevent COVID-19. Another study (Chaachouay et al., 2021) found that Moroccan herbalists used 20 plant species from 14 families in COVID 19 prevention and treatment. In the present study, Lamiaceae and Rutaceae families jointly ranked utmost position representing the largest number of plant species (3 species; which is 11.54% of the total number) in each family. This result is completely identical and consistent with the results of Chaachouay et al., (2021) but shows small deviations from Khadka et al., (2021). Chaachouay et al., (2021) showed that the Lamiaceae family occupies the highest number of medicinal plants utilized by herbalists in the prevention and treatment of COVID-19 symptoms. On the contrary, Khadka et al., (2021) reported that Apiaceae is the predominant family where Lamiaceae jointly ranked 2nd position with Zingiberaceae and Amaryllidaceae. The results of quantitative data analysis such as RFC and UV in our study show that *Camellia sinensis, Allium sativum, Allium cepa, Azadirachta indica, Zingiber officinale, Ocimum tenuiflorum, Nigella sativa,* and *Phyllanthus emblica* are the most frequently used plant species by Bangladeshi respondents in the prevention and management of COVID-19 symptoms. Besides, Chaachouay et al., (2021), Khadka et al., (2021), and Nguyen et al., (2021) mentioned that these plant species as useful in the prevention and treatment of COVID-19 symptoms and utilized by Moroccan, Nepali as well as Vietnamese people respectively. Khadka et al., (2021) stated *Zingiber officinale* was the most cited species by Nepali people whereas *Eucalyptus globulus,* followed by *Azadiracta indica* was the most mentioned species by Moroccan herbalists (Chaachouay et al., 2021). Nguyen et al., (2021) reported that *Zingiber officinale* Rosc., *Allium sativum* L., and *Perilla frutescens* (L.) Britt. were the most frequently used herbal remedies by Vietnamese adults. They used these herbal medicines to treat different COVID symptoms like sore throat, fever, cough, and nasal congestion.

The most frequently used plant parts aforementioned ethnobotanical studies conducted in Bangladesh are somewhat varied with our results. Most of the previous ethnobotanical studies have stated that the leaves are the most used parts, but in this study, we found that fruits are the most used parts (39%) followed by leaves (29%) in the treatment of COVID-19 symptoms. However, our findings are similar to some ethnobotanical studies (Baharvand-Ahmadi et al., 2016; Mussarat et al., 2014) where fruits are the most commonly used plant parts.

According to the respondents, the two most common methods of using these plants and plant-derived products were direct oral intake and the other was steam inhalation. Most of the respondents mentioned that when they faced symptoms of respiratory problems like difficulty in breathing or shortness of breath, they took steam inhalation through the nose and mouth, which were prepared by evaporating a variety of spicy plant ingredients in boiling water. Khadka et al., (2021) also mentioned that boiling different parts with hot water is the most common method of preparation. Steam inhalation has traditionally been used for decades as a home remedy for common colds and respiratory tract infection symptoms including fever, feeling unwell, feeling chilled, loss of appetite, headache, muscle aches, and pains (Brewster et al., 2020; Singh et al., 2017). For example, Bay leaves (*Cinnamomum tamala*), Cardamom (*Elettaria cardamomum*), cumin (*Cuminum cyminum*), black pepper (*Piper nigrum*), clove (*Syzygium aro-maticum*), and cinnamon (*Cinnamomum verum*) were boiled altogether in water and its vapor was steam inhaled through the nose and mouth at 3–4 times in a day. Some participants even mentioned that they drunk this mixed water directly in their mouths. Besides, for symptoms, such as sore throat, dry cough, loss of taste or smell, diarrhoea, fatigue, etc., the juice made from these plant remedies was taken orally singly or mixed with honey, tea, or vinegar. For example, basil leaf (*Ocimum tenuiflorum*) juice was taken directly in the mouth or mixed with honey to cure dry cough and sore throat. It may also be mentioned that the juice prepared from ginger (*Zingiber officinale*) rhizome was mixed with honey and taken 4 times a day to cure voice loss symptoms. Besides, ginger rhizomes were also sliced into pieces and mixed with boiled green tea, and taken 5–8 times a day.

5.3. Previous ethnomedicinal records of the studied plant species

People from different marginalized and ethnic communities have been relying on traditional plant-based remedies for the treatment of various ailments from generation to generation. They treat various gastroenteritis and respiratory systems diseases that are closely related to COVID-19 symptoms such as fever or chills, cold, cough, flu, headache, diarrhoea, tiredness/fatigue, sore throat, loss of taste or smell, asthma, shortness of breath, or difficulty breathing, etc., using traditional plant-based knowledge at their home. There are many strong and important reports about the similar use of these plant species not only in Bangladesh but also all over the world especially in other parts of South Asia. Several ethnobotanical studies (Biswas et al., 2010; Chowdhury and Koike, 2010; Faruque et al., 2019; Islam et al., 2014, 2019; Khan et al., 2015b; Mollik et al., 2010; Uddin et al., 2012; Uddin and Hassan, 2014; Islam et al., 2020) (see **Appendix B)** accomplished among marginalized communities and ethnic minorities in different regions of Bangladesh and other countries. These studies have shown that *Ocimum tenuiflorum, Allium cepa, Allium sativum , Azadiracta indica, Cinamomum tamala, Punica granatum, Phyllanthus emblica, Vitex negundo, Zingiber officinale, Psidium guajava, Nigella sativa,* and *Camellia sinensis* has traditionally been used to treat a variety of diseases similar to COVID-19 symptoms. Kayani et al., (2014) stated that *Allium sativum* L. (Asthma, whooping cough, respiratory disorders), *Azadiracta indica* Adr. Juss. (Asthma), *Camellia sinensis* (L.) O.Ktze. (Coughing up with blood), *Capsicum annuum* L. (Asthma, whooping cough, cold), *Citrus reticulate* Blanco (Flu), *Coriandrum sativum* L. (Asthma, cough, bronchitis), *Cuminum cyminum* Linn. (Dry cough, cold), *Phylanthus emblica* L. (Asthma, bronchitis), *Psidium guajava* L. (Old cough, bronchitis, whooping cough), and *Punica granatum* L. (Whooping cough, tuberculosis, cold and flu) are used to treat different respiratory disorders by the inhabitants of Gallies at Abbottabad in northern Pakistan.

5.4. Antiviral activity of the studied plant species

Previously published research data obtained from pre-clinical and clinical studies (see **Appendix C)** show that different extracts of the reported plant species in our study such as aqueous, ethanol, methanol, and other extracts of various plant parts as well as its bioactive compounds have proved its inhibitory activity against different types of RNA (ssRNA/dsRNA) and/or DNA (ssDNA/dsDNA) viruses that cause widespread infectious diseases including cold/flu and other respiratory infections including coronavirus and severe acute respiratory syndrome coronavirus (Jang et al., 2020; Keyaerts et al., 2007; Roshdy et al., 2020), influenza (Hayashi et al., 2007; Lee et al., 2012; Onishi et al., 2020; Song et al., 2005; Yang et al., 2014) & parainfluenza (Priya and Kumari, 2017; Weber et al., 1992), procine reproductive and respiratory syndrome virus (Fabros et al., 2018; Ge et al., 2018), rhinovirus (Denyer et al.,

1994; Weber et al., 1992), *Measles morbillivirus* (Meléndez-Villanueva et al., 2019), Newcastle Disease Virus (Doostmohammadian et al., 2020; Harazem et al., 2019; Mahmood et al., 2018), and adenovirus (Colpitts and Schang, 2014; Karimi et al., 2020; Liu et al., 2009). Besides, plant extracts and bioactive compounds of the reported plant species show antiviral activity against a variety of viruses such as the human immunodeficiency virus (Asres et al., 2001; Estari et al., 2012; Geuenich et al., 2008; Kannan et al., 2012; Liu et al., 2005), Avian influenza virus (H9N2) (Ghoke et al., 2018; Sornpet et al., 2017), herpes simplex virus (Houston et al., 2017; Kurokawa et al., 1995; Siqueira et al., 2020; Xiang et al., 2011), hepatitis A virus (Battistini et al., 2019; Seo et al., 2017; Seo and Choi, 2017), dengue virus (Hall et al., 2017; Parida et al., 2002; Raekiansyah et al., 2018), etc.

Green tea and black tea derived from the leaves of the *Camellia sinensis* plant contain polyphenols called epigallocatechin-3-gallate (EGCG) and theaflavins, respectively. These both compounds exhibit antiviral activity against a variety of viruses, especially against positive-sense single-stranded RNA viruses (Chowdhury et al., 2018; Ge et al., 2018; Jang et al., 2020; H. Wang et al., 2016; Weber et al., 2015; Yang et al., 2012).

In an *in vitro* study, Jang et al., (2020) reported that tea polyphenols EGCG and theaflavin exhibited inhibitory action against the SARS-CoV-2 3CL-protease in a dose-dependent manner with the IC_{50} values of 7.58 μg/ml and 8.44 μg/ml for EGCG and theaflavin, respectively. They did not find any cytotoxicity on HEK293T cells by both EGCG and theaflavin at the concentrations tested up to 40 μg/ml.

Garlic (*Allium sativum* L.) is another important and potential antiviral candidate. Many pre-clinical and clinical investigations (Keyaerts et al., 2007; Wang et al., 2017, 2020; Weber et al., 1992) revealed the antiviral activity of fresh garlic extract and its organosulfur compounds (OSCs) against a variety of viruses, especially positive and negative-sense single-stranded RNA viruses. The OSCs namely allicin and its derivatives (alliin, diallyl sulfide (DAS), diallyl disulfide (Garlicin), methyl allyl thiosulfinate) derived from garlic are mainly responsible for their antiviral properties (Khubber et al., 2020; Rouf et al., 2020; Wang et al., 2017; Weber et al., 1992). Also, a non-organosulfur proteinous compound namely lectin derived from garlic has been reported antiviral activity against SARS-CoV via inhibition of early viral attachment (Keyaerts et al., 2007).

Many *in vitro* studies provide anti-viral evidence that juice extract (Moradi et al., 2020; Núñez et al., 2015), polyphenols (Haidari et al., 2009; Moradi et al., 2019; Sundararajan et al., 2010), ellagitannins, punicalagin, punicalin and ellagic acid derived from pomegranate (*Punica granatum* L.) can attenuate various types of ssRNA/dsRNA and ssDNA/dsDNA viral infections by blocking the HCV NS3/4A protease activity (Reddy et al., 2014) and blocking CD4 and coreceptors CXCR4/CCR5 binding ability of HIV-1 (Neurath et al., 2004).

The antiviral literature study of the plants we reported further reveals that *Zingiber officinale*, *Piper nigrum*, *Cinnamomum verum*, *Psidium guajava*, *Azadirachta indica*, and *Nigella sativa* plants showed strong antiviral responses against various types of RNA and/DNA viruses **(Appendix C)**. Roshdy et al., (2020) developed a herbal extract namely EGYVIR which constitutes a combination of *Piper nigrum* seeds extract with *Curcuma longa* (Turmeric) root extract. EGYVIR is reported as a potent immunomodulatory herbal extract that has promising antiviral activity against SARS-CoV-2.

All but 3 plant species reported in our study namely *Citrus aurantiaca*, *Cinnamomum tamala*, and *Elettaria cardamomum* exhibited antiviral activity against several RNA (ssRNA/dsRNA) and DNA (ssDNA/dsDNA) viruses. This report cannot be assumed that these 3 species do not have any antiviral activity, but that there is no research report on any type of antiviral activity that has been found in these 3 species. It may be that antiviral activity research for these 3 species has not been evaluated until now.

5.5. Reviewing of anti-inflammatory and immunomodulatory activities of the studied plants

Pneumonia (inflammation of lungs) and asthma are the key pathophysiological features of COVID-19 patients where immunity, inflammation, and oxidation processes are involved (Danzi et al., 2020). Studies on SARS-CoV and COVID-19 have shown that immune system weakness is one of the main reasons for the incidence of COVID-19 complications such as pneumonia and mortality in infected patients (Curbelo et al., 2017; Prompetchara et al., 2020; Taghizadeh-Hesary and Akbari, 2020). Researchers suggest that improving the immune systems response may be effective in reducing the incidence of pneumonia and that reducing inflammation may be effective in decreasing mortality rates from pneumonia. Besides, asthma is a complex chronic respiratory disease (CRD) connected with several inflammatory cells and proteins that comprise inflammatory eosinophils, hypersecretion of mucus, and airway hyperresponsiveness which finally creates breathing difficulty by triggering wheezing, coughing, and shortness of breath (de Oliveira et al., 2013; Tattersfield et al., 2002).

Analysis of published reports on the anti-inflammatory and immunomodulatory effects of plants recorded in this study shows that almost all plant species have beneficial effects on boosting the immune system and reducing inflammation. Many *in vitro* and *in vivo* experimental evidence (Gholamnezhad et al., 2015; Majdalawieh and Fayyad, 2015) revealed that *Nigella sativa* and its major active ingredient thymoquinone have an inherent potent ability to modulate inflammation, cellular and humoral adaptive immune responses. Gholamnezhad et al., (2015) summarized the basic and clinical evidence of anti-inflammatory and immunomodulatory aspects of *N. sativa* and its constituents on preventive and relieving bronchodilatory effects on obstructive respiratory diseases such as asthma, bronchiectasis, bronchitis, and chronic obstructive pulmonary disease (COPD). Boskabady et al., (2010, 2007) reported that *N. sativa* and its active ingredient have a potent antiasthmatic effect on asthmatic airways. Heo et al., (2008) reported that aqueous extract of green tea (*Camellia sinensis*) exhibits potent anti-asthmatic activity by alleviating asthmatic symptoms in the lung of ovalbumin sensitized mice, by increasing the expression levels of T-helper 1 (Th1) cell-specific anti-asthmatic biomarkers (TNF-β and interferon-γ) and decreasing the expression of anti-asthmatic cytokines. In addition, Hwang et al., (2017) reported that a water-soluble amino acid namely L-theanine, isolated from green tea (*Camellia sinensis*), showed anti-inflammatory activity in an ovalbumin (OVA)-induced murine model of asthma giving protective effects on asthmatic responses, particularly airway inflammation and oxidative stress modulation. L-theanine represses OVA-induced mucus production and inflammatory cell infiltration in the respiratory tract and blood vessels. L-theanine also reduces the production of immunoglobulin E (IgE), monocyte chemoattractant protein-1 (MCP-1), IL-4, IL-5, IL-13, tumor necrosis factor-alpha (TNF-α), and interferon-gamma (IFN-γ) in bronchoalveolar lavage fluid (BALF). Many studies revealed that tea bioactive compounds (polyphenols; epigallocatechin gallate (EGCG), theaflavin (TF), alkaloids; caffeine and its intermediates, theophylline, and theobromine) have immunomodulatory competence and anti-inflammatory properties which can enhance and modulate innate immunity response (Ranjith-Kumar et al., 2010; Y. Wang et al., 2016). Chowdhury and Barooah, (2020) suggested that tea bioactive compounds modulate innate immunity and could mitigate the unprecedented COVID-19 pandemic.

Many *in vivo* and *in vitro* studies have revealed that *Punica granatum* L. fruit, and its juice, extract, peel powder, and oil, employ anti-proliferative, anti-inflammatory (BenSaad et al., 2017; Lee et al., 2010) anti-oxidant (Pontonio et al., 2019), and immunomodulatory properties by attenuating different respiratory conditions such as asthma (Barwal et al., 2009; de Oliveira et al., 2013), lung fibrosis, lung cancer, COPD, and alveolar inflammation via modulating various mechanisms (Shaikh and Bhandary, 2021) such as through inhibiting eosinophils, decreasing cytokines like IL-1β and IL-5, and attenuating protein levels in the lungs (de Oliveira et al., 2013).

In an *in vitro* study, Hodge et al., (2002) reported that garlic (*Allium sativum*) extract may aid to resolve inflammation linked with inflammatory bowel disease (IBD) and could be a potential therapeutic use in IBD treatment. IBD is a term for 2 conditions as Crohn's disease and ulcerative colitis showing the main symptoms are diarrhoea, fever, fatigue, abdominal pain, loss of taste or smell/loss of appetite, etc., (https://www.cdc.gov/ibd/what-is-IBD.htm), and these symptoms are very similar to COVID-19 diseases. Hodge et al., (2002) also showed that garlic extract significantly inhibits Th1 and decreases the production of inflammatory cytokines such as monocyte IL-12, monocyte tumor necrosis factor-alpha (TNF-α), IL-1α, IL-6, IL-8, T-cell interferon-gamma (IFN-γ), IL-2, and TNF-α. Mohi El-Din et al., (2014) reported that garlic extract inhibits the development of asthma in the lungs of albino rats by inducing an anti-inflammatory effect. A study by YOUN et al., (2008) reported that garlic can modulates innate immune responses that could reduce the risk of many chronic diseases. They demonstrated that the ethyl acetate fraction of garlic inhibited the lipopolysaccharide-induced dimerization of Toll-like receptors 4, which inhibits the activation of nuclear factor-kappaB (NF-κB) and the expression of cyclooxygenase 2 and inducible nitric oxide synthase.

Zingiber officinale (Ginger) is an important spice and herbal remedy commonly used for the treatment of respiratory disorders in traditional medicine and having anti-inflammatory and immunomodulatory effects reported in various *in vitro* and *in vivo* studies. Studies revealed that *Z. officinale* ameliorates allergic asthma (A.M. Khan et al., 2015; Rouhi et al., 2006) via suppression of Th2-mediated immune response by decreasing in mRNA expression levels of IL-4 and IL-5 (A.M. Khan et al., 2015). Other studies showed that *Zingiber officinale* extracts relieving coughing, and acute tracheitis-induced chest pain (Roohi Broujeni et al., 2009), rheumatoid arthritis, and osteoarthritis (Haghighi et al., 2003; Roohi Broujeni et al., 2009) in patients. A recent study stated that the combination of *Z. officinale* and *Echinacea* can alleviate the clinical symptoms of COVID-19 such as coughing, dyspnea, and muscle pain, and reduce the hospitalization rate of suspected COVID-19 outpatients (Mesri et al., 2021).

Oliveira et al., (2015) found that *Allium cepa* L. extract and quercetin have potential antiasthmatic effects that relax the tracheal rings and reduces the total number of cells in bronchoalveolar lavage (BAL) and eosinophil peroxidase (EPO) in the lungs by reducing the production of inflammatory cytokines known to cause asthma. In another study, Marefati et al., (2018) reported that the application of *A. cepa* extract reduced the total number of White blood cells (WBCs) and lung inflammatory cells in the ovalbumin sensitized Wister rat and showed effectiveness against asthma. In the same study, they noted that *A. cepa* extract modulates immunity by reducing the IL-4 and IgE cytokines and increasing IFN-γ, and the IFN-γ/IL-4 ratio in sensitized rats. Besides, Dawud et al., (2016) and Ghorani et al., (2018) autonomously suggested the potential therapeutic effect of *A. cepa* on airway diseases such as asthma. They reported that aqueous-alcoholic extract of *A. cepa* has anti-inflammatory and preventive effects on tracheal responsiveness and lung inflammation in asthmatic Wistar rats

by decreasing the total WBCs and Phospholipases A2 (PLA2) level, and also decreasing the neutrophil, eosinophil, and monocyte counts but increasing lymphocytes counts in the Blood and bronchoalveolar fluid (BALF). Cherk Yong et al., (2019) mentioned that quercetin-loaded liquid crystalline nanoparticles (LCN) could be a potential therapeutic drug for asthma as they show significant efficacy in suppressing the production of key pro-inflammatory cytokines such as IL-1β, IL-6, and IL-8 in the human primary bronchial epithelial cell line.

Jang et al., (2011) demonstrated that methanolic extract of *Capsicum annuum* L. fruit inhibits ovalbumin-induced airway inflammation and oxidative stress in a mouse model of asthma by reducing the pathophysiological signs of allergic airway disease and increasing the inflammatory cell recruitment to the airways, airway hyperresponsiveness, and increased levels of Th-2 cytokines.

Cinnamaldehyde, a bioactive compound isolated from *Cinnamomum verum* showed anti-inflammatory activity by reducing allergic symptoms in the allergic rhinitis (AR) rat model (Hancı et al., 2016). AR is a risk factor for the development of asthma that occurs in individuals and is related to inflammation of the upper respiratory tract (Yawn, 2008). Moreover, Hancı et al., (2016) mentioned that cinnamaldehyde reduced vascular congestion along with plasma cell, eosinophil, as well as inflammatory cell infiltration into the lamina propria.

Two alkaloid compounds namely synephrine and stachydrine from Pericarpium Citri Reticulatae (PCR, *Citrus reticulata*) have shown anti-asthmatic activity *in vitro* (Fu et al., 2019). The alkaloid fractions showed anti-asthmatic activity against histamine-induced experimental asthmatic Guinea pigs by down regulating the expression of eosinophils in BALF and serum IgE, IL-4, and IL-5 levels.

Moreover, all the reported plants, *Psidium guajava, Azadirachta indica, Phyllanthus emblica, Ocimum tenuiflorum, Syzygium aromaticum, Piper nigrum, Coriandrum sativum, Cuminum cyminum, Mentha piperita L., Ananas comosus, Cinnamomum tamala, Spondias mombin, Elettaria cardamomum,* and *Malus domestica,* have been reported for their anti-inflammatory and immuno-stimulating properties in alleviating various respiratory diseases symptoms which are similar to COVID-19 symptoms (Fig. 11**. and Appendix D).**

5.6. Attitudes and perceptions of patients towards the use of HMBHR in the management of COVID-19 symptoms

According to the majority of respondents who participated in this study, they relied more on plants and plant-derived traditional home remedies (HMBHR) than on hospital-based allopathic treatments for COVID-19 management. In some cases, they even put plant-based traditional home remedies on top. They cited the lack of adequate COVID-19 specialized hospitals, the deficit of adequate intensive care unit (ICU) beds and ventilation systems in hospitals, and, above all, the absence of effective drugs for COVID-19 treatment; and which has increased their reliance on plant-based traditional remedies and preferred treatment at home. An example is a 37-years-old employed woman who was diagnosed with other diseases including diabetes and was hospitalized with COVID-19 left the hospital and returned home and started receiving plant-based remedies at home as her condition continued to deteriorate in the hospital due to the adverse environment. She was then gradually recovered from COVID-19. She mentioned that the steam inhalation of hot water with basil leaves made her feel much more comfortable than the nebulizer in times of shortness of breath and/or difficulty breathing. She, therefore, believes that plant-based home remedies have healed her.

5.7. Limitations of the study

This study encompassed some limitations due to the COVID-19 pandemic situation. First, it was not possible to conduct face-to-face interviews with most respondents. Second, since most of the plants and plant-derived products used in COVID-19 treatment were collected from local marketplaces and some plants are not native to Bangladesh. Thus, herbarium sheets and/or voucher specimens of all the plants cannot be prepared and stored except for a few. However, these limitations can be overcome in future research by taking some specific steps. Firstly, face-to-face interviews with respondents can be conducted using Zoom and other conventional video conferencing platforms subject to easy availability. In addition, they can be interviewed face-to-face, ensuring proper health safety and rules and maintaining social distance. Samples of plant products can be collected from the local market and preserved in fluid preservatives following standard laboratory methods instead of preparing herbarium sheets.

6. Conclusion

The present study reveals that the Bangladeshi COVID-19 patients used 26 different plants and their products to manage and mitigate the COVID-19 symptoms. Literature review analysis supports the antiviral properties of these investigated plants, especially against several positive-sense (+) single-stranded RNA viruses. Review analysis also showed the anti-inflammatory and immunomodulatory effects of these plants in the human body. These all shreds of evidence support the effective use of these plants and their products in the prevention and management of COVID-19 symptoms. It also shows strong evidence, rationales, and scientific claims for the efficacy of COVID-19 treatment. Thus, the plants studied in this investigation might play an important role as safe home-based therapeutics for protecting us from the deadly pandemic COVID-19 viral infection. This study may be a very plausible platform for exploring plant-based drugs and vaccines for COVID-19 therapy through *in vitro* and/or *in vivo* pharmacological studies. Although several COVID-19 vaccine candidates have already been developed. However, there arise mixed responses among the public about their actual effectiveness. Moreover, the vaccine is not readily available to the marginalized population. On the other hand, these plant-based traditional remedies are easily accessible to marginalized people. Its side effects are considered as very low and negligible and their use and utilization are recognized as safe. Therefore we recommend that patients with mild symptoms of COVID-19 can easily use plant-based traditional therapies that could reduce the overall risk of COVID-19 such as morbidity and mortality.

7. Data availability

All the data related to this article exist in the main body of the article and as an appendix in the supplementary material.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sjbs.2021.07.036.

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