Role of botanical essential oils as a therapy for controlling coronavirus (SARS-CoV-2) disease (Covid-19)

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Abstract: **- This review paper presented on the basis of extensive literature survey updated the importance of plant essential oils in controlling many diseases, particularly coronavirus (SARS-CoV-2) disease outbreak. Plant essential oils are valuable natural products, and used as a raw materials in aromatherapy, phytotherapy, perfumery, cosmetics, spices and nutrition. Aromatic plants produced a diversity of chemical constituents with the potential to inhibit viral replication. Essential oils have several biological properties such as antibacterial, antifungal, antiviral, antioxidant, anti-inflammatory, wound-healing and anti-cancer effects in *in vitro* and *in vivo*. Therefore, essential oils have been analyzed and described as good antiviral agents against respiratory tract viral infections, hence are excellent prospective candidate against coronavirus. Thus, essential oils and their constituents can hopefully be considered in near future for more clinical assessment and possible applications in controlling the coronavirus pandemic. However, some of the plant essential oils are very toxic and poisonous and therefore, oral consumption should be avoided. Further detailed clinical trial experiments should be conducted for the scientific validation.**

Key words: **Antiviral, aromatherapathy, coronavirus, essential oils, herbal medicine, oil therapy, toxicity,**

I. INTRODUCTION

The global outbreak of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) disease (covid-19) is an ongoing pandemic and a public gravest health emergency (Malabadi et al., 2021a, 2021b). The SARS-CoV-2 is a new strain of coronavirus that appeared in China in December 2019, and the viral disease is named as covid-19 (Zhang et al., 2020a, 2020b, 2020c; Zheng et al., 2009; Zhou et al., 2020a, 2020b; Zhu et al., 2020). SARS-CoV-2 is a beta-coronavirus responsible for the COVID-19 pandemic (Shin et al., 2020; Yang, 2021; Xu et al., 2020; Malabadi et al., 2021a, 2021b). Symptoms of COVID-19 can be relatively non-specific and infected people may be asymptomatic (Shin et al., 2020; Yang, 2021). The coronavirus can infect cells of the lungs, kidneys, heart and intestine, resulting in the organ damage leading to the multiple organ dysfunction syndrome (Shin et al., 2020; Yang, 2021; Wu et al., 2020a, 2020b). Infection with these highly pathogenic coronaviruses (SARS-CoV-2) could result in the acute respiratory distress syndrome (ARDS) and acute lung injury (ALI) followed by the failure of the lungs function and death (Shin et al., 2020; Yang, 2021; Wu et al., 2020a, 2020b). Therefore, interaction between coronavirus, SARS-CoV-2 and the host may be responsible for its unusual high morbidity and mortality (Zhang et al., 2020a, 2020b, 2020c; Zheng et al., 2009; Zhou et al., 2020a, 2020b; Zhu et al., 2020). People infected with COVID-19 generally develop signs and symptoms including mild respiratory symptoms, fever, common cold, running nose, severe headache, dry cough, fatigue, shortness of breath, and loss of smell on an average of 5–6 days after infection but may ranges from two to fourteen days (Shereen et al., 2020; Wu et al., 2020a, 2020b; Wang et al., 2020; V'kovski et al., 2020). Furthermore, coronavirus-2 (SARS-CoV-2) is zoonotic infecting both animal and human (Shereen et al., 2020; Shin et al., 2020; Wu et al., 2020a, 2020b; Wang et al., 2020). Airborne transmission, particularly *via* nascent aerosols from human atomization, is highly virulent and represents the dominant route for the transmission of covid-19 disease (Shin et al., 2020; Yang, 2021; Malabadi et al., 2021a). Coronaviruses have been identified in human and several avian hosts as well as in various mammals, including pigs, chicken, camels, bats, Himalayan palm civets, mice, dogs, and cats (Wu et al., 2020a, 2020b; Wang et al., 2020; Shin et al., 2020; Malabadi et al., 2021a, 2021b). SARS-CoV-2 is a RNA enveloped coronavirus responsible for the pandemic of the Severe Acute Respiratory Syndrome. RNA viruses are characterized by a high mutation rate, up to a million times higher than that of their hosts (Zhu et al., 2020; Shin et al., 2020; Yang, 2021). The pathogen, severe acute respiratory syndrome coronavirus (SARS-CoV-2) shared a phylogenetic similarity to SARS-CoV (about 79%) and Middle East respiratory syndrome (MERS-CoV) (about 50%) (Zhang et al., 2020a, 2020b, 2020c; Zheng et al., 2009; Zhou et al., 2020a, 2020b; Zhu et al., 2020). Furthermore, the genome sequence of coronavirus (SARS-CoV-2) also showed phylogenetic similarity to one of the species of bats (80%)

(Shin et al., 2020; Zhang et al., 2020a, 2020b, 2020c). Therefore, coronavirus (SARS-CoV-2) is originated from bats and bats are the primary hosts for the spread of the covid-19 disease (Zhang et al., 2020a, 2020b, 2020c; Shin et al., 2020; Yang, 2021; Shereen et al., 2020). The novel coronavirus (SARS-CoV-2) originated from the Hunan seafood market at Wuhan, Hubei, China where bats, snakes, raccoon dogs, palm civets, and other animals were sold, and viral disease was rapidly spread up and becomes global pandemic (Shin et al., 2020; Tang et al., 2020; Wu et al., 2020a, 2020b; Wang et al., 2020; Yang, 2021; Zhang et al., 2020a, 2020b, 2020c).

The outbreak of second wave of coronavirus (SARS-CoV-2) variant with double mutilations (B.1.617) in India is out of control and leading to the larger infections and death. India is in the midst of a devastating second wave of COVID-19. For the past several weeks, cases and deaths have skyrocketed. India is recording more than a quarter million cases per day. B.1.617 is also spreading quickly in India. Over the past few months, it has become the dominant strain in the state of Maharashtra and West Bengal (Doucleff, 2021) Several studies have linked the two key mutations in B.1.617 with an increased ability for the virus to evade the immune system (Doucleff, 2021). So, most likely, COVD-19 vaccines will still work against B1.617, but they could be slightly less effective. There are also signs that people who have already had COVID-19 can be reinfected more easily with this strain. Therefore, re-infections may be driving this second wave, explosive surge in India (Doucleff, 2021).

Currently the outbreak of this new variant (B.1.167) with double mutations in India is the major health concern. The B.1.617 genome has at least 15 mutations, with two specific mutations in the spike protein (Sample, Ian,19 April 2021). This new variant (B.1.617) with double mutations is also detected in UK, and Canada (BBC News, 2021). The transmission rate is very high leading to the large number of viral infections and death. This has led to the forced lockdown, strict home isolation has been implemented by the Government of India in order to curb the outbreak of viral disease. This new variant, called B.1.617, was initially detected in India with two mutations, the E484Q and L452R (Double mutant strain). Mutations in the spike gene can make the virus inherently "better" at infecting people or can help the virus to escape neutralising antibodies. This means if the virus mutates in the "right way", it can reinfect someone who has already recovered from covid-19 (Sample, Ian, 19 April 2021). The so-called “double mutation” coronavirus found in India can be considered as a variant of concern (VOC) because of its significant rapid spread and leading to the death of infected people. The B.1.617 strain’s mutations are feared to make the variant spread faster and partially evade immunity. This new variant is believed to be largely responsible for India’s current second wave of the COVID-19 pandemic, with infection rates and hospitalisations on the rise once again. The B.1.617 variant strain has all the hallmarks of a very dangerous virus. Mutations at sites E484 and L452 have been observed separately, but this is the first major viral lineage that combines the two. Double mutation" refers to B.1.617's mutations in the SARS-CoV-2 spike protein's coding sequence at E484Q and L452R. The two mutations are 1) E484Q. The mutation at position 484, a glutamic acid-to-glutamine substitution, confers the variant stronger binding potential to hACE2 (the human ACE2 receptor), as well as better ability to evade hosts' immune systems, to B.1.617 in comparison to other variants. 2) L452R. The mutation at position 452, a leucine-to-arginine substitution, confers stronger affinity of the spike protein for the ACE2 receptor and decreased recognition capability of the immune system. This new variant, (B.1.617) which has a so-called double mutation, is thought to be fuelling India's deadlier new wave of cases, and has already begun to overwhelm its hospitals and crematoriums. WHO has concluded that "Having two of these mutations, which have been seen in other variants around the world, are concerning," Further, there was a similarity with mutations that will increase transmission as well as to reduce neutralization, possibly stunting the ability of vaccines to curb them. Therefore, both mutations are known to decrease although not completely eliminate the binding of the antibodies created by infection and vaccination. This new strain underscores the insidious nature of viruses, and threatens to thwart containment efforts in India, despite measures such as the world's largest lockdown last year. Viruses mutate all the time, as the part of evolutionary biology. Some mutations weaken the virus while others may make it stronger, enabling it to proliferate faster or cause more infections (Malabadi et al., 2021a).

One good news is that indigenously developed covid-19 vaccine Covaxin (India's indigenous COVID-19 vaccine by Bharat Biotech, Hyderabad, Telangana, is developed in collaboration with the Indian Council of Medical Research (ICMR) and National Institute of Virology (NIV), Pune, neutralises the double mutant variants of SARS-CoV-2 and works against new strain. Therefore, Bharath Biotech, Covaxin has now received Emergency USE Authorizations for covid-19 treatment in India. In addition to this, another covid-19 vaccine, Covishild (Serum Institute of India, Pune, Maharashtra, India) has also neutralises the double mutant variants of SARS-CoV-2. This has been tested only in few blood samples of the infected people. Large scale clinical trials are undergoing and results are yet to be confirmed.

Herbal plants are a natural source of many important phytochemicals and widely used in the pharmaceutical, food and cosmetic industries (Malabadi et al., 2021a; Swamy et al., 2016; Ojah, 2020; Asif et al., 2020; Ma and Yao, 2020; Ahmad et al., 2021; Teixeira et al., 2013). Essential oils are the complex volatile compounds, synthesized naturally in different plant parts during the process of secondary metabolism (Swamy et al., 2016; Teixeira et al., 2013). A wide variety of herbal plants are available in the Indian subcontinent, and they are the backbone of Indian traditional herbal medicinal system, Ayurveda and Siddha (Malabadi et al., 2021a; Kulkarni et al., 2020; Swamy et al., 2016;

Malabadi, 2008; Malabadi and Vijayakumar, 2008; Malabadi et al., 2009, 2010a, 2010b, 2011a, 2011b; Malabadi et al., 2012a, 2012b, 2012c, 2012d; Malabadi et al., 2016a, 2016c, 2016d; Malabadi et al., 2017a, 2017b; Malabadi et al.. 2018). Essential oils have the great potential in the field of biomedicine as they effectively destroyed the several bacterial, fungal, and viral pathogens (Swamy et al., 2016; Teixeira et al., 2013). The presence of different types of aldehydes, phenolics, terpenes, and other antimicrobial compounds means that the essential oils are effective against a diverse range of pathogens (Swamy et al., 2016; Teixeira et al., 2013). Essential oils have tremendous business potential on the global market owing to their unique flavour and fragrance properties and also biological activities (Swamy et al., 2016; Asif et al., 2020; Teixeira et al., 2013). There are a wide-range of essential oils, and their components have been clinically proven to possess the antiviral properties (Swamy et al., 2016; Malabadi et al., 2021a; Ojah, 2020; Asif et al., 2020; Ma and Yao, 2020; Ahmad et al., 2021; Silva et al., 2020; Kompelly et al., 2019). Essential oils are employed in aromatherapy and for the treatment of several diseases including cardiovascular disease, diabetes, Alzheimer's, and cancer (Swamy et al., 2016; Teixeira et al., 2013). In addition, the use of synthetic chemicals for the control of pathogenic microorganisms is limited because of their carcinogenic effects, acute toxicity, and environmental hazard potential (Swamy et al., 2016; Teixeira et al., 2013). In this regard, the exploitation of essential oils to control epidemic multidrug resistant pathogenic microorganisms can be useful to combat various infectious diseases (Swamy et al., 2016; Teixeira et al., 2013). However, the effects of plant essential oils on human coronaviruses are yet to be explored.

II. CORONAVIRUS (SARS-COV-2): BOTANICAL ESSENTIAL OILS

Plant based essential oils are comprised of a complex mixture of volatile phytochemicals from diverse classes including monoterpenes, sesquiterpenes, and phenylpropanoids (Asif et al., 2020; Ma and Yao, 2020; Ojah, 2020; Vimalanathan and Hudson, 2014; Juergens et al., 2003, 2020; Tshibangu et al., 2020). Essential oils of medicinal plants have an extensive applications in medicinal chemistry, pharmaceuticals, aromatherapy particularly in perfume and soap industries (Ojah, 2020; Tshibangu et al., 2020). Thus medicinal plants continue to be a main source of new lead bio-active molecules (Malabadi et al., 2021a, 2021b; Ahmad et al., 2021; Tshibangu et al., 2020; Ojah, 2020). Essential oils are odorous and volatile compounds found in plants and are stored in special fragile secretary structures, such as glands, secretary hairs, secretary ducts, secretary cavities or resin ducts (Ojah, 2020; Tshibangu et al., 2020; Asif et al., 2020; Ma and Yao, 2020). Essential oils of plants are hydrophobic, soluble in alcohol, non-polar or weakly polar solvents but only slightly soluble in water (Ojah, 2020; Asif et al., 2020; Ma and Yao, 2020). Essential oils are among the plant-derived antiviral molecules that are being employed in phytomedicine, and are considered as prospective drug candidate against recent outbreak of deadly coronavirus (Nadjib, 2020; Ojah, 2020; Tshibangu et al., 2020; Asif et al., 2020; Ma and Yao, 2020). Essential oils have the ability to hamper the growth of a diverse range of pathogens because of the presence of natural compounds produced by the organs of plants. Importantly, the unique aroma and other bioactive properties of an essential oil depends on its chemical constituents (Swamy et al., 2016). Essential oils are usually colourless or pale yellow, with exception of the blue essential oil of chamomile (*Matricaria chamomilla*) and the most are liquid of lower density compared to water with few exceptions of the essential oil obtained from sassafras, cinnamon and clove (Ojah, 2020; Tshibangu et al., 2020; Asif et al., 2020; Ma and Yao, 2020). Essential oils can be classified based on the number of carbon chains formed from basic isoprene units; hydrocarbons, esters, oxides, lactones, alchols, aldehydes and ketones (Asif et al., 2020; Ma and Yao, 2020; Tshibangu et al., 2020; Ojah, 2020).

Essential oils are the main active molecules in aromatic plants, and are the mixtures of different lipophilic and volatile substances (Tshibangu et al., 2020; Ojah, 2020; Asif et al., 2020; Ma and Yao, 2020). Essential oils of plants possess various applications mainly in health, cosmetic, agriculture and food industries (Ojah, 2020; Tshibangu et al., 2020; Asif et al., 2020; Ma and Yao, 2020). Biological properties of essential oils include not only antimutagenic, anticancer, antioxidant, antiprotozoal activities but also anti-inflammatory, antimicrobial, immuno-modulatory and antiviral that can be useful in COVID-19 treatment (Ojah, 2020; Asif et al., 2020; Ma and Yao, 2020; Tshibangu et al., 2020; Nadjib, 2020). Aromatic plants have been used since decades for the treatment of various ailments such as malaria, diabetes, mental disorders, cancer, hypertension, respiratory disorders etc (Tshibangu et al., 2020; Asif et al., 2020; Ma and Yao, 2020; Tshibangu et al., 2020; Nadjib, 2020). Aromatherapy utilizes various essential oils that can be issued through topical application, massage, inhalation or water immersion to stimulate a desired therapeutic response (Ojah, 2020; Asif et al., 2020; Ma and Yao, 2020; Tshibangu et al., 2020; Nadjib, 2020). Essential oils are colorless pleasant smelling liquids with high refractive index (Ojah, 2020; Asif et al., 2020; Ma and Yao, 2020; Tshibangu et al., 2020; Nadjib, 2020). Essential oils are composed of saturated and unsaturated hydrocarbons, alcohol, aldehydes, esters, ethers, ketones, oxides, phenols and terpenes which may produce characteristic odours (Ojah, 2020; Asif et al., 2020; Ma and Yao, 2020; Tshibangu et al., 2020; Nadjib, 2020). Essential oils are neither acidic nor alkaline. They have the ability to go into the body tissues and literally become free radical scavengers (Ojah, 2020; Asif et al., 2020; Ma and Yao, 2020; Tshibangu et al., 2020; Nadjib, 2020). Aromatherapy is well known throughout the world particularly in India, Africa, Europe, China, Japan, Thailand, and Nepal. Aromatic plants are boiled and steam is inhaled to treat colds, coughs or flu (Ojah, 2020; Tshibangu et al., 2020; Asif et al., 2020; Ma and Yao, 2020; Nadjib, 2020). Aromatherapy can provide

respiratory disinfection, treatment of respiratory disorders, decongestant and psychological benefits (Ojah, 2020; Tshibangu et al., 2020; Asif et al., 2020; Ma and Yao, 2020; Nadjib, 2020). Molecules that enter the nose or mouth pass to the lungs, and from there, to other parts of the body (Tshibangu et al., 2020; Ojah, 2020; Asif et al., 2020; Ma and Yao, 2020; Nadjib, 2020). They can reach the brain, affect the limbic system, which is linked to the emotions; the heart rate, breathing, memory, stress and hormone balance and then can have a subtle, yet holistic effect on the body (Tshibangu et al., 2020; Ojah, 2020; Asif et al., 2020; Ma and Yao, 2020; Nadjib, 2020). Essential oils are used as flavouring agents. Flavours are added to food to enhance their taste and aroma. Flavouring in vanilla, is isolated from vanilla beans and methyl salicylate, which has a characteristic minty taste and odour (Ojah, 2020; Tshibangu et al., 2020; Asif et al., 2020; Ma and Yao, 2020; Nadjib, 2020). Essential oils and their terpene constituents may be accepted as natural alternative to synthetic skin penetration enhancers (Ojah, 2020; Tshibangu et al., 2020).

Essential oils of plants are characterised by the antibacterial, antifungal, antioxidant, and antiviral properties (Tshibangu et al., 2020; Schnitzler et al., 2010; Ma and Yao, 2020; Brochot et al., 2017; Asif et al., 2020; Kamalabadi et al., 2018; Vimalanathan and Hudson, 2014; Juergens et al., 2003, 2020). Essential oils of plants have long been known to have anti-inflammatory, immunomodulatory, bronchodilatory, and antiviral properties and are being proposed to have the activity against SARC-CoV-2 virus (Ojah, 2020; Kulkarni et al., 2020; Asif et al., 2020; Kumar et al., 2020; Sharma and Kaur, 2020a, 2020b; Thuy et al., 2020; Silva et al., 2020; Juergens et al., 2003, 2020; Tshibangu et al., 2020). Enveloped viruses are known to respond sensitively to essential oils (Schnitzler et al., 2010; Asif et al., 2020; Tshibangu et al., 2020; Ojah, 2020). Owing to their lipophilic nature, essential oils are advocated to penetrate viral membranes easily leading to the membrane disruption (Asif et al., 2020; Tshibangu et al., 2020; Ojah, 2020). Moreover, essential oils contain multiple active phytochemicals that can act synergistically on multiple stages of viral replication and also induce positive effects on host respiratory system including bronchodilation and mucus lysis (Asif et al., 2020; Tshibangu et al., 2020; Ojah, 2020). These essential oils are found to be active against a wide variety of viruses, such as influenza virus (IFV), human herpesviruses (HSV), human immunodeficiency virus (HIV), yellow fever virus, and avian influenza (Ma and Yao, 2020; Asif et al., 2020; Tshibangu et al., 2020; Ojah, 2020). HSV (-1 and -2) are known to cause many life-threatening diseases (Kulkarni et al., 2020; Asif et al., 2020; Kumar et al., 2020; Schnitzler et al., 2010; Sharma and Kaur, 2020a, 2020b; Silva et al., 2020; Thuy et al., 2020; Tshibangu et al., 2020; Ojah, 2020).

In another recent study reported by Tshibangu et al., (2020), the aromatic plants and their essential oils are active against a large number of viruses (Herpes virus-1, Herpes virus-2, HIV, Adeno virus, Hepatite B Virus, Enterovirus 71, JUNV, etc.) and even against SARS-CoV-1 which has 96% of the same genetic background with SARS-CoV-2 (Tshibangu et al., 2020; Ojah, 2020; Asif et al., 2020; Kumar et al., 2020). Aromatic plants and their essential oils exhibit high antiviral activities against several types of viruses (Tshibangu et al., 2020; Ojah, 2020; Asif et al., 2020; Kumar et al., 2020). This evidence stemming from several experimental studies means that some compounds derived from essential oils could act as inhibitors of COVID-19 (Tshibangu et al., 2020; Ojah, 2020; Asif et al., 2020; Kumar et al., 2020). Molecular docking investigations and pharmacoinformatics of some compounds derived from essential oils with SARS-CoV-2 protease are in progress to identify the potential inhibitors of the virus (Tshibangu et al., 2020; Ojah, 2020; Nadjib, 2020; Asif et al., 2020; Kumar et al., 2020).

Essential oils can enter the body easily by inhalation. Due to their volatility, they can be inhaled easily through the respiratory tract and lungs, which can distribute them into the bloodstream (Tshibangu et al., 2020; Ojah, 2020; Nadjib, 2020; Asif et al., 2020; Kumar et al., 2020). In general, the respiratory tract offers the most rapid way of entry into the body system followed by the dermal pathway (Tshibangu et al., 2020; Ojah, 2020; Nadjib, 2020; Asif et al., 2020; Kumar et al., 2020). Vapour form of essential oils was also found to be safe against monolayers of epithelial cells. Inhalation of essential oils has a significant role in controlling the central nervous system (Tshibangu et al., 2020; Ojah, 2020; Ojah, 2020; Nadjib, 2020; Asif et al., 2020; Kumar et al., 2020). Human exposure to essential oils through diet or environment is widespread. In most cases, essential oils can be absorbed from the food matrix or as pure products and cross the blood brain barrier easily (Tshibangu et al., 2020; Ojah, 2020; Nadjib, 2020; Asif et al., 2020; Kumar et al., 2020). One of the study concluded that essential oils in vapour form could benefit people suffering from influenza (Vimalanathan and Hudson 2014; Asif et al., 2020; Tshibangu et al., 2020; Ojah, 2020; Nadjib, 2020; Kumar et al., 2020). Carvacrol and its isomer thymol obtained from oregano have been shown to inhibit viral host cell fusion via depletion of viral cholesterol from the HIV-1 envelope membranes, thus blocking the entry of the virus into the host system (Mediouni et al. 2020; Tshibangu et al., 2020; Ojah, 2020; Nadjib, 2020; Asif et al., 2020; Kumar et al., 2020). The essential oils of plants have the lipophilic nature property and therefore, potential to intercalate into the lipid double layer of the viral envelope (Asif et al., 2020; Tshibangu et al., 2020; Ojah, 2020; Nadjib, 2020; Kumar et al., 2020). Subsequently, the fluidity of the membranes is changed and, at a higher concentration, the membranes are even ruptured (Wink, 2020). Major mechanisms through which essential oils induce antiviral actions are, direct actions on free viruses, inhibition of steps involved in virus attachment, penetration, intracellular replication, and release from host cells and inhibition of vital enzymes (Ma and Yao, 2020; Schnitzler et al., 2010; Tshibangu et al., 2020; Ojah, 2020; Nadjib, 2020; Asif et al., 2020; Kumar et al., 2020).

Plant essential oils are known for their antiviral components and one or more of the essentials may prove to be potential cures for COVID-19 (Silva et al., 2020; Tshibangu et al., 2020; Ojah, 2020; Nadjib, 2020; Asif et al., 2020; Kumar et al., 2020; Silva et al., 2020). Some active components of the essential oils are terpinenes, pinenes, caryophyllene, eugenol, linalool, and camphor (Tshibangu et al., 2020; Silva et al., 2020 Silva et al., 2020; Jahan et al., 2021). Essential oil components of *Laurus nobilis* L. (*Lauraceae*), has β-ocimene, α- and β-pinene, and 1,8-cineole have been hypothesized to be potential therapeutics against COVID-19 through inhibiting the main protease (Mpro) of the virus (Tshibangu et al., 2020; Silva et al., 2020; Jahan et al., 2021). In an *in silico* study with 171 essential oil components from various plants, best docking scores to Mpro were observed with (*E*)-β-farnesene, (*E*,*E*)-α-farnesene, (*E*,*E*)-farnesol, and (*E*)-nerolidol (Jahan et al., 2021; Tshibangu et al., 2020; Silva et al., 2020).

At present, only computer-aided docking and few *in vitro* studies are available which showed anti-SARC-CoV-2 activities of essential oils (Kulkarni et al., 2020; Asif et al., 2020; Kumar et al., 2020; Schnitzler et al., 2010; Sharma and Kaur, 2020a, 2020b; Silva et al., 2020; Thuy et al., 2020; Jahan et al., 2021). Therefore, *in vitro* and *in vivo* studies are warranted to establish the safe dose and clinical efficacy of essential oils against SARC-CoV-2 (Asif et al., 2020; Nadjib, 2020). The multiple pharmacological attributes of plant essential oils, a combination approach whereby essential oils with established pharmacokinetic and pharmacodynamic properties are administered with synthetic drugs is suggested to combat coronaviral disorder and its associated complications (Asif et al., 2020; Nadjib, 2020). Furthermore, essential oils and their major components have displayed potent antiviral activity to other coronaviruses, such as SARS-CoV-1, although the mechanism of action of these oils and their components were found to be mainly through inhibition of viral replication (Senthil Kumar et al., 2020). Senthil Kumar et al., (2020) reported that geranium and lemon essential oils and their major compounds, citronellol, geraniol, limonene, linalool, and neryl acetate, could downregulate ACE2 expression in epithelial cells, thereby blocking virus entry into host cells, and eventually preventing viral infection. However, further studies are highly warranted to conclude the underlying molecular mechanisms of this inhibitory effect (Senthil Kumar et al., 2020).

Oral ingestion of essential oils needs attention due to the potential toxicity of some oils. Essential oils are very toxic and higher concentration are poisonous too and oral consumption might leads to death. Ingested essential oil compounds may then be absorbed and delivered to the rest of the body by the bloodstream and then distributed to the other parts of the body (Tshibangu et al., 2020; Ojah, 2020). Once essential oil molecules are in the body, they interrelate with physiological functions by three distinct modes of action which may be pharmacological, physiological or psychological mixture (Tshibangu et al., 2020; Ojah, 2020; Ma and Yao, 2020; Schnitzler et al., 2010; Tshibangu et al., 2020; Ojah, 2020; Nadjib, 2020; Asif et al., 2020; Kumar et al., 2020). Biological activity of essential oils may be due to one of the compounds or due to the entire mixture (Tshibangu et al., 2020; Ojah, 2020). Essentials oils showed antibacterial, fungicidal, relaxant, stimulating, antidepressant effect and can be very effective therapeutic agent and used for external and topical applications mixture (Tshibangu et al., 2020; Ojah, 2020; Ma and Yao, 2020; Schnitzler et al., 2010; Nadjib, 2020; Asif et al., 2020; Kumar et al., 2020). Essential oils are known for their therapeutic properties and, used in the treatment of various infections caused by both pathogenic and non-pathogenic diseases (Tshibangu et al., 2020; Ojah, 2020; Ma and Yao, 2020; Schnitzler et al., 2010; Nadjib, 2020; Asif et al., 2020; Kumar et al., 2020).

After the confirmation of primary scientific evidences about anti-SARC-CoV-2 potentials of essential oils and their active components, various essential oils selling and extraction companies claimed about efficacy of their essential oils bearing products against COVID-19 (Asif et al., 2020). These claims were immediately noticed by the Food and Drug Administration (FDA) authority of USA and other authorities, and warning letters were issued to the companies selling essential oils with these claims (Asif et al., 2020).

Following are the few important essential oils of medicinal plants used for controlling many disease due to extensive applications in medicinal chemistry, aromatherapy and pharmaceuticals.

*1) Ravintsara oil (*Cinnamomum camphora)-Madagascar

Ravintsara oil is extracted and distilled from the leaves of *Cinnamomum camphora* belongs to the family *Lauraceae* in Madagascar (Blanchard, 2007; Ojah, 2020**;** Ankita et al., 2014; Costa et al., 2010; da Silva et al., 2020; Guo et al., 2017; Loizzo et al., 2008; Patne et al., 2020). True Ravintsara (*Cinnamomum camphora*) essential oils contain at least 45% of 1,8-cineole (Loizzo et al., 2008; Minami et al., 2003). *Cinnamomum camphora* in Madagascar is a very different species than the camphor trees grown in Asia. **Ravintsara oil is very toxic, poisonous and oral consumption of the oil should be avoided.** Ravintsara oil is more similar to Eucalyptus and Camphor. Furthermore, eucalyptol, the primary chemical constituent of Ravintsara, makes its aroma uniquely and ideal for use in a soothing massage. Ravintsara oil is perfect for personal and home use, and aroma of oil helps to create a relaxing, open environment in even the stuffiest rooms. In addition to aromatic benefits, Ravintsara oil also contains surface cleansing properties when applied topically to the skin and general home surfaces. Rather than being rich in camphor, Ravintsara oil also contains higher concentration of 1,8-cineole (45-55%) (Blanchard, 2007; Ankita et al., 2014; Costa et al., 2010; da Silva et al., 2020; Guo et al., 2017; Loizzo et al., 2008; Patne et al., 2020). Ravintsara oil has an invigorating camphoraceous scent and some chemical similarity to eucalyptus radiata or globulus (Blanchard, 2007; Ankita et al.,

2014; Costa et al., 2010; da Silva et al., 2020; Guo et al., 2017; Loizzo et al., 2008; Patne et al., 2020). During recent outbreak of coronavirus (SARS-CoV-2), Ravintsara oil is found inhibiting the coronavirus under *in vitro* and *in vivo* due to its antiviral properties (Ojah, 2020; Patne et al., 2020; Loizzo et al., 2008). Therefore, further clinical evidence is yet to be concluded. Ravintsara oil is an excellent germ fighter and has antiviral, analgesic, anti-inflammatory, and anti-spasmodic properties which can calm muscles and soothe coughs (Blanchard, 2007; Ankita et al., 2014; Costa et al., 2010; da Silva et al., 2020; Guo et al., 2017; Loizzo et al., 2008; Patne et al., 2020). Ravintsara oil can support the lungs and energetically can boost mood, help one relax, and support feelings of confidence. The main chemical, 1,8 cineole, generally present in copious amounts in Ravintsara oil and has been linked to cognitive enhancement and improved focus and work performance (Juergens et al., 2003, 2020). Therefore, Ravintsara oil may also help one to better focus and support work or study (Blanchard, 2007; Ankita et al., 2014; Costa et al., 2010; da Silva et al., 2020; Guo et al., 2017; Loizzo et al., 2008; Patne et al., 2020; Minami et al., 2003; Juergens et al., 2003, 2020). Ravintsara oil extracted from the leaves of *Cinnamomum camphora* in Madagascar sometimes is also known as Ho Leaf Oil. The oil from the bark of this tree is commonly called Ho Wood (Blanchard, 2007; Ankita et al., 2014; Costa et al., 2010; da Silva et al., 2020; Guo et al., 2017; Loizzo et al., 2008; Patne et al., 2020; Ojah, 2020; Minami et al., 2003).

2) Ravensara oil (Ravensara aromatica Sonnerat)-Madagascar

Ravensara oil is extracted and distilled from the leaves of *Ravensara aromatica* belongs to the family *Lauraceae* in Madagascar (Andrianoelisoa et al., 2010; Ramanoelina et al., 2006; Patne et al., 2020; Costa et al., 2010; da Silva et al., 2020; Ojah, 2020). It is a shrub of the rain forests of Madagascar that can reach 5 meters in height. The oval leaves are green, and the flowers are composed of 5 very persistent sepals (Andrianoelisoa et al., 2010; Ramanoelina et al., 2006; Patne et al., 2020; Costa et al., 2010; da Silva et al., 2020; Minami et al., 2003). The leaves and the fruits have the reputation of being aphrodisiacs (Andrianoelisoa et al., 2010). **Ravensara oil is very toxic, poisonous and oral consumption of the oil should be avoided**. The essential oil of aromatic Ravensare contains monoterpene hydrocarbons, monoterpene alcohols, sesquiterpene hydrocarbons, phenols, esters and monoterpene oxides and Limonene, germacrene-D (Andrianoelisoa et al., 2010; Costa et al., 2010; Ramanoelina et al., 2006; Patne et al., 2020). Ravensare oil mainly contains methyl chavicol (79.7%), methyl eugenol (8.5%) and limonene (3.1%) (Patne et al., 2020; Costa et al., 2010; Andrianoelisoa et al., 2010). The chemical composition of *Ravensara aromatica* bark is characterized by a high amount of methyl chavicol (83–98%), whatever the chemotype (Andrianoelisoa et al., 2010; Ojah, 2020). The aromatic Ravensare oil has decontracting, anti - inflammatory, stimulating properties of the immune and circulatory system. Ravensare oil is also sedative tonic, de-stressing, antiseptic oil, antimicrobial, and antiviral properties **(**Astani et al., 2010**;** Andrianoelisoa et al., 2010; Ramanoelina et al., 2006; Patne et al., 2020; da Silva et al., 2020). During recent outbreak of coronavirus, Ravensare oil to be tested against SARS-CoV-2 under *in vitro* and *in vivo* conditions (Ojah, 2020; Patne et al., 2020; da Silva et al., 2020; Minami et al., 2003). However, clinical trials are not yet confirmed and experiments still lacking the scientific evidences.

3) Tea tree oil (Melaleuca alternifolia)-Australia

Tea tree oil (*Melaleuca alternifolia*), the volatile essential oil derived mainly from the Australian native plant *Melaleuca alternifolia* belong to the family *Myrtaceae* (Carson et al., 2006; Garozzo et al., 2009, 2011; Capetti et al., 2020; Brun et al., 2019; Patne et al., 2020). Tea tree oil (TTO) is produced by steam distillation of the leaves and terminal branches of *Melaleuca alternifolia* endemic to Australia (Carson et al., 2006; Garozzo et al., 2009, 2011; Capetti et al., 2020; Brun et al., 2019). **Tea tree oil (TTO) can be toxic if ingested, as evidenced by studies with animals and from cases of human poisoning. Therefore, oral consumption of Tea tree oil should be avoided and used only for the external topical applications.** Tea Tree Oil is a complex mixture of terpenes and other hydrocarbons produced metabolically in the leaves of *Melaleuca alternifolia* an Australian native species is also known as the Narrow Leaved Tea Tree. Employed largely for its antimicrobial properties, Tea tree oil (TTO) is incorporated as the active ingredient in many topical formulations used to treat cutaneous infections (Capetti et al., 2020; Carson et al., 2006; Garozzo et al., 2009, 2011; Capetti et al., 2020; Astani et al., 2010; Brun et al., 2019; Patne et al., 2020). It is widely available over the counter in Australia, Europe, and North America and is marketed as a remedy for various ailments (Carson et al., 2006; Garozzo et al., 2009, 2011; Capetti et al., 2020; Brun et al., 2019; Li et al., 2013; Usachev et al., 2013). Tea tree oil is anti-bacterial (Acne, oral care, hand sanitiser, body odour, minor wounds or lesions), anti-fungal (Dandruff, mould, toenail, feet, HVAC/air treatment), anti-inflammatory (minor wounds, grazes, insect bites), anti-yeast (Feminine care, oral care), acaricidal (Ticks, mites), and antiviral (Home, industrial, personal care) properties (Carson et al., 2006; Garozzo et al., 2009, 2011; Capetti et al., 2020; Brun et al., 2019; Li et al., 2013; Usachev et al., 2013). The other common uses of Tea tree oil is used in 1) Hand sanitisers – formulations with around 70% alcohol and 5-10% Tea tree oil (TTO) are most common. The ethanol evaporates quickly while the Tea tree oil (TTO) remains much longer on the skin potentially providing additional protection through its antimicrobial efficacy. 2) Vaporisers or HVAC inserts – many homes and offices are choosing to use Tea tree oil (TTO) in a vaporiser unit or in an air conditioning unit to provide potential protection from airborne viruses and other microorganisms. 3) Surface cleaning products – formulations with Tea tree oil (TTO) are proving popular for spraying on and wiping down surfaces. Many anecdotal reports of tea tree

oil being added to daily cleaners to provide the additional potential protection against microorganisms (Carson et al., 2006; Garozzo et al., 2009, 2011; Capetti et al., 2020; Brun et al., 2019; Li et al., 2013; The Australian Tea Tree Industry Association (ATTIA Ltd)- Fact sheet-May 17, 2020). Despite some progress, there is still a lack of clinical evidence demonstrating efficacy against bacterial, fungal, or viral infections. Large randomized clinical trials are now required to cement a place for Tea tree oil (TTO) as a topical medicinal agent.

Tea tree oil (TTO) comprises of various monoterpenes and sesquiterpenes as well as other aromatic compounds (Patne et al., 2020). The monoterpenes terpinen-4-ol, α-terpinene, α-terpinene, 1, 8-cineole, p-cymene, α-terpineol, α-pinene, terpinolenes, limo-nene, and sabinene account for 80-90% of the Tea tree oil (TTO) (Patne et al., 2020; Carson et al., 2006; Garozzo et al., 2009, 2011; Capetti et al., 2020; Brun et al., 2019; Li et al., 2013). Tea tree oil (TTO) can help to get rid of the herpes simplex virus, which causes cold sores, as well as viruses that cause the common cold and the flu. Monoterpenes combination in Tea tree oil (TTO) shows synergetic anti-viral actions. Active components of tea tree oil (TTO) showed strong anti-viral activity (Patne et al., 2020; Carson et al., 2006; Garozzo et al., 2009, 2011; Capetti et al., 2020; Brun et al., 2019; Li et al., 2013). All these properties suggested the probability of the effectiveness of tea tree oil (TTO) against Covid-19 (Patne et al., 2020).

4) Lemon Balm Oil (Melissa officinalis L)

Lemon balm (*Melissa officinalis* L.,) belongs to a family *Lamiaceae*, is a perennial plant, can be found in its natural environment in the eastern part of the Mediterranean area, as well as in the temperate zones of Asia and North America (Nurzyńska-Wierdaka et al., 2014; Sharafzadeh et al., 2011; Abdel-Naime et al., 2016; Ozarowsk et al., 2016; Moradkhani et al., 2010). Currently in India lemon balm (*Melissa officinalis* L.,) is cultivated in Karnataka, Gujarat, Punjab, Tamilnadu, Kerala, Maharashtra, Andhra Pradesh, Kashmir, and Uttrakhand (Verma et al., 2015). Dried or fresh leaves and top aerial section of the plant which are consumable. Fresh leaves of lemon balm add a magical flavour to many dishes, oils, vinegars and herbal liqueurs. Fresh or dried leaves make a refreshing tea, either cold or hot (Verma et al., 2015). Lemon balm is a versatile culinary herb which can be used to flavour for different types of dishes, from beverages, to appetizers, desserts (Verma et al., 2015). It can be added to salads, sandwiches, soups, stews, butters, cheeses, fish, stuffings for poultry, egg dishes, vegetables, fruit cups, jams, jellies, sauces, herb vinegar, wine, fruits punch, cakes, custards, ice cream, cookies, and cheesecakes (Verma et al., 2015). Lemon balm (*Melissa officinalis*) is used in phytotherapy for the prevention and treatment of nervous disturbances of sleep (Nurzyńska-Wierdaka et al., 2014; Sharafzadeh et al., 2011; Abdel-Naime et al., 2016; Ozarowsk et al., 2016; Moradkhani et al., 2010).

Lemon balm oil has medicinal properties like refreshing, as tonic, carminative, diaphoretic, surgical dressing for wounds, gastrointestinal disorders, sedative-hypnotic strengthening the memory and headache, sedative, carminative, digestive, diaphoretic antioxidant, antimicrobial, antiviral, antidepressant, psychoneurological, antispasmodic and stimulant activity, antidiabetic, and antitumor properties (Verma et al., 2015; Nurzyńska-Wierdaka et al., 2014; Sharafzadeh et al., 2011; Abdel-Naime et al., 2016; Ozarowsk et al., 2016; Moradkhani et al., 2010). Lemon balm oil has been used externally to treat herpes, sores, gout, insect bites and other skin diseases (Verma et al., 2015). Lemon balm is also known as a hormonal herb due to its antithyroid activity (Nurzyńska-Wierdaka et al., 201).

Lemon balm (*Melissa officinalis* L.,) has antiviral activity against herpes simplex virus type 2, influenza virus A2, influenza viruses and myxoviruses in vitro and vaccinia virus. In one of the study, aqueous extract of the lemon balm leaves inhibited haemagglutination induced by newcastle disease virus or mumps virus (Verma et al., 2015). Aqueous extracts of the leaves of Lemon balm (*Melissa officinalis* L.,) have been reported to have activity against semliki forest virus (Verma et al., 2015). Lemon balm attracts bees, and if it is rubbed on inside of empty beehives it will attract new bee swarms (Verma et al., 2015). Lemon balm is also used as an insect repellent (Verma et al., 2015). It is a prominent antimicrobial agent against food-borne pathogens and spoilage bacteria. In vitro testing has identified its anti-HIV activity against HIV-1 reverse transcriptase and antitumor activity (Verma et al., 2015). Therefore, during recent outbreak of coronavirus (SARS-CoV-2), Lemon balm (*Melissa officinalis* L.,) was suggested as an alternative therapy for the control of covid-19 (Patne et al., 2020). Clinical trials are yet to be concluded for the scientific validation.

Lemon balm (*Melissa officinalis* L.,) is grown for pharmaceutical purposes and to obtain essential oil, and is used in therapy which contains up to 0.3% of essential oil (Verma et al., 2015; Nurzyńska-Wierdaka et al., 2014; Sharafzadeh et al., 2011; Abdel-Naime et al., 2016; Ozarowsk et al., 2016; Moradkhani et al., 2010). The glandular trichomes are produced and start to release oil at a very early stages of plant growth (Verma et al., 2015; Nurzyńska-Wierdaka et al., 2014; Sharafzadeh et al., 2011; Abdel-Naime et al., 2016; Ozarowsk et al., 2016; Moradkhani et al., 2010). The lemon balm oil is obtained by hydrodistillation from air-dried leaves was light yellow in color and characterized by a fresh lemon scent (Nurzyńska-Wierdaka et al., 2014; Sharafzadeh et al., 2011; Abdel-Naime et al., 2016; Ozarowsk et al., 2016; Moradkhani et al., 2010).

The main active constituents of lemon balm oil (*Melissa officinalis* L) are volatile compounds (*e.g*., geranial, neral, citronellal, and geraniol), triterpenes (*e.g*., ursolic acid and oleanolic acid), and phenolics (*e.g*., cis-and trans-RAisomers, caffeic acid derivatives, luteolin, naringin, and

hesperidin) (Nurzyńska-Wierdaka et al., 2014; Sharafzadeh et al., 2011; Abdel-Naime et al., 2016; Ozarowsk et al., 2016; Moradkhani et al., 2010). The chemical characterization of lemon balm oil (*Melissa officinalis* L) confirmed the presence of geranial (45.2% and 45.1%) and neral (32.8% and 33.8%); citronellal (8.7% and 0.4%), geraniol (trace amounts and 0.6%), and geranyl acetate (0.5% and 3.0%), as well as, among others, isogeranial, *E*-caryophyllene, caryophyllene oxide, germacrene D, and carvacrol (Nurzyńska-Wierdaka et al., 2014; Sharafzadeh et al., 2011; Abdel-Naime et al., 2016; Ozarowsk et al., 2016; Moradkhani et al., 2010).

5) Eucalyptus oil (Eucalyptus globulus)

Essential oils obtained from eucalyptus (*Eucalyptus globulus*) belongs to family *Myrtaceae* are traditionally used to treat various respiratory ailments including pharyngitis, bronchitis, and sinusitis (Asif et al., 2020; Patne et al., 2020). **Eucalyptus oil is very toxic and poisnous at higher concentrations** and mainly used in soap industries, toilet, surface cleaning liquids, and topical applications. Signs of eucalyptus poisoning might include stomach pain and burning, dizziness, muscle weakness, small eye pupils, feelings of suffocation, and some others. Therefore, oral consumption of Eucalyptus oil should be avoided since the oil is very poisonous and might leads to death. Eucalyptus oil and its active constituent, 1,8-cineole (eucalyptol) have an *in vitro* antiviral activities against various strains of viruses including enveloped mumps viruses (MV) and herpes simplex viruses (HSV-1 and HSV-2) and influenza A (H1N1) virus under *in vitro* assays (Asif et al., 2020; Brochot et al., 2017). Because of the antiviral activity of eucalyptus oil and eucalyptol against respiratory viruses, multiple researchers have attempted to explore the antiviral efficacy of eucalyptus oil and its active ingredients against SARC-CoV-2 using in vitro assays and molecular docking techniques (Patne et al., 2020; Asif et al., 2020; Sharma and Kaur, 2020a, 2020b). The 1,8-cineole is more extensively studied for its pharmacological potentials against various respiratory ailments (Juergens et al. 2003, 2020). 1,8-cineole (eucalyptol) is one of the components of Vicks VapoRub™ which is known to have nasal decongestant effects when applied to nose or inhaled as vapours in warm water (Asif et al., 2020; Juergens et al., 2003, 2020). Eucalyptol is also known to have mucolytic and bronchodilatory properties (Asif et al., 2020; Juergens et al., 2020). Eucalyptus oil is also very toxic and has also been shown to have disinfection properties and inhibited the growth of viruses on various utensils and filter devices (Asif et al., 2020; Usachev et al., 2013; Patne et al., 2020). Therefore, eucalyptus oil and its active constituent, i.e. eucalyptol (1,8-cineole) in the prevention and treatment of COVID-19 has been proposed (Patne et al., 2020; Asif et al., 2020). However, clinical trials are yet to be confirmed for the scientific validation.

6) Garlic oil (Allium sativum)

Garlic oil (*Allium sativum)* belong to the family *Amaryllidaceae* is one of the traditional medicinal plant with antimicrobial, antibacterial, antiviral, antioxidant, anti-inflammatory properties commonly used in all the dishes (Asif et al., 2020; Patel et al., 2018). Garlic has been used as a medication to treat common cold, throat infections, running nose, influenza, and other kinds of infections for centuries. The compounds such as allyl disulphide (28.4%), allyl trisulphide (22.8%), allyl (*E*)-1-propenyl disulphide (8.2%), allyl methyl trisulphide (6.7%), and diallyl tetrasulphide (6.5%) were identified as the main constituents of garlic essential oil (Asif et al., 2020). In case of garlic, 17 compounds were studied for their activities against ACE2 protein and viral main protease (Mpro/6LU7) of SARC-CoV-2. ACE2 is involved in the viral invasion of host cells, while Mpro is involved in viral replication. All the 17 compounds studied showed interactions with host protein (ACE2) as well as with viral proteases, indicating that garlic oil has a great potential to treat COVID-19 patients (Asif et al., 2020; Thuy et al. 2020). Therefore, on the basis of these docking and *in vitro* studies, it is proposed that garlic essential oils and their isolated constituents, especially Diallyl sulphide (DAS), have the potential to prevent the entry of virus into host cells as well as to activate molecular antioxidant pathways that decreased the secretions of culprit pro-inflammatory cytokine (Asif et al., 2020). Clinical trials are yet to be confirmed for the scientific validation.

7) Essential oil of Laurus nobilis

The essential oil of *Laurus nobilis* belongs to the family *Lauraceae* is one of the medicinal plant which comprises approximately 2500 species (Basak and Candan, 2013). The genus *Laurus* is found in Europe and consists of the two species *Laurus azorica* and *Laurus nobilis* (Basak and Candan, 2013). Indian bay leaf tree is an aromatic medicinal plant known as *Cinnamomum tamala*. The leaf used to flavour and season food, just like the European bay leaf, commonly known as Bay Laurel (*Laurus nobilis*). Indian bay leaf is commonly known as tejpat, tezapatta, Malabar leaf, Indian bark, Indian cassia, or malabathrum, is a tree in the family *Lauraceae* that is native to India, Bangladesh, Nepal, Bhutan, and China. *Laurus nobilis* is known for the antimicrobial, analgesic, anti-inflammatory, antitumoral, acetylcholine esterase inhibiting properties of the essential oil (Basak and Candan, 2013). The chemical composition of the essential oil from *Laurus nobilis* L. leaves was analyzed by GC/GC-MS and resulted in the identification of 29 compounds, representing 99.18% of the total oil. 1,8-cineole (68.82%), 1-(S)-*α*-pinene (6.94%), and R-(+)-limonene (3.04%) were determined to be the main components (Basak and Candan, 2013). The essential oil of *Laurus nobilis* L. is used in the production of soap and also as an aroma in the food and cosmetics industries; dry fruits and dry leaves are used for adding fragrance to food and consumed as tea, respectively (Basak and Candan, 2013). Therefore, essential oils of *Laurus nobilis* L that are rich in b-ocimene, 1, 8-cineole, a-pinene, and b-pinene possessed strong antiviral properties that can be effective in the

treatment against SARS-CoV-2. Clinical trials are yet to be confirmed for the scientific validation (Patne et al., 2020).

Roviello and Roviello, (2021) in Italy reported that mild climate, higher average sunlight exposure and the Mediterranean diet, which includes the consumption of foods containing polyphenols and natural compounds with potential antiviral activities, could have all contributed in the defence against the pandemic coronavirus (SARS-CoV-2) outbreak (Roviello and Roviello, 2021). Further, more than forty compounds discovered in bay laurel (*Laurus nobilis*) a typical Mediterranean evergreen tree of common culinary use, and found that nine of them had a significantly high affinity for SARS-CoV-2 main protease Mpro, one of the most important targets in the anti-COVID-19 therapeutic strategies (Roviello and Roviello, 2021). Among these laurel-derived ligands, lauruside 5 emerged from the study as the most promising candidate as a potential Mpro inhibitor (Roviello and Roviello, 2021).

8) Rosemary oil (Rosmarinus officinalis L.)

Rosemary (***Rosmarinus officinalis* L.)** belongs to the family *Lamiaceae*, is a medicinal plant of Mediterranean origin that has been distributed throughout different areas of the world (González-Minero et al., 2020; Kompelly et al., 2019). *Rosmarinus officinalis* is a woody, perennial herb with fragrant, evergreen, needle like leaves and white, pink, purple or blue flowers and found throughout India (Kompelly et al., 2019). *Rosmarinus officinalis* is an ancient plant considered to be medicinal in the European Pharmacopoeia (González-Minero et al., 2020; Kompelly et al., 2019). It has many medicinal properties, and its extracts have been used (mainly orally) in folk medicine. The family *Lamiaceae* which contains several genera—such as *Salvia*, *Lavandula*, and *Thymus*—that are commonly used in cosmetics, due to their high prevalence of antioxidant molecules (González-Minero et al., 2020). One of these plants is rosemary (*Rosmarinus officinalis*), a plant with medicinal properties, of which extracts appear in the composition of hundreds of cosmetics (González-Minero et al., 2020). Rosemary oil is used as a food seasoning, due to its chemical compound constituents responsible for the anti-bacterial, anti-fungal, anti-oxidant, anti-cancer, anti-proliferative, antimicrobial, hepatoprotectivity, anti-diabetic, anti-inflammatory, anti-depressant, anti-obesity, ulcerative colitis, neuroprotective properties (Kompelly et al., 2019). On the other hand, the bioactivities of rosemary extracts include properties such as anti-inflammatory, anti-diabetic, hepatoprotective and anti-microbial activity. These bioactivities are related to the phenolic compound constituents (mainly caffeic acid, rosmarinic acid and carnosic acid (Kompelly et al., 2019). Rosemary is a perennial shrub that grows in the wild or is cultivated. It has glandular hairs that emit fragrant volatile essential oils (mainly monoterpenes) in response to drought conditions in the Mediterranean climate (González-Minero et al., 2020). It also contains diterpenes and other polyphenolic molecules (González-Minero et al., 2020). The derivatives of rosemary were formulated in essential oils for massages and aromatherapy, rosemary alcohol, gels, shampoos, soaps, rosemary water, cleansing milk, deodorant, anti-wrinkle cream, aftershave lotion, hydrating facial cream, cream for the eye contour area, etc (González-Minero et al., 2020).

At least 150 molecules are known to be present in the volatile essential oil and fewer in the non-volatile fraction, such as carnosic acid, ursolic acid, oleanolic acid, flavonoids, and phenolic acids (rosmarinic acid) (González-Minero et al., 2020). These molecules are precursors of plant derivatives with a high antioxidant capacity. Rosemary is widely used in cosmetic preparations as a fragrance and as a skin conditioner in safe concentrations (González-Minero et al., 2020). Rosemary preserves cosmetics from degradation and has a great potential to be used topically. It absorbs UV light well and is a bactericidal and antifungal agent (González-Minero et al., 2020). Its anti-alopecia properties are also being studied. Thus far, it is only known that the benefits of this plant are associated with the synergistic action of its molecules or through synergistic action with other plant extracts (González-Minero et al., 2020).

The principal components of Rosemary oils were found to be 1,8-cineol (33.08-55.5 %), camphor (13.55-18.13 %), α-pinene (8.58-9.32 %), β-pinene (2.0–9.0%), α-terpineol (6.79- 8.17 %), camphene (5.07-5.58 %), borneol (4.08-5.48 %), limonene (3.19-3.04 %) and p-cymene (2.42-3.11 %) (Kompelly et al., 2019; Patne et al., 2020). Rosemary oil is rich in 1, 8- Cineole, rosmarinic acid, camphor, caffeic acid, ursolic acid, betulinic acid, carnosic acid and carnosol which shows strong anti-viral effects (Kompelly et al., 2019; Patne et al., 2020). In traditional medicine, the leaves of *R. officinalis* are used based on their anti-bacterial activities, carminative and as analgesic in muscles and joints (Kompelly et al., 2019). The rosemary's essential oils and extracts obtained from flowers and leaves are used to treat minor wounds, rashes, headache, dyspepsia, circulation problems, but also as an expectorant, diuretic and anti-spasmodic in renal colic (Kompelly et al., 2019).

Rosemary extract has demonstrated the antiviral effects against herpes viruses and hepatitis A, which affects the liver (Patne et al., 2020). Therefore, Rosemary essential oil can be effective against COVID-19, assuming the activity of its chief chemical constituents like 1, 8- Cineole, α-pinene, β-pinene, (Patne et al., 2020). Clinical trials are yet to be confirmed for the scientific validation.

9) Bergamot Oil (Synonym Citrus x bergamia Risso & Poit.)

Bergamot essential oil (BEO) is the result of the mechanical manipulation (cold pressing) of the exocarp (flavedo) of the hesperidium of *Citrus limon* (L.) Osbeck Bergamot Group (synonym *Citrus* x *bergamia* Risso & Poit.) (Valussi et al., 2021). It is chemically dominated by monoterpene hydrocarbons (i.e., limonene), but with significant percentages of oxygenated monoterpenes (i.e., linalyl acetate) and of non-volatile oxygen heterocyclic

compounds (i.e., bergapten) (Valussi et al., 2021). Bergamot essential oil (BEO) was described to possess melanogenic, antinociceptive, antiproliferative, sedative, anxiolytic, neuroprotective, antioxidant, and antimicrobial activities (Valussi et al., 2021). The pharmacological properties of Bergamot essential oil (BEO) are Relaxing, calming, anxiolytic, antinociceptive, anti-inflammatory, antiviral, and antimicrobial (Valussi et al., 2021).

The main volatile compounds in the oil are limonene (37.2 %), linalyl acetate (30.1%), linalool (8.8%), γ-terpinene (6.8%) and β-pinene (2.8%) and in smaller quantities geranial and β-bisabolene (Patne et al., 2020). Bergamot oil and its chief active compound citronellal showed inhibitory action against influenza virus (Patne et al., 2020). So, it may show inhibitory action against the SARS-CoV-2 virus (Patne et al., 2020). Clinical trials are yet to be confirmed for the scientific validation.

The Bergamot essential oil (BEO) is very toxic at higher concentrations (Valussi et al., 2021). The most relevant concerns about Bergamot essential oil (BEO) toxicology regards its photosensitive and melanogenic properties, traditionally ascribed to its content in furocoumarins (psoralens) such as bergapten, which may be even photo-mutagenic if applied alone as a pure substance (Valussi et al., 2021). Cases of adverse effects caused by Bergamot essential oil (BEO) application reported that aromatherapy (sauna with vaporized BEO followed by artificial or natural sunbathing) can cause skin photosensitivity (Valussi et al., 2021). The oral intake of large amounts of Bergamot essential oil (BEO) can be associated with neurological symptoms (muscle cramps, fasciculations, paraesthesias and blurred vision) (Valussi et al., 2021).

10) Juniperus oxycedrus Oil (cade oil)

The genus *Juniperus* L. belongs to the *Cupressaceae* family, representing about 70 species all over the world, and widely distributed throughout the forests of the temperate and cold regions of the northern Hemisphere, from the far north to the Mediterranean (Fadel et al., 2019; Alan et al., 2016). The essential oils were obtained from leaves, berries and twigs by yielding 0.02%, 2.12% and 0.01% (Fadel et al., 2019; Alan et al., 2016). The major compounds were determined manoyl oxide (32.8%) and caryophyllene oxide (11.9%) in leaf oil, myrcene (44.6%), α-pinene (19.9%) and germacrene D (15.5%) in berry oil, manoyl oxide (35.4%) and caryophyllene oxide (16.8%) in twig oil (Fadel et al., 2019; Alan et al., 2016). The other constituents were α-Pinene (27.4%) and β-myrcene (18.9%). Other recognized compounds were α-phellandrene (7.1%), limonene (6.7%), epibicycloses-quiphellandren (2.3%) and δ-cadinene (2.2%). All the phyto-constituents have inhibitory action against SARS-CoV-1 virus (Loizzo et al., 2008; Patne et al., 2020).

Juniper tar (cade oil) is distilled from the branches and wood of *Juniperus oxycedrus* is also **very toxic at higher concentrations**. The poisoning caused convulsions, collapsus, acute pulmonary oedema, renal failure and hepatotoxicity. Therefore, oral consumption should be avoided and a very low concentrations of cade oil (*Juniperus oxycedrus*) is used for topical applications.

*11) Thyme oil (*Thymus vulgaris)

Thyme oil (*Thymus vulgaris*) belongs to the mint family *Lamiaceae* is a tiny perennial aromatic shrub, evergreen or semi-evergreen herbaceous plants (Swamy et al., 2016; Boruga et al., 2014; Reddy et al., 2014; Teixeira et al., 2013). It is growing up to 15-30 cm tall by 40 cm wide. Thyme is cultivated in most of the European countries, together with France, Spain, Italy, Bulgaria, Romania, Portugal, Germany, and UK (Swamy et al., 2016; Boruga et al., 2014; Reddy et al., 2014; Teixeira et al., 2013). Currently Thyme is also growing in India (Karnataka, Tamilnadu, Kerala, Maharashtra). The major chemical components of Thyme oil (*Thymus vulgaris*) are p-cymene (8.41%), γ-terpinene (30.90%) and thymol (47.59%) (Swamy et al., 2016; Boruga et al., 2014; Reddy et al., 2014; Teixeira et al., 2013). The other chemical compounds are linalool, carvacrol, 1,8-cineole, eugenol, camphor, camphene, α-pinene, borneol, and α -pinene (Swamy et al., 2016; Reddy et al., 2014; Teixeira et al., 2013).

Thyme essential oil (*Thymus vulgaris*) has antiseptic, antimicrobial, astringent, anthelmintic, medicinal drug tonic, carminative, disinfectant, antiviral and anti-inflammatory activities (Swamy et al., 2016; Reddy et al., 2014; Boruga et al., 2014; Teixeira et al., 2013). Thyme is used for skin issues like oily skin, sciatica, acne, dermatitis, skin condition and bug bites (Swamy et al., 2016; Reddy et al., 2014;Boruga et al., 2014; Teixeira et al., 2013). In aromatherapy, the distinct types, thymol, 'red thyme oil', linalol kind for its terribly light soft action and thuyanol for antiviral properties are used (Swamy et al., 2016; Reddy et al., 2014; Boruga et al., 2014; Teixeira et al., 2013). Thyme essential oil (*Thymus vulgaris*) is useful in the treatment of assorted intestinal infections and infestations, like hookworms, ascarids, gram-positive and gram-negative bacterium, fungi and yeasts as well as *Candida albicans*. Its active constituent, thymol, is active against enterobacteria and cocci bacteria (Swamy et al., 2016; Reddy et al., 2014; Boruga et al., 2014; Teixeira et al., 2013). Thyme may also improve liver functioning, and act as an appetite stimulant. It will be used in the treatment of cartilaginous tube, bronchial and urinary infections. Used as a gargle, Thyme is helpful in treatment of laryngitis and inflammation. the main component of the volatile oil of thyme, thymol, is active against enterobacteria and cocci bacteria (Swamy et al., 2016; Reddy et al., 2014; Boruga et al., 2014; Teixeira et al., 2013; Syamasundar et al., 2008). On the basis of antiviral property, Thyme oil (*Thymus vulgaris*) has been proposed as an alternative therapy for controlling coronavirus (SARS-CoV-2) during recent outbreak (Patne et al., 2020). Clinical trials are yet to be concluded for the scientific validation.

Syamasundar et al., (2008) has also reported the higher content of thymol in Indian species of *Thymus vulgaris* and is a good source for flavour industry. This study also concluded that forty eight compounds were detected among which 36 compounds, which constituted 98.63% of the oil were identified, with thymol (61.6%), p-cymene (11.2%), ϒ-terpinene (7.4%), methyl thymol (3.9%), methyl carvacrol (3.3%) and β-caryophyllene (2.3%) as major chemical constituents in Indian species of *Thymus vulgaris* (Syamasundar et al., 2008). Therefore, this study concluded that the thyme (*Thymus vulgaris*) can be cultivated in India and is a potential source of thymol as well as its essential oil (Syamasundar et al., 2008).

12) *Achillea clavennae* (**Family**- *Asteraceae*; **Parts used**-Leaves and flowers; **Major chemical compounds**-Camphor, myrcene, 1,8-cineole, β-caryophyllene, linalool, geranyl acetate) (Swamy et al., 2016).

13) **Cinnamon Oil (***Cinnamomum zeylancium* or *Cinnamomum vervun* (**Family-***Lauraceae***; Parts used**- bark, leaves**; Major chemical compounds-** Cinnamaldehyde -65-80% and eugenol -5-10%) (Swamy et al., 2016).

14) *Copaifera officinalis* (**Family**- *Fabaceae***; Parts used**-Essential oil**; Major chemical compounds-** β-Caryophyllene, β -bisabolene, germacrene B, α-copaene, germacrene D, α -humulene, £-cadinene) (Swamy et al., 2016).

15) *Artemisia longifolia* (**Family**- *Asteraceae* **; Parts used**-Aerial parts**; Major chemical compounds**- Alpha-pinene, camphene, 1,8-cineole) (Swamy et al., 2016).

16) *Artemisia frigida* (**Family**- *Asteraceae* **; Parts used**-Aerial parts**; Major chemical compounds**- 1,8-Cineole, methylchavicol, camphor) (Swamy et al., 2016).

17) *Piper nigrum* (**Family**- ***Piperaceae* ; Parts used**-Essential oil**; Major chemical compounds-** Limonene, £-3-carene, α -pinene, β -caryophyllene, β -pinene, sabinene, α -felandeno, myrcene, para-cymene, linalool, terpinolene, β -selinene, 1,8 cineole, α -terpinene, eugenol, terpinen-4-ol, camphene, safrole) (Swamy et al., 2016).

18) *Salvia lavandulifolia* (**Family**- *Lamiaceae* **; Parts used**-Essential oil **; Major chemical compounds**- Camphor, α -thujone, beta-thujone, camphene, α -pinene, terpineol) (Swamy et al., 2016).

19) *Thuja* sp. *(Thuja plicata, Thuja occidentalis)* (**Family**-*Cupressaceae* **; Parts used**- Essential oil **; Major chemical compounds**- Alpha-thujone and beta-thujone) (Swamy et al., 2016).

20) *Euphrasia rostkoviana* (**Family**- *Orobanchaceae* **; Parts used**- Essential oil **; Major chemical compounds**- n-Hexadecanoic acid, thymol, myristic acid, linalool) (Swamy et al., 2016).

21) **Fennel Oil (***Foeniculum vulgare)* (**Family**- *Apiaceae* **; Parts used**- Essential oil **; Major chemical compounds**-Trans-anethole, methylchavicol, limonene) (Swamy et al., 2016).

22) **Peppermint Oil (***Mentha piperita* or *Mentha balsamea*) **Family**- *Lamiaceae* **; Parts used**- Essential oil **; Major chemical compounds**- 1,8 cineole, menthol, limonene) (Swamy et al., 2016).

23) Clove oil (*Eugenia caryophyllata*) (also known as *Syzygium aromaticum*, *Eugenia aromatica*, *E. carophyllus*) **Family**- *Myrtaceae* **; Parts used**- Essential oil **; Major chemical compounds**- m-Eugenol (69.4%),Eugenol acetate (10.8%), Tyranton (7.8%) Caryophyllene (6.8%), 1, 4, 7-Cycloundecatriene, 1, 5, 9, 9-tetramethyl-, and trace amounts (<1%) of other constituents) (Swamy et al., 2016).

24) Oregano Oil: (*Origanum vulgare*) **Family**- *Lamiaceae* **; Parts used**- Essential oil **; Major chemical compounds**- p-cymene, γ-terpinene, caryophyllene, spathulenol, germacrene-D, β-fenchyl alcohol, and δ-terpineol) (Swamy et al., 2016).

25) ***Theileria orientalis* Oil (Family**-*Theileriidae*; **Parts used**- Essential oil) (Swamy et al., 2016).

III. CONCLUSION

This review paper summarises the latest updates on the use of essential oils of medicinal and aromatic plants as an alternative therapy for controlling the coronavirus (SARS-CoV-2) disease (covid-19) outbreak. Medicinal plants have been used worldwide by indigenous populations, playing an important role in the treatment of human and animal diseases. Medicinal plants continue to be the main source of new lead bio-active molecules. Virucidal activity of essential oils, which are lipophilic by nature, is probably due to the disruption of the viral membrane or interference with viral envelope proteins involved in the host cell attachment. The reactivity of essential oils depends upon the nature of their functional groups and orientation. Essential oils are considered to be potent against a diverse range of pathogens. Therefore, further research should focus on exploring the molecular mechanisms of essential oils and their individual chemical compounds. Hence there is a ray of hope in near future for the application of essential oils of botanicals could be used to protect from viral pandemic outbreak.

However, some of the essential oils of plants are very toxic and poisonous which is a major concern and oral consumption should be avoided. Further, much of the evidence comes from animal and *in vitro* studies and overall clinical Evidence-Based Complementary and Alternative Medicine evidence to support these herbal interventions remains weak and lacking. The data of the literature survey presented in this review paper is not enough and lacks scientific evidence. Drug regulatory framework should also be applied immediately to ensure that they conform with required standards of safety, quality, and efficacy. In addition, preclinical and clinical trial evaluations of these essential oils as agents for COVID-19 have not specifically been conducted, so further investigations related to this are warranted.

Therefore, this is just the starting point, and human clinical trials are yet to be concluded for the scientific validation.

REFERENCES

[1]. Abdel-Naime WA, Fahim JR, Fouad MA, Kamel MS (2016) Botanical studies of the leaf of *Melissa officinalis* L., Family: Labiatae, cultivated in Egypt. Journal of Pharmacognosy and Phytochemistry. 5(6): 98-104.

[2]. Ahmad S, Zahiruddin S, Parveen B, Basist P, Parveen A, Gaurav, Parveen R, Ahmad M (2021) Indian medicinal plants and formulations and their potential against COVID- 19–preclinical and clinical research. Front. Pharmacol. 11: 578970. (doi: 10.3389/fphar.2020.578970).

[3]. Alan S, Kurkcuoglu M, Sener G (2016) Composition of the essential oils of *Juniperus oxycedrus* L. subsp. oxycedrus growing in Turkey. Turk J Pharm Sci. 13(3): 300-303.

[4]. Andrianoelisoa HS, Menut C, Ramanoelina P, Raobelison F, de Chatelperron PC, Danthu P (2010) Chemical Composition of Essential Oils From Bark and Leaves of Individual Trees of *Ravensara aromatica* Sonnerat. Journal of Essential Oil Research. 22(1): 66-70. (DOI: 10.1080/10412905.2010.9700267).

[5]. Ankita S, Chandra SS, Arti T (2014) Phytochemical study and antimicrobial activities of *Cinnamomum camphora*. World J. Pharmaceutical Research. 3(2): 2287-2294.

[6]. Asif M, Saleem M, Saadullah M, Yaseen HS, Al -Zarzour R (2020) COVID‑19 and therapy with essential oils having antiviral, anti‑inflammatory, and immunomodulatory properties. Inflammopharmacology. 1-4. (https://doi.org/10.1007/s10787-020-00744-0).

[7]. Astani A, Reichling J, Schnitzler P (2010) Comparative study on the antiviral activity of selected monoterpenes derived from essential oils. Phytotherapy Research. 24: 673-679 (https://www.ncbi.nlm.nih.gov/pubmed/19653195).

[8]. Basak SS, Candan F (2013) Effect of *Laurus nobilis* L. essential oil and its main components on *α*-glucosidase and reactive oxygen species scavenging activity. Iranian Journal of Pharmaceutical Research. 12 (2): 367-379.

[9]. BBC News (2021) Coronavirus pandemic Coronavirus: 'Double mutant' Covid variant found in India (April, 2021)

[10]. Blanchard JM (2007) *Cinnamomum camphora* a cineole (**Ravintsara**), A plant for the prevention of hospital-acquired infections?. Phytotherapy. **5:** 15-20. (https://doi.org/10.1007/s10298-007-0202-1).

[11]. Boruga O, Jianu C, Mişca C, Goleț I, Gruia AT, Horhat FG (2014) *Thymus vulgaris* essential oil: chemical composition and antimicrobial activity. Journal of Medicine and Life. 7(3): 56-60.

[12]. Brochot A, Guilbot A, Haddioui L, Roques C (2017) Antibacterial, antifungal, and antiviral effects of three essential oil blends. Microbiology Open 6:e00459. (https ://doi.org/10.1002/mbo3.459).

[13]. Brochot A, Guilbot A, Haddioui L, Roques C (2017) Antibacterial, antifungal, and antiviral effects of three essential oil blends. Microbiology Open 6:e00459. (https ://doi.org/10.1002/mbo3.459).

[14]. Brun P, Bernabè G, Filippini R et al., (2019) *In vitro* antimicrobial activities of commercially available Tea Tree (*Melaleuca alternifolia*) essential oils. Current Microbiology 76: 108–116. (https://www.ncbi.nlm.nih.gov/pubmed/30421144).

[15]. Capetti F, Sgorbini B, Cagliero C et al., (2020) *Melaleuca alternifolia* essential oil: Evaluation of skin permeation and distribution from topical formulations with a solvent-free analytical method. Planta Medica. 1-9. (https://www.thieme-connect.de/products/ejournals/abstract/10.1055/a-1115-4848).

[16]. Carson CF, Hammer KA, Riley TV (2006) *Melaleuca alternifolia* (Tea Tree*)* Oil: A review of antimicrobial and other medicinal properties. Clinical Microbiology Reviews. 19(1): 50-62. (https://www.ncbi.nlm.nih.gov/pubmed/16418522).

[17]. Costa R, Pizzimentib F, Marotta F, Dugo P, Santi L, Mondello L (2010) Volatiles from steam-distilled leaves of some plant species from Madagascar and New Zealand and evaluation of their biological activity. Natural Product Communications. 5 (11): 1803-1808.

[18]. da Silva JKR, Figueiredo PLB, Byler KG, Setzer WN (2020) Essential oils as antiviral agents, potential of essential oils to treat SARS-CoV-2 infection: An in-silico investigation. Int. J. Mol. Sci. 21: 3426. (doi:10.3390/ijms21103426).

[19]. Doucleff M (2021) Correspondent, Science Desk. People Are Talking About A 'Double Mutant' Variant In India. What Does That Mean. (April, 24th 2021) (https://www.npr.org/sections/goatsandsoda/2021/04/24/988744811).

[20]. Fadel H, Benayache F, Figueredo JLCG, Chalard P, Hazmoune H, Benayache S (2019): Essential oil constituents of *Juniperusoxycedrus* L. and *Cupressussempervirens* L. (*Cupressaceae*) growing in Aures region of Algeria. Natural Product Research. (DOI: 10.1080/14786419.2019.1687473).

[21]. Garozzo A, Timpanaro R, Bisignano B, et al., (2009) *In vitro* antiviral activity of *Melaleuca alternifolia* essential oil. Letters in Applied Microbiology. 49: 806-8 (https://www.ncbi.nlm.nih.gov/pubmed/19843207).

[22]. Garozzo A, Timpanaro R, Stivala A et al., (2011) Activity of *Melaleuca alternifolia* (tea tree) oil on influenza virus A/PR/8: study on the mechanism of action. Antiviral Research. 89(1): 83-8 (https://www.ncbi.nlm.nih.gov/pubmed/21095205).

[23]. Gibbs JEM (2019) Essential oils, asthma, thunderstorms, and plant gases: a prospective study of respiratory response to ambient biogenic volatile organic compounds (BVOCs). J Asthma Allergy. 12:169–182.

[24]. González-Minero FJ, Bravo-Díaz L, Ayala-Gómez A (2020) *Rosmarinus officinalis* L. (Rosemary): An ancient plant with uses in personal healthcare and cosmetics. Cosmetics. 7: 77. (doi:10.3390/cosmetics7040077).

[25]. Guo X, Cui M, Deng M, Liu X, Huang X, Zhang X, Luo L (2017) Molecular differentiation of five *Cinnamomum camphora* chemotypes using desorption atmospheric pressure chemical ionization mass spectrometry of raw leaves. Nature-Scientific Reports. 7:46579. (DOI: 10.1038/srep46579).

[26]. Jahan R, Paul AK, Jannat K, Rahmatullah M (2021) Plant Essential Oils: Possible COVID-19 Therapeutics. Natural Product Communications. 16(2): 1. (DOI: 10. 1177/ 1934 578X 21996149).

[27]. Juergens UR, Dethlefsen U, Steinkamp G, Gillissen A, Repges R, Vetter H (2003) Anti-inflammatory activity of 1.8-cineol (eucalyptol) in bronchial asthma: a double-blind placebo-controlled trial. Respir Med. 97:250–256. (https ://doi.org/10.1053/rmed.2003.1432).

[28]. Juergens LJ, Worth H, Juergens UR (2020) New perspectives for mucolytic, anti-inflammatory and adjunctive therapy with 1,8-cineole in COPD and asthma: review on the new therapeutic approach. Adv Therapy. 37:1737–1753. (https ://doi.org/10.1007/s1232 5-020-01279 -0).

[29]. Kamalabadi M, Astani A, Nemati F (2018) Anti-viral effect and mechanism of carvacrol on herpes simplex virus type 1. Int J Med Lab. 5:113–122.

[30]. Kompelly A, Kompelly S, Vasudha B, Narender B (2019) *Rosmarinus officinalis* L.: an update review of its phytochemistry and biological activity, Journal of Drug Delivery and Therapeutics. 9(1):323-330. (DOI: http://dx.doi.org/10.22270/jddt.v9i1.2218).

[31]. Kumar A, Choudhir G, Shukla SK, Sharma M, Tyagi P, Bhushan A, Rathore M (2020) Identification of phytochemical inhibitors against main protease of COVID-19 using molecular modeling approaches. J Biomol Struct Dyn. (https ://doi.org/10.1080/07391102.2020.17721 12).

[32]. Kulkarni SA, Nagarajan SK, Ramesh V, Palaniyandi V, Selvam SP, Madhavan T (2020) Computational evaluation of major components from plant essential oils as potent inhibitors of SARS-

CoV- 2 spike protein. J. Molec Struct. 1221:128823. (https ://doi. org/10.1016/j.molst ruc.2020.12882 3).

[33]. Li X, Duan S, Chu C, Xu J et al., (2013) *Melaleuca alternifolia* concentrate inhibits in vitro entry of influenza virus into host cells. Molecules. 18: 9550-66. (https://www.mdpi.com/1420-3049/18/8/9550).

[34]. Loizzo MR, Saab AM, Tundis R, Statti GA, Menichini F, Lampronti I, Gambari R, Cinatl J, Doerr HW (2008) Phytochemical analysis and in vitro antiviral activities of the essential oils of seven Lebanon species. Chemistry & Biodiversity. 5(3): 461-70.

[35]. Ojah EA (2020) Exploring essential oils as prospective therapy against the ravaging Coronavirus (SARS-CoV-2). IBEROAMERICAN JOURNAL OF MEDICINE. 04 : 322-330. (http://doi.org/10.5281/zenodo.3903594).

[36]. Ma L, Yao L (2020) Antiviral effects of plant-derived essential oils and their components: an updated review. Molecules 25:2627.

[37]. Malabadi RB, Meti NT, Chalannavar RK (2021a) Role of herbal medicine for controlling coronavirus (SARS-CoV-2) disease (COVID-19). International Journal of Research and Scientific Innovations. 8(2): 135-165.

[38]. Malabadi RB, Meti NT, Chalannavar RK (2021b) Applications of nanotechnology in vaccine development for coronavirus (SARS-CoV-2) disease (Covid-19). International Journal of Research and Scientific Innovations. 8(2): 191-198.

[39]. **Malabadi RB**, Kolkar KP, Meti NT, Chalannavar RK (2021c) Recent updates on role of herbal medicine for **Alzheimer's disease** (Dementia). International Journal of Current Research in Biosciences and Plant Biology. **8(1)**, xxx-xxx. (**doi:** https://doi.org/10.20546/ijcrbp.2020.801.xxx).

[40]. **Malabadi RB, Chalannavar RK** (2020) Safed musli (*Chlorophytum borivilianum*): Ethnobotany, phytochemistry and pharmacological updates. Int. J. Curr. Res. Biosci. Plant Biol. 7(11): 25-31.

[41]. **Malabadi RB** (2008) Production of edible vaccines for oral immunization in transgenic plants, current and future prospective. Journal of Phytological Research. 21(1): 1-10.

[42]. Malabadi RB, Vijaykumar S (2008) Evaluation of antifungal property of medicinal plants. Journal of Phytological Research. 21(1):139-142.

[43]. Malabadi RB, Mulgund GS, Nataraja K (2009) Triacontanol induced somatic embryogenesis and plantlet regeneration in *Catharanthus roseus*. Journal of Medicinal and Aromatic Plant Sciences. 31: 147-151.

[44]. Malabadi RB, Mulgund GS, Nataraja K (2010a) Evaluation of antifungal activity of selected medicinal plants. Journal of Medicinal and Aromatic Plant Sciences. 32(1):42-45.

[45]. Malabadi RB, Parashar A, Ganguly A, Suresh MR (2010b) Expression of dengue virus envelope protein in a different plant system. Faculty Research and Development day, Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, Canada, 19th November 2010. Abstract No-69, page.

[46]. **Malabadi RB**, Ganguly A, Teixeira da Silva JA, Parashar A, Suresh MR, Sunwoo HH (2011a) Overview of plant-derived vaccine antigens: dengue virus. J. Pharm. Pharm. Sci. 14: 400–413.

[47]. Malabadi RB, Vijayakumar S, Mulgund GS, Nataraja K (2011b) Induction of somatic embryogenesis in papaya (*Carica papaya*). Research in Biotechnology. 2(5):40-55.

[48]. Malabadi RB, Chalannavar RK, Meti NT, Mulgund GS, Nataraja K, Vijayakumar S (2012a) Synthesis of antimicrobial silver nanoparticles by callus cultures and *in vitro* derived plants of *Catharanthus roseus*. Research in Pharmacy. 2(6);18-31.

[49]. Malabadi RB, Meti NT, Mulgund GS, Nataraja K, Vijayakumar S (2012b) Synthesis of silver nanoparticles from *in vitro* derived plants and callus cultures of *Costus speciosus* (Koen.); Assessment of antibacterial activity. Research in Plant Biology. 2(4):32-42.

[50]. Malabadi RB, Mulgund GS, Meti NT, Nataraja K, Vijayakumar S (2012c) Antibacterial activity of silver nanoparticles synthesized by using whole plant extracts of *Clitoria ternatea*. Research in Pharmacy. 2(4):10-21.

[51]. Malabadi RB, Lokare-Naik S, Meti NT, Mulgund GS, Nataraja K, Vijayakumar S (2012d) Synthesis of silver nanoparticles from *in vitro* derived plants and callus cultures of *Clitoria ternatea*; Evaluation of antimicrobial activity. Research in Biotechnology. 3(5): 26- 38.

[52]. **Malabadi RB,** Chalannavar RK, Sowmyashree K, Supriya S, Nityasree BR, Gleiser RM, Meti NT, Vijayakumar S, Mulgund GS, Gani RS, Nasalapure A, Chougale R, Masti S, Chougale A, Divakar MS, Kasai D, Odhav B, Baijnath H (2016a) Ebola virus: Updates on plant made vaccine development. International Journal of Research and Scientific Innovations. 3(6):4-12.

[53]. Malabadi RB, Chalannavar RK, Meti NT, Gani RS, Vijayakumar S, Mulgund GS, Masti S, Chougale R, Odhav B, Sowmyashree K, Supriya S, Nityasree BR, Divakar MS (2016c) Insulin plant, *Costus speciosus*: Ethnobotany and pharmacological updates. Int.J. Curr. Res. Biosci. Plant Biol. 3(7): 151-161.

[54]. Malabadi RB, Chalannavar RK, Meti NT, Vijayakumar S, Mulgund GS, Gani RS, Supriya S, Sowmyashree K, Nityasree BR, Chougale A, Divakar MS (2016d) Antidiabetic Plant, *Gymnema sylvestre* R. Br., (Madhunashini): Ethnobotany, phytochemistry and pharmacological updates. International Journal of Current Trends in Pharmacobiology and Medical Sciences. **1**(4): 1-17.

[55]. **Malabadi RB**, Chalannavar RK, Supriya S, Nityasree BR, Sowmyashree K, Mulgund GS, Meti NT (2017a) **Dengue** virus disease: Recent updates on vaccine development. International Journal of Research and Scientific Innovations. 4(7):08-29.

[56]. **Malabadi RB**, Chalannavar RK, Supriya S, Nityasree BR, Sowmyashree K, Mulgund GS, Meti NT (2017b) Dengue virus disease: Current updates on the use of *Carica papaya* leaf extract as a potential herbal medicine. International Journal of Research and Scientific Innovations. 4(8):36-50.

[57]. **Malabadi RB,** Chalannavar RK, Supriya S, Nityasree BR, Sowmyashree K, Meti NT (2018) Role of botanical drugs in controlling dengue virus disease. International Journal of Research and Scientific Innovations. 5(7): 134-159.

[58]. Mediouni S et al., (2020) Oregano oil and its principal component carvacrol inhibit HIV-1 fusion into target cells. J Virol. (https ://doi. org/10.1128/jvi.00147 -20).

[59]. Moradkhani H, Sargsyan E, Bibak H, Naseri B, Sadat-Hosseini M, Fayazi-Barjin A, Meftahizade H. (2010) *Melisa officinalis* L., a valuable medicinal plant: A review. Journal of Medicinal Plants Research. 4: 2753-2759.

[60]. Minami M, Kita M, Nakaya T, Yamamoto T, Kuriyama H, Imanishi J (2003) The inhibitory effect of essential oils on herpes simplex virus type-1 replication in vitro. Microbiol Immunol. 47(9):681-4. (doi: 10.1111/j.1348-0421.2003.tb03431.x.).

[61]. Nadjib BM (2020) Effective antiviral activity of essential oils and their characteristic terpenes against coronaviruses: An update. J Pharmacol Clin Toxicol. 8(1):1138.

[62]. Nurzyńska-Wierdaka R, Bogucka-Kockab A, Szymczakc G (2014) Volatile constituents of *Melissa officinalis* leaves determined by plant age. Natural Product Communications. 9 (5): 703-706.

[63]. Ozarowski M, Mikolajczak PL, Piasecka A et al., (2016) Influence of the *Melissa officinalis* leaf extract on long-term memory in scopolamine animal model with assessment of mechanism of action. Evidence-Based Complementary and Alternative Medicine. 2016: 17 Article ID 9729818. (http://dx.doi.org/10.1155/2016/9729818).

[64]. Patel VJ, Biswas Roy S, Mehta HJ, Joo M, Sadikot RT (2018) Alternative and natural therapies for acute lung injury and acute respiratory distress syndrome. Biomed Res Int. 2476824. (https :// doi.org/10.1155/2018/24768 24).

[65]. Patne T, Mahore J, Tokmurke P (2020) Inhalation of essential oils: Could be adjuvant therapeutic strategy for covid-19. International J. Pharmaceutical Sciences and Research. 11(9): 4095-4103.

[66]. Ramanoelina P, Gaydou EM, Rasoarahona J (2006) Chemical composition of *Ravensara aromatica* Sonn. leaf essential oils from Madagascar. Journal of Essential Oil Research. 18(2): 215-17.

[67]. Reddy PV, Kandisa RV, Varsha PV, Satyam S (2014) Review on *Thymus vulgaris* traditional uses and pharmacological properties. Med. Aromat Plants. 3(3):1-3. (DOI: 10.4172/2167-0412.1000164).

[68]. Roviello V, Roviello GN (2021) Lower COVID‐19 mortality in Italian forested areas suggests immunoprotection by Mediterranean plants. Environmental Chemistry Letters. 19:699–710.

[69]. Sample, Ian (19 April 2021). "What do we know about the Indian coronavirus variant?". *The Guardian*. London. Retrieved 20 April 2021.

[70]. Schnitzler P, Astani A, Reichling J (2010) Antiviral effects of plant derived essential oils and pure oil components. Lipids Essent Oils Antimicrob Agents. (https ://doi.org/10.1002/97804 70976 623.ch10).

[71]. Senthil Kumar KJ, Gokila Vani M, Wang CS, Chen CC, Chen YC, Lu LP, Huang CH, Lai CS, Wang SY (2020) Geranium and Lemon essential oils and their active compounds downregulate angiotensin-converting enzyme 2 (ACE2), a SARS-CoV-2 spike receptor-binding domain, in epithelial cells. Plants. 9; 770. (doi:10.3390/plants9060770).

[72]. Sharafzadeh S, Khosh-Khui M, Javidnia K. (**2011**) Aroma profile of leaf and steam of lemon balm (*Melissa officinalis* L.) grown under greenhouse conditions. Advances in Environmental Biology. 5: 547-550.

[73]. Sharma AD, Kaur I (2020a) Jensenone from eucalyptus essential oil as a potential inhibitor of COVID 19 corona virus infection. Res Rev Biotech Biosci. 7:59–66.

[74]. Sharma AD, Kaur I (2020b) Eucalyptol (1,8 cineole) from eucalyptus essential oil a potential inhibitor of COVID 19 corona virus infection by molecular docking studies. Preprints: 2020030455.

[75]. Shereen MA, Khan S, Kazmi A, Bashir N, Siddique R (2020) COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. Journal of Advanced Research. 24 : 91–98.

[76]. Shin MD, Shukla S, Chung YH, Beiss V, Chan SK, Ortega-Rivera OA, Wirth DM, Chen A, Sack M, Pokorski JK, Steinmetz NF (2020) COVID-19 vaccine development and a potential nanomaterial path forward. Nature Nanotechnology. 15:646-655.

[77]. Silva J, Figueiredo P, Byler K, Setzer W (2020) Essential oils as antiviral agents. Potential of essential oils to treat SARS-CoV-2 infection: an in-silico investigation. Int J Mol Sci 21(10) :3426. (https ://doi. org/10.3390/ijms2 11034 26).

[78]. Swamy MK, Akhtar MS, Sinniah UR (2016) Antimicrobial Properties of Plant Essential Oils against Human Pathogens and Their Mode of Action: An Updated Review. Evidence-Based Complementary and Alternative Medicine. Article ID 3012462. 21 (http://dx.doi.org/10.1155/2016/3012462).

[79]. Syamasundar KV, Srinivasulu B, Stephen A, Ramesh S, Rao RR (2008) Chemical composition of volatile oil of *Thymus vulgaris* L. from Western Ghats of India. Journal of Spices and Aromatic Crops. 17 (3) : 255–258.

[80]. Tang X, Wu C, Li X, Song Y, Yao X, Wu X et al., (2020) On the origin and continuing evolution of SARS-CoV-2. Natl Sci Rev. (https ://doi.org/10.1093/nsr/ nwaa0 36).

[81]. Teixeira B, Marques A, Ramos C et al., (2013) "Chemical composition and antibacterial and antioxidant properties of commercial. Evidence-Based Complementary and Alternative Medicine 17 essential oils." Industrial Crops and Products. 43(1): 587–595.

[82]. The Australian Tea Tree Industry Association (ATTIA Ltd)- Fact sheet - Tea Tree Oil Antiviral Properties-17th May 2020; Tea Tree Oil and the SARS-CoV-2 coronavirus pandemic. ABN 48 077 019 204. PO Box 903, Casino NSW 2470, Australia. 1-4.

[83]. Thuy BTP et al., (2020) Investigation into SARS-CoV-2 resistance of compounds in garlic essential oil. ACS Omega. 5:8312–8320. (https ://doi.org/10.1021/acsom ega.0c007 72).

[84]. Tshibangu DST, Matondo A, Lengbiye EM et al., (2020) Possible effect of aromatic plants and essential oils against COVID-19: Review of their antiviral activity. Journal of Complementary and Alternative Medical. 11(1): 10-22. (JOCAMR.60656. ISSN: 2456-6276).

[85]. Usachev EV, Pyankov OV, Usacheva OV, Agranovski IE (2013) Antiviral activity of tea tree and eucalyptus oil aerosol and vapour. J Aerosol Sci 59:22–30. (https ://doi.org/10.1016/j.jaero sci.2013.01.004).

[86]. Valussi M, Donelli D, Firenzuoli F, Antonelli M (2021) Bergamot Oil: Botany, Production, Pharmacology. Encyclopedia. 1: 152–176. (https://doi.org/10.3390/encyclopedia1010016).

[87]. Verma PPS, Singh A, Laiq-ur-Rahaman, Bahl JR (2015) Lemon balm (*Melissa officinalis*.L.,), An herbal medicinal plant with broad therapeutic uses and cultivation practices: A review. International Journal of Recent Advances in Multidisciplinary Research. 02 (11): 0928-0933.

[88]. Vimalanathan S, Hudson J (2014) Anti-influenza virus activity of essential oils and vapors. Am J Essent Oils Nat Prod. 2:47–53.

[89]. V'kovski P, Kratzel A, Steiner S, Stalder H, Thie V (2020) Coronavirus biology and replication: Implications for SARS-CoV-2. Nature Reviews Microbiology. 1-16. (https://doi.org/10.1038/ s41579-020-00468-6).

[90]. Wang C, Horby PW, Hayden FG, Gao GFA (2020) Novel coronavirus outbreak of global health concern. Lancet. 395: 470–473.

[91]. Wink M (2020) Potential of DNA intercalating alkaloids and other plant secondary metabolites against SARS-CoV-2 causing COVID-19. Diversity. 12:175.

[92]. Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, Hu Y, Tao ZW, Tian JH, Pei YY, Yuan ML, Zhang YL, Dai FH, Liu Y, Wang QM, Zheng JJ, Xu L, Holmes EC, Zhang YZ (2020a) A new coronavirus associated with human respiratory disease in China. Nature. 579 (7798): 265-269.

[93]. Wu YQ, Zou L, Yu X, Sun D, Li SB, Tang L, Yang JR, Chen XY, Wu YG, Fang H (2020b) Clinical effects of integrated traditional Chinese and western medicine on COVID-19: A systematic review. Shanghai J. Tradit. Chin. Med. 1–8.

[94]. Xu X, Chen P, Wang J, Feng J, Zhou H, Li X et al., (2020) Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission. Sci China Life Sci. 1–4.

[95]. Yang (2021) Application of nanotechnology in the COVID-19 pandemic. International Journal of Nanomedicine. 6 :623–649.

[96]. Zhang D, Zhang B, Lv JT, Sa RN, Zhang XM, Lin ZJ (2020a) The clinical benefits of Chinese patent medicines against COVID-19 based on current evidence. Pharmacol. Res. 157:104882. (doi: 10.1016/j.phrs.2020.104882).

[97]. Zhang E, Du RH, Li B, Zheng XS, Yang XL, Hu B, Wang YY, Xiao GF, Yan B, Shi ZL, Zhou P (2020b) Molecular and serological investigation of 2019-nCoV infected patients: Implication of multiple shedding routes. Emerging Microbes and Infections. 9: 386-89.

[98]. Zhang R, Lib Y, Zhangc AL, Wangd Y, Molinae MJ (2020c) Identifying airborne transmission as the dominant route for the spread of COVID-19. Proc. Natl. Acad. Sci. USA. 117(26): 14857–14863.

[99]. Zheng N, Xiaa R, Yang C, Yin B, Li Y, Duan C, Liang L, Guo H, Xie Q (2009) Boosted expression of the SARS-CoV nucleocapsid protein in tobacco and its immunogenicity in mice. Vaccine. 27: 5001–5007.

[100]. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W et al., (2020a) Discovery of a novel coronavirus associated with the recent pneumonia outbreak in humans and its potential bat origin. Nature. 579: 270–273. (doi: 10.1038/s41586-020-2012-7).

[101]. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W et al., (2020b) A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 579: 270–273.

[102]. Zhu N, Zhang D, Wang W et al., (2020) China novel coronavirus investigation research team. A novel coronavirus from patients with pneumonia in China 2019. N Engl J Med. 382:727-33.