



# Antiviral perspectives of economically important Indian medicinal plants and spices

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## Abstract

Human respiratory diseases caused by viral infections leads to morbidity. Among infectious diseases, viral infections associated with the respiratory tract remain the primary reason for global deaths due to their transmissibility. Since immemorial, traditional Indian medicinal plants, their extracts, and several phytochemicals can treat various diseases. Sources for this review paper are data derived from a peer-reviewed journal that emphasizes the economic importance of medicinal plants. Several plant-based medicines have been reported to be effective against multiple viral infections, including the Human Adenovirus, Enterovirus, Influenza virus, Hepatitis virus, etc. This review emphasizes use of the Indian medicinal plants like as *Withania somnifera* (Ashwagandha, Winter Cherry), *Moringa oleifera* (Drumstick), *Ocimum tenuiflorum* (Tulsi), *Azadirachta indica* (Neem), *Curcuma longa* (Turmeric), *Terminalia chebula* (Chebulic Myrobalan), *Punica granatum* (Pomegranate) and the Indian household spices (ginger, garlic and black pepper). It further describes their secondary phytoconstituents extraction procedure, mode of action and the potential application to improve clinical outcomes of neutraceuticals against various viral infections.

**Keywords** Antiviral Mechanism · Medicinal Plants · Viral infections · Spices · Phytochemicals

## Introduction

Medicinal plants have been used in ancient civilizations to treat different diseases. People have preferred natural remedies even as mainstream medication's cost and adverse effects have escalated. The World Health Organization (WHO) stated that 80% of the world population has started relying on medicinal plants for their primary health care. Due to their low cost and easy availability, phytochemicals are increasingly important in developing new medication candidates (Mukherjee, 2019; Nazeam et al., 2020). Numerous studies have explored antiviral, antioxidant, anti-inflammatory, and anti-cancer activities of various classes of phytochemicals extracted from these medicinal plants. Recent findings have demonstrated that plant-derived medications can fight virus strains resistant to standard antiviral drugs

and hence, there is an urgent need to explore such novel natural antiviral medicines.

Viruses are tiny intracellular parasites with either RNA or DNA as their core genetic material and are proteinaceous capsids. The small RNA genome size encodes capsid structural proteins and other viral replication proteins. Some viruses have a lipid envelope that consists of a lipid bilayer from the host cell (Forouharshad and Ajallouei, 2021). Viruses can infect a wide range of organisms and cause widespread of diseases in humans. Furthermore, the high contagiousness of viral diseases causes epidemics and pandemics in developed countries (Zhou et al., 2020). This conveys the need for developing efficient and economical antiviral drugs.

Previous literatures have demonstrated that natural antiviral agents found in herbal remedies exhibit antiviral action through many mechanisms like inhibiting viral entrance, replication, and the building of surface cell receptors for specific virus-host infections. Specific bioactive constituents of various medicinal plants like *Heracleum maximum Bartr.*, Secomet-V extracted from *Trifolium* species (Kotwal et al., 2005), *Pandanus*

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*amaryllifolius Roxb* exhibited antiviral activity against numerous human viruses like influenza, human immunodeficiency virus (HIV), Hepatitis B Virus (HBV), Human Corona Virus (HCV), and Human Papillomavirus (HPV) (Thabti et al., 2020). Pandanin was extracted from the leaves of *Pandanus amaryllifolius Roxb*. Plant-derived chemicals such tannins, alkaloids, and flavones exhibit antiviral action in vitro (Ooi et al., 2004). Although, the low water solubility and poor bioavailability of these active components remain an important concern.

This review mainly deals with a variety of medicinal plants found predominantly in South-Asian regions like *Terminalia chebula*, *Ocimum sanctum* (Panchal and Parvez, 2019), *Withania somnifera*, *Moringa oleifera*, *Azadirachta indica*, *Zingiber officinale* (Zadeh and Kor, 2014), *Allium sativum*, *Piper nigrum* (Gorgani et al., 2017), *Curcuma longa* and *Punica granatum*, their classification (summarized in Table 1), geographical distribution, extraction protocols for their specific phytoconstituents and antiviral activity of these particular phytoconstituents (Pandit, 2020;

**Table 1** A summary of classification of the medicinal plants discussed in this review

Sl. N	Kingdom	Phylum	Subphylum	Class	Order	Family	Species & Common name	References
1	Plantae	Tracheophyta	Magnoliopsida	Eudicotyledon	Myrtales	Combretaceae	<i>Terminalia chebula</i> (Chebulic Myrobalan)	Shaikh et al. (2016), Chang et al. (2019), Ekambaram et al. (2020)
2	Plantae	Tracheophyta	Angiospermae	Eudicotyledon	Lamiales	Lamiaceae	<i>Ocimum sanctum</i> (Tulsi)	Panchal and Parvez (2019), Cohen (2014), Mohapatra et al. (2020)
3	Plantae	Tracheophyta	Angiospermae	Dicotyledons	Tubiflorae	Solanaceae	<i>Withania somnifera</i> (Ginseng)	Wadhwa et al. (2017a), Lopresti et al. (2019), Rawat and Bisht (2014), Kaul et al. (2016)
4	Plantae	Tracheophyta	Angiospermae	Rosids	Brassicales	Moringaceae	<i>Moringa Oleifera</i> (Drumstick)	Onyishi et al. (2015) Kurokawa et al. (2016)
5	Plantae	Spermatophyta	Angiospermae	Dicotyledonae	Rutales	Meliaceae	<i>Azadirachta indica</i> (Neem)	Singh et al. (2016), Alzohairy (2016), Atawodi and Atawodi (2009)
6	Plantae	Spermatophyta	Angiospermae	Liliopsida	Zingiberales	Zingiberaceae	<i>Zingiber officinale</i> (Ginger)	Gamage et al. (2020), Mao et al. (2019), (Liu et al. (2019)
7	Plantae	Tracheophyta	Magnoliophyta	Liliopsida	Liliales	Liliaceae	<i>Allium sativum</i> L. (Garlic)	Batiha et al. (2020), Donma and Donma (2020)
8	Plantae	Spermatophyta	Magnoliophyta	Magnoliopsida	Piperales	Piperaceae	<i>Piper nigrum</i> L. (Black Pepper)	Donma and Donma (2020), Nag and Chowdhury (2020), Gorgani et al. (2017)
9	Plantae	Spermatophyta	Angiospermae	Monocotyledonae	Zingiberales	Zingiberaceae	<i>Curcuma longa</i> (Turmeric)	Amalraj et al. (2017), Carolina Alves et al. (2019), Chao et al. (2018), Paulucci et al. (2013)
10	Plantae	Spermatophyta	Angiospermae	Monocotyledonae	Myrtales	Punicaceae	<i>Punica granatum</i> (Pomegranate)	Moradi et al. (2019), Howell and D'Souza (2013), Lansky and Newman (2007)



Tungmunnithum et al., 2018; Zitterl-Eglseer and Marschik, 2020).

## Mechanism of virus entry into the host cell

### Antiviral mechanism of action

#### Attachment of virus to cell receptors to initiate a signaling cascade

Viruses multiply when they bind to their receptor molecules. Similarly, it suppresses Zika and Chikungunya virus by binding to the cell surface (Mounce et al., 2017). Phytochemicals can stop viruses including poxvirus, flavivirus, herpesvirus, and orthomyxovirus from spreading (Chen et al., 2013).

### Virus replication

Retroviruses require RNA as their genetic material; therefore, RNA polymerases like RNA-dependent RNA polymerase (RdRp) duplicate the viral genome. Viruses multiply by inhibiting or starting helpful host biological processes. A transcriptional transactivator (Tat) that targets the reduction in helper T-cells is required to combat the Human Immunodeficiency Virus (HIV) (Vajragupta et al., 2005).

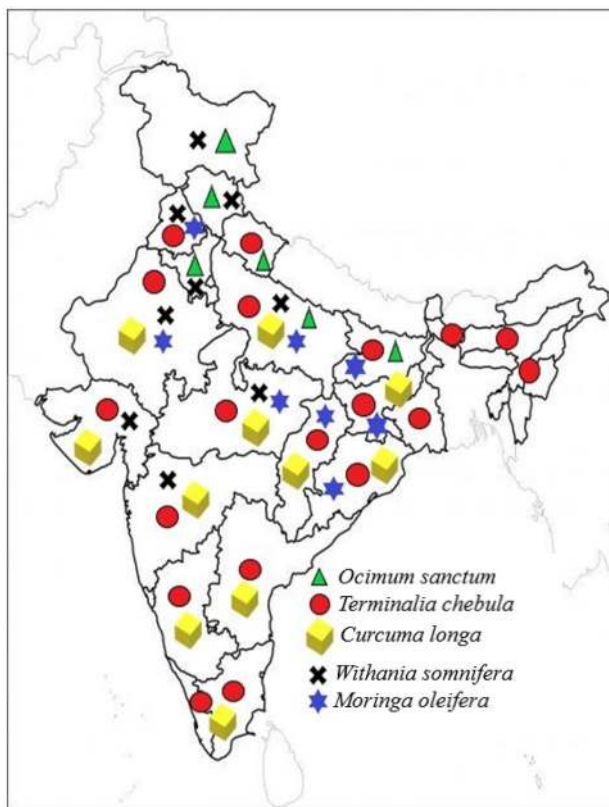
#### Phytochemicals suppress intercellular signaling cascades for downregulation of viral replication

Virion particles damage the host cell after integrating into the host genome. Activation of the NF- $\kappa$ B, PI3K/Akt, MAPK, and Ubiquitin Protease System (UPS) signaling pathways allows viruses to enter cells and replicate. Phytochemicals fight viruses by altering cellular signaling pathways (Kumar et al., 2018).

**Attention to signaling pathways** In addition to translation, Akt regulates apoptosis, autophagy, RNA splicing, and autophagy activity (Diehl and Schaal, 2013).

**Transcription of cellular components** Transcription and translation convey genetic information from generation to generation. Non-enveloped viruses require cellular transcription co-activators to express their genes (Ding, 2010).

**Post-translation modifications** After translational changes, dicer detects viral RNA and silences it. To decreased viral gene expression, it cleaves and clears foreign double-stranded RNA before delivering it into the host organisms RNAi pathway (Asikainen et al., 2008; Näär et al., 2001). The phytochemical action suppresses viral replication, causing illness in the host (Fig. 1).



**Fig. 1** Geographical distribution of medicinal plants in India. The data has been collected from various sources: (Cohen, 2014; Panchal and Parvez, 2019; Treml et al., 2020; Amalraj et al., 2017; Narinderpal et al., 2013; Kurokawa et al., 2016)

## Medicinal plants

### *Terminalia chebula* (Chebulic Myrobalan)

The plant is extensively grown in South East Asian countries like India, Sri Lanka, Bhutan, Nepal, Bangladesh, Cambodia, Myanmar, Vietnam, Indonesia, Philippines, Egypt, Thailand, etc. In India, it is found extensively in tropical deciduous forests and moist areas and distributed at an altitude of 1500 m high in the Himalayas, Sub-Himalayan areas ranging from West Bengal to North-East states, South India. The flowers appear from April–August, fruits start growing between November to March. Seeds are fallen off starting in January and can be stored for medicinal uses (Shaikh et al., 2015; Treml et al., 2020).

### Ethnomedicinal use of *Terminalia chebula*

*Terminalia chebula* (*T. chebula*), a traditional medicine, belongs to the genus *Terminalia*, the family Combretaceae. Its common name is Chebulic Myrobalan, Haritaki (Hindi), Manahi (Manipuri). *T. chebula* is widely grown in

the North-eastern regions of India and extends to the Indo-Burma region, also found in tropical areas like Andhra Pradesh, Karnataka, Kerala. *T. chebula* Retz. (Fam. Combretaceae), is considered as the ‘King of Medicine’ in Tibet because of its extraordinary healing power during treatment (Chang et al., 2019; Pouységu et al., 2011; Rathinamoorthy and Thilagavathi, n.d.). The whole plant, i.e., leaves, roots, and fruits, has several medicinal properties due to active phytochemicals. *T. chebula* is a deciduous tree ranging from medium to large-sized; at the height of 15–30 m, trunk, 1 m in diameter leaves are opposite and alternating, with big glands on the petiole. A petiole of 1–3 cm extends 8–10 cm from the base of the leaf. Drupes (fruits) are wrinkled, 3–5 cm long, ellipsoidal or ovoid forms, yellow to brown—yellowish flowers with terminal spikes and firm seeds. *T. chebula* is one of the main constituents present in ‘Triphala.’ Fruits, leaves, barks of *T. chebula* have various potentials to treat ailments (Hussell and Bell, 2014). Phytoconstituents include polyphenols, tannins, anthocyanins, flavonoids, alkaloids, and glycosides. For example, they can help heal wounds and fight cancer. They can also help protect the brain from damage caused by viruses and bacteria. *T. chebula* has a lot of hydrolyzable tannins (Chang et al., 2019). Tannins are polyphenols with two or more slightly different phenol rings. In addition to their astringent taste, they can limit digestive enzymes and nutrient absorption. These include blood pressure management, immunological response defensive mechanisms, anti-inflammatory, antioxidants, and antibacterial activities (Priya et al., 2019). They can chelate metal ions like Fe, i.e., antioxidant synergists, due to primary metabolite activities. Tannins exhibit antioxidant, anti-inflammatory, antimicrobial activities, etc. Studies have shown that flavonoids like quercetin exert an anti-inflammatory effect by inhibiting nuclear transcription factor-kappa- B (NF-κB) mediated pro-inflammatory molecules like cytokines, cyclooxygenase, nitric oxide to trigger immunological responses (Alamgeer et al., 2020; Shibata et al., 2014). Moreover, excessive ROS generation by macrophages destroyed genetic material, lipids, proteins, and lipoproteins (Riaz et al., 2017).

#### Anti-viral activity of Chebulic Myrobalan

*T. chebula* has phytochemicals such as chebulagic acid, chebulinic acid, glycosides, tannins, resins, flavonoids, triterpenoids, and steroids. They exhibit antibacterial, anti-viral, anti-inflammatory, hepatoprotective, anticarcinogenic, cardioprotective properties. *T. chebula* possessed an excellent antiviral activity against the cytomegalovirus. The aqueous water extract of the plant inhibits the plaque formation of human cytomegalovirus (HCMV). According to reports, cyclosporine-treated mice had a lower lung tissue count than those treated with aqueous plant extracts (Yukawa et al.,

1996). *T. chebula* extracts coupled with acyclovir have anti-HSV-1 action (Fig. 3) (Kesharwani et al., 2017). Chebulagic acid and chebulinic acid are potent novel inhibitors of viral replication that target the neuraminidase glycoprotein. It outperformed oseltamivir and zanamivir for treatment and preventing influenza (Air, 2012; Li et al., 2020). The acetone extract of *T. chebula* Retz showed an antiviral effect by restricting the multiplication against swine influenza virus A (Dhanani et al., 2017). Herpes Simplex Virus (HSV-1 and HSV-2) are double-stranded DNA viruses that cause orofacial and genital herpes with a significant risk of HIV infection through sexual interaction. HSV-2 is a sexually transmitted virus that infects over 500 million individuals annually. Getting rid of HPV and keeping it from spreading to mucosal surfaces via the peripheral nerve systems is difficult due to its intracellular infection in neural ganglia.

Chelulagic acid, chebulinic acid, and punicalagin are antiviral compounds in ethanolic extracts. Secondary metabolites inhibited adhesion, replication, penetration, and dissemination of secondary infections thereby attacking viral glycoproteins that connects to host cell receptors (Kesharwani et al., 2017). In vitro trials for COVID-19 treatment had showed tannic acid (gallotannin), the primary ingredient in *T. chebula*, aided in the proteolytic cleavage of the 3CL Protease (3-chymotrypsin-like protease) (Chang et al., 2019; Joshi et al., 2020; Rathinamoorthy and Thilagavathi, n.d.) (Table 3).

#### Other biological applications

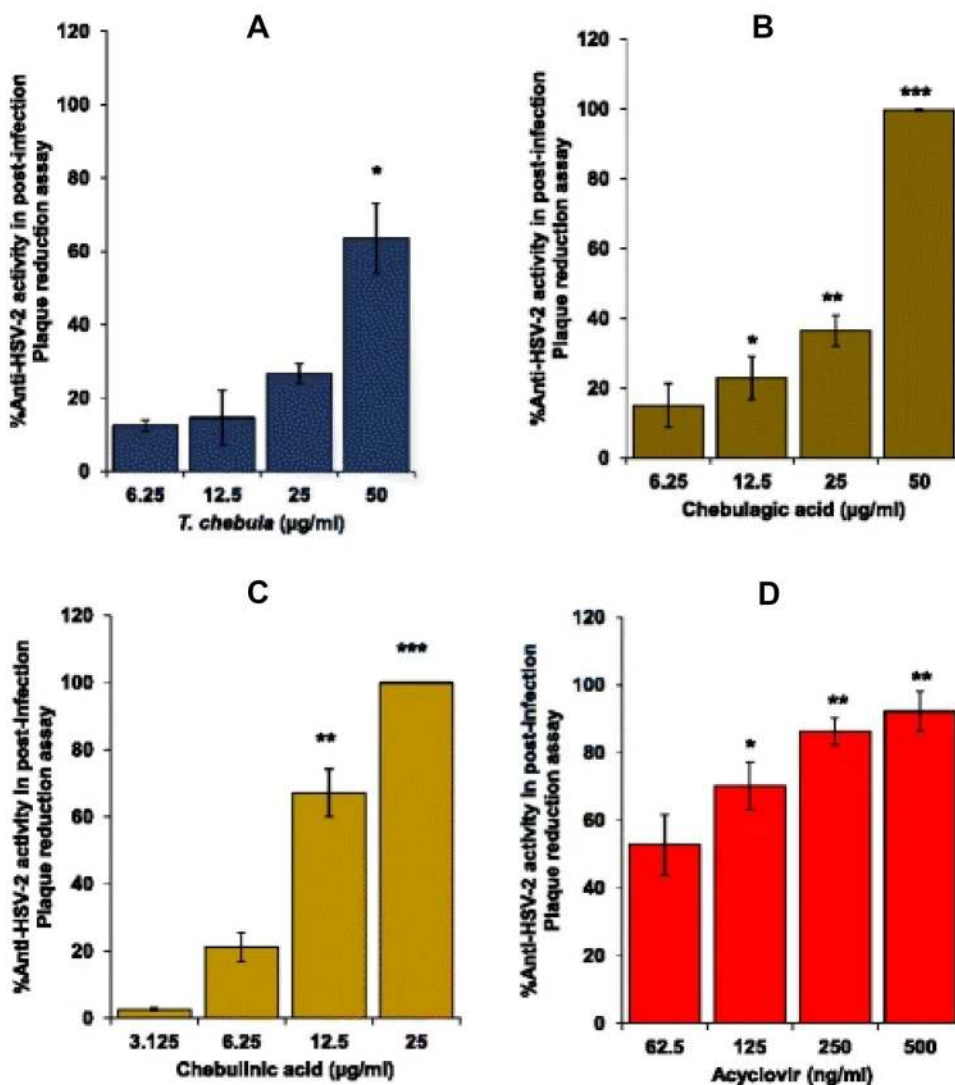
Tannin molecules are employed to detect mutagens. The oxygen-free radicals that cause cancer and mutagens interact with macromolecules. Tannins have anti-carcinogenic and anti-mutagenic effects that protect cells from oxidative stress. They have the tendency to block superoxide radicals formation, providing antioxidant capabilities and protection against cellular damage (Lin et al., 2013). Tannins were used for antiarthritic efficacy studies as it suppressed proinflammatory cytokines, biochemical markers that bone destruction, synovial inflammation in histopathological studies. Studies had shown that it possessed anticancer activities leading to apoptosis, autophagy, reactive oxygen species production. Reddy et al. showed anti-proliferative activity against HCT-15, K562, COLO-205 (Chang et al., 2019; Priya et al., 2018; Reddy et al., 2009) (Fig. 2).

#### *Ocimum sanctum* (Tulsi)

*Ocimum sanctum* is an annual decorative herb. It is a member of the Lamiaceae family, one of the most prominent families in the Plant Kingdom. Tulsi plant species have been discovered throughout Asia, Africa, Malaysia, South and North America. The plant can be found from the



**Fig. 2** Anti-HSV-2 activity of various components of *T. chebula* extract compared to acyclovir using plaque reduction assay. Vero cells growing as monolayer in 24-well culture plate were infected with HSV-2 (100 PFU/well) followed by 1% low melting point agarose overlay medium containing varying concentration of the 50% ethanolic extract of *T. chebula*, chebulagic acid, chebulinic acid and acyclovir. After 48 h incubation, plates were processed to assess the number of plaques. Reproduced with permission from (Kesharwani et al., 2017)



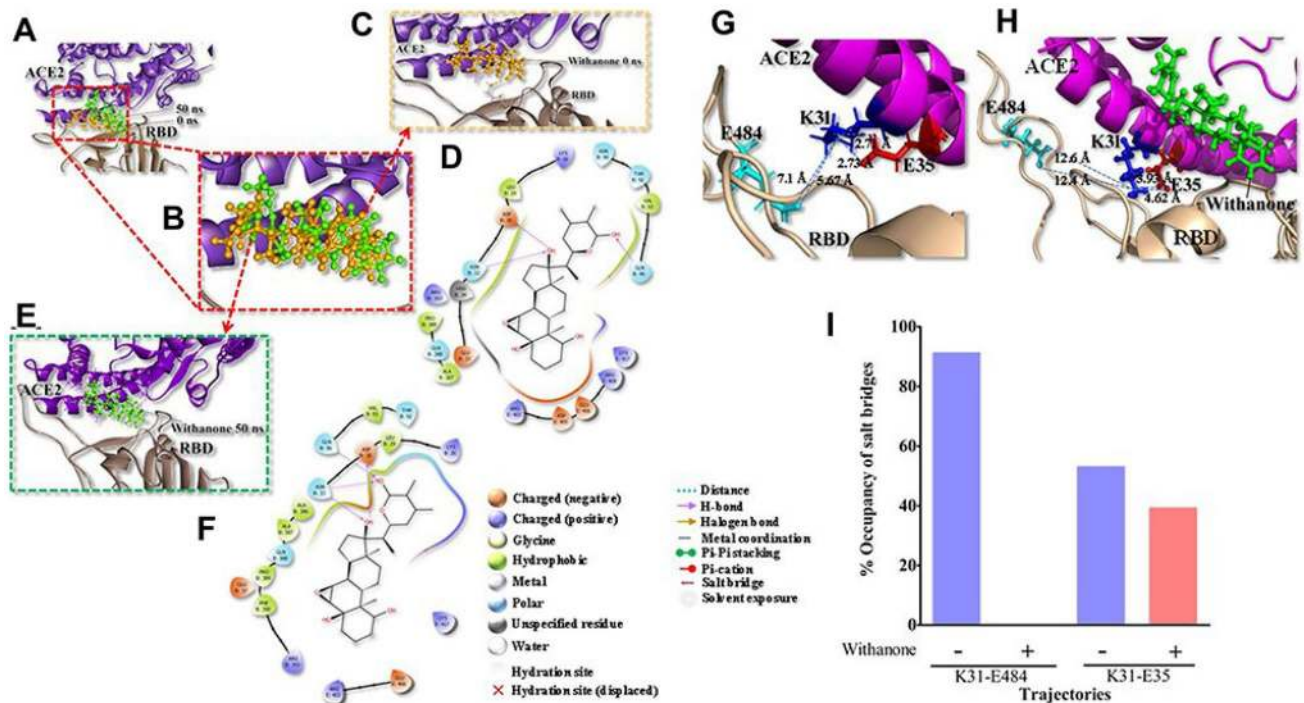
Andaman and Nicobar Islands to the Himalayas at up to 1800 m. This scented shrub grows 30–60 cm tall with green or purple leaves clustered on the opposing branch. The aromatic plant's stems are hairy, simple, broad, oblong, or acute leaves with whole, subserrate, or dentate edges. The whitish fruits are tiny. The fruits are small and yellowish. Flowers are purplish, with a hairy tube and rarely long branched. It is a tropical and subtropical edible perineal plant (Cohen, 2014; Panchal and Parvez, 2019).

#### Ethnomedicinal use of *Ocimum sanctum*

*Ocimum sanctum* (*Ocimum tenuiflorum*), also known as Tulsi is considered as the 'Queen of herbs' used in medicinal and religious purposes as a sacred plant according to Hindu spiritual rituals. It is a perineal plant used in Ayurveda and Unani medicine systems to serve holistic health and heal different diseases. It comes in two varieties: black

tulsi (Krishna Tulsi) and green tulsi (Rama Tulsi) (Cohen, 2014). Herbal remedy for stress alleviation, stomach ulcers, inflammation, cardiovascular disease prevention, and anti-allergens. Other substances found in *Ocimum* plants include phenolic acids, flavones, saponins, alkaloids, and tannins. Essential oils, oleoresin, and balsam are volatile compounds found in woods, bark, stems, leaves, flowers, and fruits of aromatic plants (Labra et al., 2004). Due to the scent expressing its essence and the activity of the active bioactive molecule, essential oils were suited for a variety of uses in cosmetic items such as fragrances and pain relief balms (Panchal and Parvez, 2019). Tulsi's active phytochemicals have antioxidant, anti-cancer, anti-inflammatory, anti-viral, anti-microbial, and neuroprotective effects. Tulsi usage benefits the immune system, nervous system, gastrointestinal tract, reproductive diseases, renal system, and blood circulation. Plants with aromatic or astringent properties are employed in agriculture as pesticides, herbicides, and





**Fig. 3** Withanone docks at the interface of the ACE2-RBD complex and shifts slightly towards the center of the interface, modulating several molecular interactions in the process. Reproduced with permission from (Balkrishna et al., 2021)

nutrient supplements for plant growth. Its nutritional value includes minerals (zinc, iron), vitamins A and C, chlorophyll, and other phytonutrients (Bano et al., 2017; Verma et al., 2019).

**Anti-viral activity of Tulsi**

The new Coronavirus (CoV) has a genomic core encased in a protein spike envelope. CoV infection causes respiratory and gastrointestinal issues (Kumar, 2020; Mohapatra et al., 2020). According to research, the plant’s aerial aqueous-alcoholic extract contains flavonoids and polyphenolic groups. Blocks ACE II receptors in the nasopharynx, preventing CoV replication. Structured substances such as luteolin-7-O-glucuronide and chlorogenic acid bind covalently to the viral enzyme’s active residue Cys145 and irreversibly suppress its action (Fig. 3) (Mohapatra et al., 2020). In silico studies show tulsi consists methyl eugenol, oleanolic acid, and ursolic acid have high receptor-acceptor binding efficiency against viral attachment spike glycoprotein and RNA dependent RNA polymerase for reproduction. According to research, these compounds bind to SARS-CoV-2 protease more effectively than Lopinavir/Ritonavir and Remdesivir to impede attachment and replication (Kumar, 2020). Triterpenoids like ursolic acid, flavonoids like apigenin, and monoterpenes like linalool, myrcene, and carvone have anti-viral activity. In bronchitis, they prevent DNA replication

and disseminated lung infection. Essential oils like eugenol, as well as *O. sanctum* extracts, have anti-viral efficacy against viruses like IHNV, poliovirus type 3, herpes virus, HBV and New Castle Disease Virus (Bhuiyan et al., 2020). HSV1 can cause encephalitis and meningitis by establishing latency in the sensory neurons ganglion area of the CNS. GMK (African Green Monkey) cells were cocultured with viruses (HSV-1 strain F and HSV-2 strain G) to show the antiviral activity of *O. sanctum* (dichloromethane and methanol extracts). Terpenoids and polyphenols (catechins) blocked hyaluronic acid (HA) protein binding, preventing H9N2 virus entered into cells. It shows virucidal, therapeutic, and prophylactic activities *in ovo* model system (Ghoke et al., 2018). Combined with acyclovir, apigenin has potent antiviral activity against (HSV-1 and HSV-2). Myricetin and scutellarein bind to the SARS-CoV helicase, preventing virus replication (Lin et al., 2014). Scutellarein is an RNA-dependent RNA polymerase polymerization activator that recruits the RNA enzyme for viral replication. Thus, tulsi’s active phytochemicals can be employed to enhance the immune system and fight viral infections (Pandit, 2020) (Table 3).

**Other biological applications**

Tulsi is a potent medicinal herb that supports a holistic, healthy living. The ingredients obtained from



various extracts had been used widely in cosmetics for many years (Bhuiyan et al., 2020; Verma et al., 2019). The extracts showed antibacterial, antimicrobial, anti-cancer, and anti-inflammatory activities (Cohen, 2014; Panchal and Parvez, 2019). Tulsi pastes has shown anti-bacterial activities to treat ringworms. Essential oils, including camphor, eucalyptol, and eugenol, work well against resistant bacterial and fungus strains (Yamani et al., 2016). Tulsi with high eugenol content, inhibits the Nf-kB driven pathway, as well a COX-2 inhibitor.

### ***Withania somnifera* (Winter Cherry)**

*Withania somnifera* is widely grown in tropical and sub-tropical dry and semi-arid areas in Maharashtra's sub-tropical and temperate areas, Madhya Pradesh, Gujarat, Rajasthan, Punjab, Haryana, Telangana, and the Himalayan region above 1700 m.

#### **Ethnomedicinal use of *Withania somnifera***

*Withania somnifera* (Ashwagandha) of the family Solanaceae, also commonly known as “Indian Winter cherry” or “Indian ginseng”, has been used as a tonic for more than 3000 years (Narinderpal et al., 2013). Its traditional herbal preparation Rasayana is said to promote wealth and mental health. Anxiety, arthritis, impotence, amnesia, cancer, neurodegenerative diseases and cardiovascular diseases are all treated with plant extracts. Withanolides, a major component of *W. somnifera*, promote steroidal activity (Wadhwa et al., 2017b) to improve male characteristics such as sexual health, body mass, mental well-being, cognitive power, cardiovascular and metabolic activities, steroid hormones help increase testosterone and DHEA-S levels. Lesser amounts of these active ingredients are present in withanolides derived from steroid oxidation (Lopresti et al., 2019). The tuberous root is the main component used in medical extractions. External uses include healing wounds and treating burns, rashes, tumors, and other skin conditions (Alves et al., 2013; Rawat and Bisht, 2014).

#### **Anti-viral activity of winter cherry**

Triethyleneglycol (TEG) an active component of Ashwagandha, has shown antimicrobial potential for disinfection of virus (H1N1) & bacteria without causing any side effects. The newly identified COVID-19 interacted with the host cell's ACE2 via its spike protein's RBD. Molecular docking simulation revealed that Withanone could bind in the interface of the AEC2-RBD complex (Dhanani et al., 2017). Withanone reduced the electrostatic binding force of attraction of the ACE2-RBD complex. A decrease in electrostatic interactions between the ACE2-RBD complexes

blocks or weakens COVID-19 entry, the researchers concluded. The current HIV/AIDS treatment regimen includes two nucleoside analogs and one protease inhibitor. Due to its high cost, resistance, and non-availability, patients were prescribed Immu-25, a polyherbal formulation of *Tinospora cordifolia*, *W. somnifera*, and *O. sanctum*. It has immunopotentiating effects by increasing leukocyte count and T-cell differentiation. Drugs containing Immu-25 have boosted the immune system using immunocompromised nude mice and activate phagocytic development for the engulfment of damaged cells during viral infections (Usha et al., 2003). COVID-19 has emerged as the world's most pressing issue. The pandemic spawned the ideas of self-isolation, forced testing, quarantine, and treatment. A new human Coronavirus drug strain has been discovered. The virus's high mortality rate drives the development of antiviral drugs. A recent study used Ashwagandha molecular docking instead of a synthetic drug. Withanoside X and Quercetin glucoside from *W. somnifera* have excellent binding sites for proteins targeting the SARS-CoV-2 NSP15 endonuclease. Because of its immunomodulatory, antioxidant, and anti-inflammatory properties, it can be used as an alternative conventional drug in the treatment of Novel Coronavirus disease (Bano et al., 2017) (Table 3).

#### **Other biological applications**

*W. somnifera* known as winter cherry/ Indian ginseng has many other pharmacological studies. It is a good neurotransmitter and relevant for treating neurological disorders and a stress reliever that regenerates neurons and ganglia in a particular condition of Parkinson's, Huntington's, Alzheimer's diseases. For example, it blocks NF-kB transcription, which increases cytokines and other growth-promoting factors during inflammation, inhibits JAK/STAT signaling, which blocks anti-apoptotic, and proteasome-mediated degradation complex inhibition, which blocks apoptotic cell death (Wadhwa et al., 2017a). Because the plant has several active constituents, it is being cultivated for various pharmaceutical uses to increase biomass and produce high-quality products (Gulati and Singh, 2017). *Salmonella typhi*, *Escherichia coli*, *Pseudomonas aeruginosa*, and others have been shown to be susceptible to the leaf extract. Stems and roots, for example, are anti-cancer, anti-inflammatory, and neuroprotective. Secondary metabolites from the plant have been shown to inhibit cytokine production and apoptotic markers (Dhanani et al., 2017; Marslin et al., 2015; Wadhwa et al., 2017b) (Table 3).

### ***Moringa oleifera* (drumstick)**

*Moringa* is also known as “Mother's Best Friend” and “Miracle Tree”. For ages, for its enriched nutrient resources,



*Moringa* has been approved by the WHO as an alternate dietary food supplement to combat malnutrition. *Moringa* is a popular medicinal and nutritional plant in India. Its high tolerance for extreme weather is a rapidly spreading plant native to the southern Himalayan foothills.

**Ethnomedicinal use of *Moringa oleifera***

*Moringa oleifera* has been used as a folk medicine for millennia. *Moringa* contains amino acids, proteins, enzymes, and anti-inflammatory properties beneficial to nutrition and wound healing. Ancient cultures recognized moringa oil’s healing properties (Onyishi et al., 2015). In addition to unsaturated and essential fatty acids like linolenic acid, linoleic acid, and oleic acid, its leaves are high in micronutrients like calcium, potassium, iron, vitamin C, vitamin A, polyphenols, protein, and micronutrients like calcium, potassium, iron, vitamin C, and vitamin A. The majority of its phytochemical constituents were antimicrobial. Leaf extracts with phenolics and flavonoids are anti-herpetic (Kurokawa et al., 2016). Its roots have the property to reverse the chemotherapeutic-induced nephrotoxicity via antioxidant property (Chand et al., 2016). High-binding energy moringa constituents like kaempferol, pterygosperrin, morphine, and quercetin inhibited viral replication. These natural compounds could be investigated as COVID-19 prevention candidates (Shaji, 2020).

**Anti-viral activity of drumstick**

Beta-amyrin, a flavonoid in the aqueous extract, showed the anti-viral activity against HSV-1 and HSV-2 (Nasr-Eldin et al., 2018). Aqueous leaf extract had shown the anti-viral

effect by the reduction of HBV-C DNA (Feustel et al., 2017). Niazimini, a glycoside in the methanol extract, exhibited the inhibited properties of the *Epstein Barr* virus (Murakami et al., 1998). Chollom S. C has reported the extract of seeds showed the anti-viral properties against ND virus 100, 200, and 250 mg/ml *in ovo* assay (Chollom, 2012). Crude extract from *Moringa* leaves to possess significant anti-viral potential against the infectious bursal disease (IBD) virus (Chollom, 2012). 12-100 µg/ml of chloroformic extract inhibited Footmouth disease virus (FMDV) (Younus et al., 2015). Flavonoid quercetin had inhibited poliovirus replication by reducing the overexpression of pirin protein (Neznanov et al., 2008) (Table 3).

**Other applications**

*Moringa* leaf extracts inhibit *S. aureus* strains isolated from food and animal intestines. Nasr-Eldin et al. (Nasr-Eldin et al., 2018). *Moringa* leaf extracts have antimicrobial effects, and have been shown to inhibit the growth of *S. aureus* strains isolated from food and animal intestines (Khan et al., 2020). Seed extracts had the property of filtration, which removes the microbes and particulates (Potestà et al., 2020). Plant-based antioxidants with 1% seed extract can protect against heavy metal toxicity and oxidation. 2020 (Dilworth et al., 2020). In a recent study, methanolic extract of leaves triggered PC-3 prostate cancer cells by attacking main cellular molecules during Hedgehog signaling, resulting in inhibitory effects. Reduced mRNA expression of the GLI1 transcription factor and the SMO protein in the Hedgehog signaling pathway (Paula et al., 2017). The presence of terpenoids in the leaves extracts exhibited the

**Table 2** Activity of Phytochemical constituents present in *Moringa oleifera*

Part	Phytochemical	Activity	References
Leaves	Ethyl-(E)-2-undec-6-enoate (1),	Anti allergic	Abd Rani et al. (2019)
Leaves	Quercetin	Strong antioxidant	Lin et al. (2018)
Leaves	Kaempferol	Cancer-fighting properties	Singh et al. (2009)
Leaves	β-sitosterol-3-O-glucoside	Antimicrobial property	Abdel-Rahman Tahany et al. (2010)
Seed	Oleic acid	Potential to lower the serum cholesterol	Barbosa et al. (2019)
Seed	Glucomoringin	Inhibitory activity on beta-hexosaminidase and TNF-α release	Abd Rani et al. (2019)
Root	Stigmasterol	Production of milk by increasing estrogen level in mammary glands	Kumar et al. (2019)
Bark	Moringine	Antimicrobial property	Romeo et al. (2018)
Root	Benzyl Glucosinolate	Food additive	Chen et al. (2019)
Seeds	Moringyne	Micro nutrient	Shalini and Hn (2017)
Seeds	1-O-(4-hydroxymethylphenyl)-α-L-rhamnopyranoside	Hepatoprotective drug	Sun et al. (2019)





**Table 3** A summary of mechanism of anti-viral action of the common Indian medicinal plants

SN	Medicinal plants	Plant organs for extraction	Target virus/ Other uses	Bioactive constituents and their mechanism of action	References
1	<i>Terminalia chebula</i>	Fruits and Dry leaves extract	HSV-1 and HSV-2  Other Applications—Tins have anticarcinogenic and antimutagenic effects	Retz. restricting the multiplication against swine influenza virus A. Double-stranded DNA viruses that cause orofacial and genital herpes with a significant risk of HIV  Tannins and other secondary metabolite chemicals have been shown to block superoxide radicals, providing antioxidant capabilities and protection against cellular damage. neuroprotective and cardiotoxic  Tannic acid (gallotannin), the primary ingredient in <i>T. chebula</i> leads to proteolytic cleavage of the 3CL Protease (3-chymotrypsin-like protease)	Dhanani et al. (2017)  Lin et al. (2013)  Chang et al. (2013)
2	<i>Ocimum sanctum</i>	Dry leaves extract	Coronavirus (CoV)	Triterpenoids—Ursolic acid, flavonoids—apigenin, monoterpenes, linalool, myrcene, and carvone have antiviral activity. In silico study showed methyl eugenol, oleanolic acid, and ursolic acid have high receptor-acceptor binding efficiency against viral attachment spike glycoprotein	Kumar (2020)
3	<i>Withania somnifera</i>	Extract of flower, leaf, stem, roots	HIV/AIDS	Triethyleneglycol (TEG) an active component of Ashwagandha, has shown antimicrobial potential for disinfection of virus (H1N1) & bacteria without causing any side effects. Two nucleoside analogs and one protease inhibitor. It has immune potentiating effects by increasing leukocyte count and T-cell differentiation  Blocks NF-κB transcription, which increases cytokines and other growth-promoting factors during inflammation, inhibits JAK/STAT signaling, which blocks anti-apoptotic, and proteasome-mediated degradation complex inhibition, which blocks apoptotic cell death	Bhuiyan et al. (2020)  Wadhwa et al. (2017a)
4	<i>Moringa oleifera</i>	Leaf Aqueous extract	Other Uses  Herpes simplex virus (HSV-1 and HSV-2), HBV-C DNA	Treating neurological disorder, a stress reliever and Parkinson's, Huntington's, Alzheimer's diseases  Beta-amyryn and flavonoid	Dhanani et al. (2017), Marslin et al. (2015), Wadhwa et al. (2017b)  Nasr-Eldin et al. (2018), Feustel et al. (2017)

Table 3 (continued)

SN	Medicinal plants	Plant organs for extraction	Target virus/ Other uses	Bioactive constituents and their mechanism of action	References
		Methanol extract	Epstein Barr virus	Glycoside	Murakami et al., (1998)
		Aqueous extract	Poliovirus	Flavonoid quercetin reducing the overexpression of p17 protein	Neznanov et al. (2008)
		Seed	Other Uses	Potential to lower the serum cholesterol	Barbosa et al. (2019)
		Seed	Other Uses	Inhibitory activity on beta-hexosaminidase and TNF- $\alpha$ release	Abd Rami et al. (2019)
		Root	Other Uses	Production of milk by increasing estrogen level in mammary glands	Kumar et al. (2019)
		Seeds	Other Uses	Hepatoprotective drug	Sun et al. (2019)

antihyperglycemic effect due to the stimulation of  $\beta$  cells (Mapfumo et al., 2020) (Tables 2 and 3).

### ***Azadirachta indica* (Neem)**

#### **Ethnomedicinal use of *Azadirachta indica***

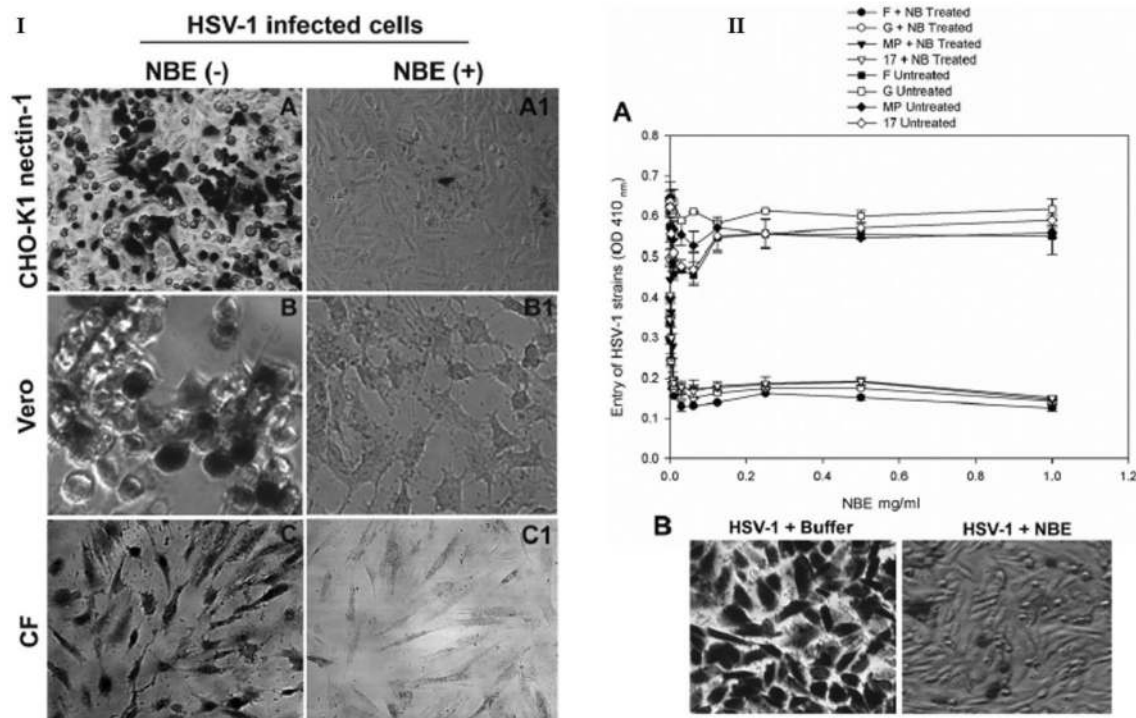
The healing properties of Neem, an Indian native, have been known for centuries. They were used for various purposes in ancient texts. Neem has been used medicinally for over a thousand years by Asians. In the recent years, the tree has been introduced to other tropical areas of America and Africa as a useful cure for various diseases. In India, neem trees are found in almost every home, with over 25 million trees in Uttar Pradesh (55.7%), Tamil Nadu (17.8%), and Karnataka (5.5%) (Singh et al., 2016)

#### **Anti-viral activity of Neem**

The first report on neem extract’s antiviral properties appeared in the Indian journal of medical science in 1969. Neem has been found to be antiviral against polio, dengue, HIV, and Coxsackie B virus. Historically, neem leaf paste was applied directly to the infected skin to treat viral diseases like chickenpox, smallpox, and warts. In mice models infected with highly infectious viral strains, neem extracts were found to provide defense against the HSV-2. In a related study, neem bark inhibited the entry of the herpes virus HSV-1. Even at low concentrations of 50 g/ml, neem bark extract effectively blocks the herpes simplex virus from entering cells (Jang et al., 2008). As a result, neem bark extracts could be used as a novel antiherpetic formulation. Other virulent strains were also kept at bay by neem bark extract (Jang et al., 2008). Several other formulations based on neem extracts like tea made from neem leaves and ointments for topical applications (such as for cold sores) are used to treat herpes infection to provide relief to the patients. Due to its anti-viral activity, neem leaves boiled in water are used during a bath at the time of infection (Fig. 4).

Water extracts of Neem leaves were reported to significantly inhibit the growth and colonization of Dengue virus type 2, a significant cause of viral hemorrhagic fever related to Ebola in in vivo animal models and confirmed by the absence of any symptoms (Rao and Yeturu, 2020). Another study also reported that neem leaf extract significantly inhibited and inactivated Coxsackie B virus replication in in vitro 1mg/ml neem leaf extract significantly inhibited plaque formation in six Coxsackie viral strains. The mechanism of action was proposed to be viricidal, interfering with the viral reproductive cycle. During the early stages of viral replication, the methanolic extract of neem leaves outperformed the chloroform extract in terms of antiviral efficacy (Rao and Yeturu, 2020). Recent pharmacological studies in the United





**Fig. 4** Anti HSV-1 activity of Neem confirmed using X-gal staining. Reproduced with permission from (Tiwari et al., 2010)

States revealed that aqueous extracts from neem leaves show moderate inhibition of viral replication in case of the HBV. Neem leaves can potentially eliminate viral infection by mere contact. In vitro, polysaccharides derived from neem extracts demonstrated antiviral activity against poliovirus. Acute poliovirus, herpes infectious virus, and dengue virus replication is prevented by neem extracts, which inactivate the virus and disrupt its replication cycle (Faccin-Galhardi et al., 2012).

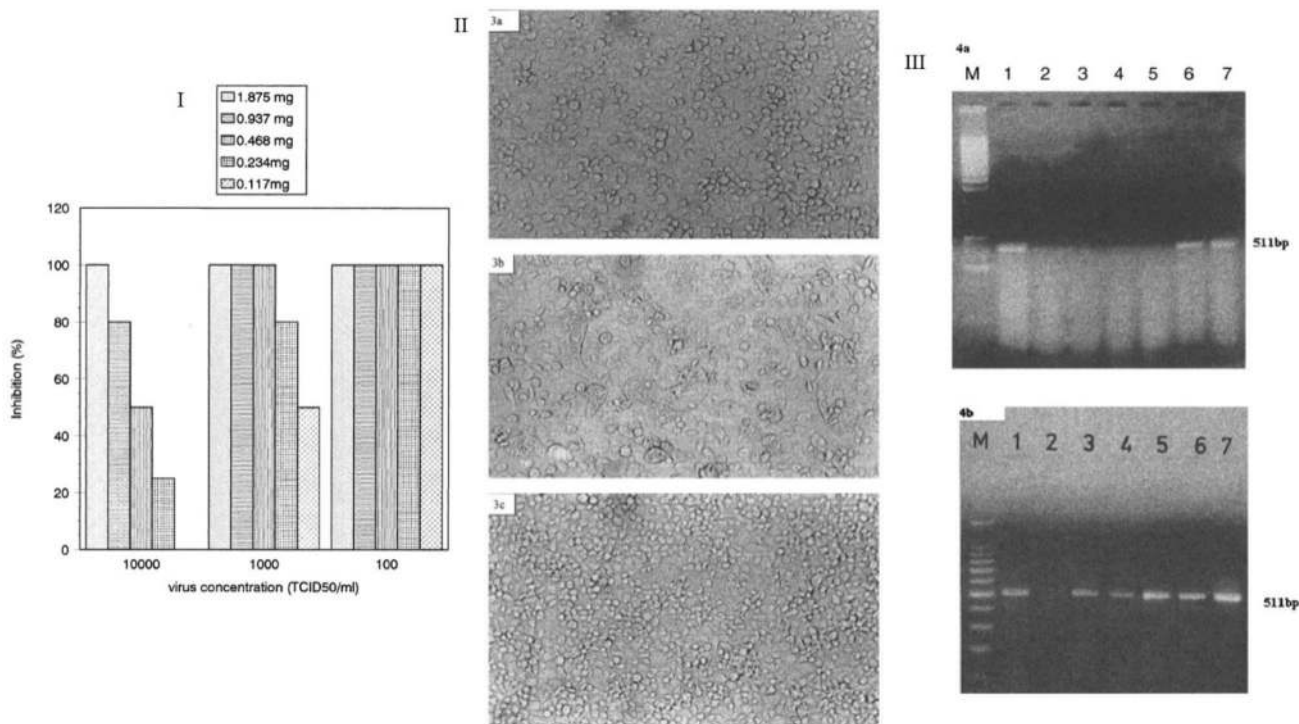
A possible application of neem to combat the COVID-19 was analyzed in a recent study (Nesari et al., 2021). Fever, cough, shortness of breath, and other respiratory complications are common symptoms of COVID-19 infection. Ayurvedic medicine has used neem extracts for centuries to treat malaria and dengue fever (Parida et al., 2002). The neem twig is also used in Ayurvedic medicine to treat cough and asthma. In traditional Indian medicine, diarrhea is treated with neem leaves. In many viral infections, neem leaf extracts have increased CD4 + T cells, dendritic cell maturation, and macrophage-mediated antigen presentation in animal models. Despite the lack of direct experimental data, it is hypothesized that neem extracts combined with modern medicines could be an effective alternative medicine to combat the symptoms and prevent COVID-19 infection (Roy and Bhattacharyya, 2020).

## Other applications

For centuries, several neem extracts have been used for various biological applications. Inflammatory, antiulcer, and contraceptive properties are found in neem formulations derived from various neem parts. Neems leaves immunomodulatory action boost the body's immune response to treat neuromuscular pain and foot infections caused by fungi termites. Neem bark and root extracts exhibit strong bio-insecticidal activity for controlling ectoparasites such as fleas and ticks and treating common skin infections like acne, psoriasis, eczema, and scabies. Other applications of using neem extracts include the treatment of tetanus, orchitis, otitis, kidney swelling, abscess in the ear, urinary infection, and rheumatism (Fig. 5).

Also, neem extract mimics hormones, interfering with parasite nutrition and egg hatching.

Its anticlotting phytoconstituents make it helpful in treating snake venom and insect bites. Other neem seeds and leaf products have practical uses, such as antiseptic creams, soaps, repellents, ointments, etc. (Biswas et al., 2002; Kumar and Navaratnam, 2013; Patil et al., 2013; Upadhyay et al., 1992).



**Fig. 5** Inhibitory potential of various concentrations of NL aq. Ext on different concentrations of Dengue virus type-2. Reproduced with permission from (Parida et al., 2002)

## Indian household spices

### *Zingiber officinale* (Ginger)

#### Ethnomedicinal use of *Zingiber officinale*

The rhizome of ginger is widely used as a medicinal constituent due to its unique nutritional and medicinal properties. Infectious and non-infectious diseases are treated with *Z. officinale* in combination or alone in Ayurveda, Homeopathy, Unani, Siddha, Chinese and Tibetan medicine. The most common uses of Ginger includes application as antimicrobial, antioxidant, anticancer, analgesic, nephroprotective, antidiabetic, hepato-protective, larvicidal, immunomodulatory and anti-inflammatory activities (Gamage et al., 2020).

#### Anti-viral activity of Ginger

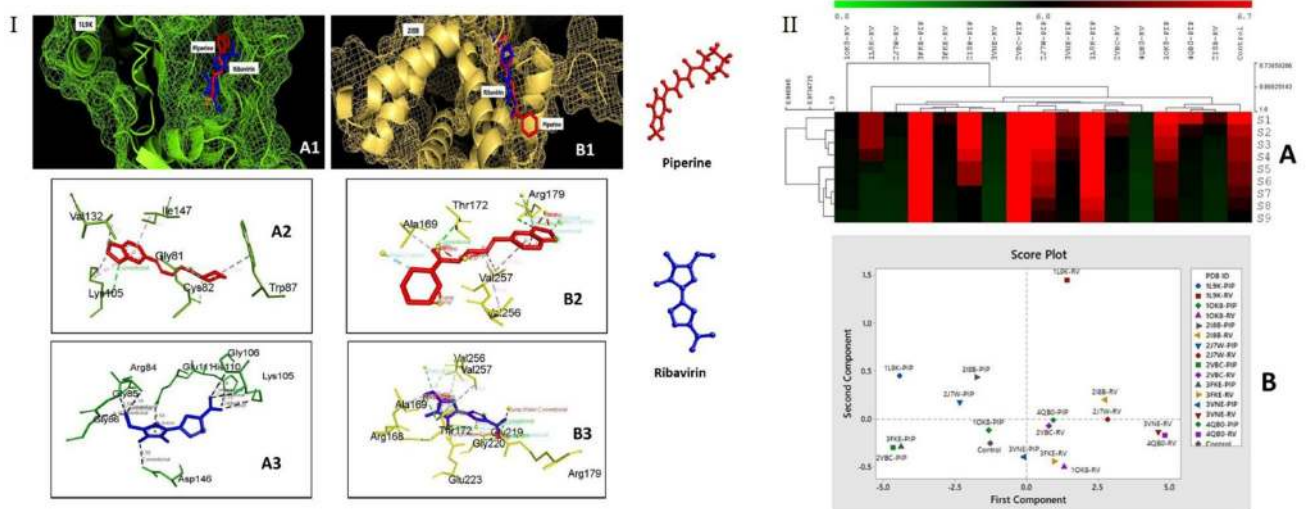
Several studies have reported the anti-viral properties of ginger against of range of viruses. The plant’s fresh rhizome is proven to be effective against the Human Respiratory Syncytial Virus (HRSV) infection This effect is thought to work by reducing HRSV-induced plaque formation in respiratory mucosal cell lines. Higher levels of *Z. officinale* also increase mucosal cell secretion of IFN- $\beta$ , which helps fight viral infections by inhibiting viral attachment and

colonization. This effect also helps prevent common cold and associated fever due to the mucous secretions and helps to manage complications arising due to asthma and cough (Chang et al., 2013). Several studies found antiviral properties in *Z. officinale* extracts against the deadly Hepatitis C viral infection. One study found that the plant extract effectively inhibits viral replication in Hep G2 cells infected with Hepatitis C, affecting viral RNA directly. In another study, *Z.officinale* reduced viral loads and maintained levels of liver function markers like Alanine aminotransferase (ALT), aminotransferase (AST), and fetoprotein. This finding holds in support with the fact that the Indian Ayurveda recommends using ginger in treating liver associated diseases and infectious conditions associated with the liver (El-adawi et al., 2011) (Fig. 6).

Ginger is commonly used in treating intestinal infections. Aqueous extracts of *Z. officinale* are proven to exhibit antiviral activity against Feline Calicivirus, a stand-in for Human Norovirus, which causes food borne infections in the alimentary channel. Allicin contains anti-influenza cytokines that contributes to its use as anti- influenza A (H1N1) agent. The inhibitory effect of ginger against the growth of Influenza A/ Aichi/2/68 virus were previously reported and was found to be mediated via macrophage activation through augmented secretion of TNF- $\alpha$  (Sahoo et al., 2016). Ginger essential oil interferes with the viral envelope’s mechanism of action,







**Fig. 6** Molecular docking and statistical analysis of interaction of piperine with anti-viral proteins and Ribavirin. Reproduced with permission (Nag and Chowdhury, 2020)

inhibiting HSV-2 adsorption (Koch et al., 2008). Clinically isolated acyclovir-resistant strains of HSV-1 were previously studied in vitro for their sensitivity to ginger oil. The study revealed that the essential oil possessed a high level of antiviral activity against acyclovir susceptible strains as well as acyclovir-resistant HSV-1 clinical isolates via significantly reducing the plaque formation (Schnitzler et al., 2007).

In in vitro studies on *Z. officinale* rhizome extracts showed excellent antiviral properties. The plant extract was found to effectively combat drug resistance in antivirals used to treat chikungunya (Kaushik et al., 2020). A virtual prediction of potential antiviral effects of ginger against SARS-CoV2 causing COVID-19 infection was reported in a recent study. The virus crosses the barriers of the host cell through a unique S protein on its surface and initiates its reproduction with the help of a key protein MPro. The results of molecular docking suggested that among the bioactive phytochemicals present in ginger such as gingerol, zingiberene, zingerone and zingiberenol could interact with the key factors involved in MPro catalytic domain. These constituents could also interfere with the S-ACE2 binding shape and intensify its binding energy hypothesizing that ginger could be used as a useful antiviral compound with good bioavailability and compatibility (Ahkam et al., 2020).

### Other Applications

The bioactive components in ginger are also reported to promote digestion, intestinal absorption, and relief from constipation and flatulence. In a small study of college students, ginger extracts were as effective as dimenhydrinate in preventing motion sickness. Ginger has some antibacterial and

antifungal properties. Ginger extracts can help reduce the flatulence caused by colonic bacteria. Ginger inhibits several bacterial species like *E. coli*, *Streptococci*, *Proteus sp*, *Salmonella*, and *Staphylococcus* species at a concentration of 2 g/ml of the spice. Ginger is known to inhibit aspergillus, a fungus that produces a carcinogen called aflatoxin. Fresh ginger juice also inhibits several other species like *A.niger*, *Mycoderma Sp*, *S.cerevisiae*, and *L.acidophilus* at appropriate temperatures. Traditionally, ginger helps to improve body's fluid flow.. It also increases cellular metabolism, relieves cramps and tension by acting on the cardiac muscles. Ginger also inhibits the release of pro-inflammatory thromboxane and prostaglandins, preventing blood clots. Ginger also lowers cholesterol levels upon intake of a cholesterol-rich diet. It also exhibits antioxidant properties. Several studies on rats reveal that ginger exerts several effects on heart rate and blood pressure having a vasodilatory effect (Mowrey and Clayson, 1982; Oladunni Balogun et al., 2020; Vaishnavi et al., 2007) (Table 4).

### *Allium sativum* (Garlic)

#### Ethnomedicinal use of *Allium sativum*

Garlic is one of the most widely used homemade spices. Garlic has long been used both prophylactically and therapeutically. It is widely used in foods and medicines. Garlic and its extract have been used medicinally for many years, with the most common being relief from asthma, common colds, asthma, and hypertension, etc.. Garlic is also widely used to prevent cardiovascular disease. Garlic's antimicrobial and



**Table 4** A summary of various biological applications of common Indian household spices and plants

Sr. No	Spice	Other applications	References
1	<b>Zingiber officinale (Ginger)</b>	<ul style="list-style-type: none"> <li>• Bioactive components: promote digestion, intestinal absorption, prevent motion sickness and provide relief from constipation and flatulence</li> <li>• Increases cellular metabolism, relieves cramps and tension by acting on the cardiac muscles</li> <li>• Antibacterial: inhibit <i>E. coli</i>, <i>Streptococci</i>, <i>Proteus sp</i>, <i>Salmonella</i>, and <i>Staphylococcus</i> species at a concentration of 2 g/ml</li> <li>• Antifungal: inhibit <i>Aspergillus</i>, <i>Mycoderma Sp</i>, <i>S.cerevisiae</i>, and <i>L.acidophilus aspergillus</i></li> <li>• Inhibits the release of pro-inflammatory thromboxane and prostaglandins, preventing blood clots</li> <li>• Lowers cholesterol levels and has antioxidant properties</li> </ul>	Mowrey and Clayson (1982), Oladunni Balogun et al. (2020), Vaishnavi et al. (2007)
2	<b>Allium sativum (Garlic)</b>	<ul style="list-style-type: none"> <li>• Antibacterial: inhibit <i>Acid-fast Staphylococcus</i>, <i>Vibrio</i>, <i>Salmonella</i>, <i>Proteus</i>, and <i>Mycobacterium species</i></li> <li>• Antifungal: bioactive components like allicin inhibit a broad range of fungi</li> <li>• Anti-thrombotic, anti-atherosclerotic properties and vasorelaxant activity</li> <li>• Bioactive compounds like organosulphur compounds are immunomodulatory, antioxidant, and anti-inflammatory</li> <li>• Anticancer activity: inhibiting cell replication, invasion, and metastasis, increasing the expression of specific enzymes and hormones, generating ROS and activating the caspase pathway</li> <li>• Antioxidant property protects liver</li> <li>• Chemoprotective role: Piperine, enhance liver enzymes activity involved in biotransformation in a dose-dependent manner</li> <li>• Increases digestive enzymes and bile secretion in the intestines and pancreas</li> <li>• Immunomodulatory properties: stimulate cellular and humoral immune responses</li> <li>• Analgesic and anti-inflammatory properties</li> <li>• Piperine is a bio-enhancer because it increases drug bioavailability</li> </ul>	Bayan et al. (2014), Bordia et al. (1998), Singh and Singh (2008), Tesfaye and Mengesha (2015)
3	<b>Piper nigrum (Black Pepper)</b>	<ul style="list-style-type: none"> <li>• Anti-insect</li> <li>• Anti-parasite</li> <li>• Anti-infection</li> <li>• Antioxidant</li> <li>• Anti-tumor properties</li> </ul>	Gorgani et al. (2017), Mehmood and Gilani (2010), Science (2014)
4	<b>Curcuma longa (Turmeric)</b>	<ul style="list-style-type: none"> <li>• Used as home remedy against dysentery, diarrhea, and dental plaque</li> <li>• Used to treat sore throats and hoarseness, intestinal worms, ulcers, and bleeding noses</li> <li>• Topical application of ground powder relieves bleeding gums and treats periodontitis</li> </ul>	Esatbeyoglu et al. (2012), Grynkiewicz and Ślifirski (2012), Mathew and Hsu (2018), Wilken et al. (2011), Zorofchian Moghadamtousi et al. (2014)
5	<b>Punica granatum (Pomegranate)</b>	<ul style="list-style-type: none"> <li>• Used to treat sore throats and hoarseness, intestinal worms, ulcers, and bleeding noses</li> <li>• Topical application of ground powder relieves bleeding gums and treats periodontitis</li> </ul>	Su et al. (2011)

antiviral properties are attributed to allicin, a key thiosulfinate compound found in garlic.

### Anti-viral activity of Garlic

The antiviral efficacy of garlic extracts has recently been demonstrated *in vitro* against HSV-1 and HSV-2, vaccinia virus, Parainfluenza Virus 3 and Vesicular Stomatitis Virus (VSV). Garlic extract also helps relieve the symptoms of the influenza virus. Garlic consumption also reduced cytomegalovirus infection. The extract was most effective when used for a long time. Garlic extract is an effective antiviral against HSV-1. However, garlic had no effect on Coxsackie B1 virus virulence (Zadeh and Kor, 2014). A study of 146 people found that taking garlic supplements regularly for three months reduced the risk of getting a cold (Tsai et al., 1985). This is due to the presence of organosulfur compounds such as allicin, ajoene, methylallylthiosulfinate, and allyl methylthiosulfate. Ajoene, allyl alcohol, and diallyl disulphide are anti-HIV compounds in garlic. These compounds help reduce HIV virulence (Lissiman et al., 2014). Garlic compounds like diallyl disulfide and alliin have also been shown to reduce swelling in dengue infections (Ahmad, 2007). Garlic has been shown to have *in ovo* inhibitory effects against IBV, specifically the M41 and 4/91 strains (Hall et al., 2017). Garlic extracts have been shown to protect against influenza viruses *in vivo* by increasing the secretion of neutralizing antibodies. Some of the phytochemicals found in garlic have been linked to efficacy, including ajoene and allyl methyl thiosulfinate. Ajoene inhibits leukocyte adhesive communication and fusion, whereas allicin inhibits several thiol enzymes. It also inhibits HCMV replication and early viral gene expression by activating natural killer cells (NK cells), which kill virus-infected cells without any cues (Mohajer Shojai et al., 2016). Also, a recent study found that aqueous garlic extract has antiviral activity *in ovo* against a velogenic strain of Newcastle disease virus. Pretreatment results were more pronounced due to reduced virus and host cell entry. Its post-viral effects were found to be minimal, possibly due to the virus rapid reproduction cycle, which includes attachment in 10 min, viral protein synthesis in 6 h, and replication cycle in 12 h (Mehrbod et al., 2009).

The recent global pandemic COVID-19 causes fever, myalgia, dry cough, loss of appetite, fatigue, gustatory and olfactory malfunctions. Infected people have low Treg cells, natural killer cells, monocytes and macrophages, helper and cytotoxic T cells, and proinflammatory cytokines. Garlic bioactive constituents can reduce proinflammatory cytokine expression, restoring immunological balance. Thus, garlic consumption may be a potential SARS-CoV2 virus preventive measure. Garlic antiviral properties have

been documented. This perspective may be able to reverse immunological dysfunctions seen in patients infected with COVID-19 (Doostmohammadian et al., 2020).

### Other applications

Garlic has been shown to have antibacterial, antifungal, antiparasitic, and antiviral properties. Allicin and other sulfur compounds in garlic are antimicrobial. Acid-fast *Staphylococcus*, *Vibrio*, *Salmonella*, *Proteus*, and *Mycobacterium* species are all susceptible to garlic extracts. It was discovered that garlic extracts in varying concentrations (aqueous, chloroform, ethanol) inhibit bacterial growth. Allicin has antifungal activity against a wide range of fungi. Inducing nitric oxide synthesis or vasodilation via endothelial-dependent and independent pathways. Garlic has anti-thrombotic and anti-atherosclerotic properties, as well as vasorelaxant activity. Garlic extracts contain organosulphur compounds that are immunomodulatory, antioxidant, and anti-inflammatory. These compounds have anti-cancer properties in preclinical studies by inhibiting cell replication, invasion, and metastasis, and increasing the expression of specific enzymes and hormones. Garlic extract-derived DAS, DADS, and DATS have anticancer activity by generating ROS and activating the caspase pathway. To inhibit the cytoskeleton assembly and disassembly process, garlic extract, particularly garlic oil, is anti-inflammatory (Bayan et al., 2014; Bordia et al., 1998; Singh and Singh, 2008; Tesfaye and Mengesha, 2015) (Table 4).

### *Piper nigrum* (Black Pepper)

#### Ethnomedicinal use of *Piper nigrum*

*Piper nigrum* L. (Black Pepper), a dried unripe fruit often referred to as the king of spices, is almost used in every cuisine. One of the most commonly used spices has a pungent taste due to piperine, a predominant alkaloid, and other volatile chemical constituents. Piperine is present in various pepper species of the *Piperaceae* family. Piperine exhibits anti-inflammatory, antiviral, anticancer, pesticidal, and anti-depressant properties. Most importantly, piperine increases drug bioavailability (Kesarwani and Gupta, 2013).

#### Anti-viral activity of Black Pepper

Piperine, an alkaloid found in black pepper, was recently molecular docked against Dengue and Ebola virus enzymes. Piperine had the potential to inhibit Ebola virus VP35 interferon inhibitory domain and dengue methyltransferase compared to the commercial antiviral Ribavirin. Piperine had a higher affinity for viral proteins than Ribavirin, according to multivariate and clustering studies (Nag and Chowdhury,



2020). Nevirapine is known for its non-nucleoside inhibition of the reverse transcriptase enzyme of HIV-1 virus transcriptase enzyme. Piperine, found in black pepper, has been shown to increase drug bioavailability and duration of action. One study evaluated piperine's effect on nevirapine pharmacokinetics in fasting humans and found that piperine significantly increased nevirapine bioavailability (Kasibhatta and Naidu, 2007). In vitro studies reported the antiviral properties of piperamides extracted from black pepper against coxsackievirus B, rhinovirus type 2 HRV-2, and the influenza virus type A. The antiviral activity of alkaloids in black pepper chloroform extracts was highest against VSV (an enteric virus) and Human parainfluenza virus (a respiratory virus) (Priya and Kumari, 2017). An in-silico approach revealed that black pepper phytochemical such as Piperdardine and Piperanine were significantly active against COVID-19 when compared to currently used hydroxychloroquine (Sudhir and Delma, 2018).

### Other applications

Pepper has been used for centuries to treat fevers and increase bile secretion. Other uses for Piper include neurological, pulmonary, and gastrointestinal issues. Piperine is high in antioxidants and thus protects the liver. Piperine, enhance liver enzymes activity involved in biotransformation in a dose-dependent manner, and hence has a major chemoprotective role. Oral pepper consumption increases digestive enzymes and bile secretion in the intestines and pancreas. This could be attributed to pepper immunomodulatory properties such as cellular and humoral immune responses stimulation. There are immunomodulatory properties in pepper that stimulate cellular and humoral immune responses. Piperine and pepper extracts in hexane and ethanol have excellent analgesic and anti-inflammatory properties.. Piperine is a bio-enhancer because it increases drug bioavailability. A higher apparent permeability coefficient and shorter clearance time may be responsible for piperine's rapid absorption across the intestinal membrane (Gorgani et al., 2017; Mehmood and Gilani, 2010; Srinivasan, 2009) (Table 4).

### *Curcuma longa* (Turmeric)

Originating from India, the Archipelago and Southeast Asia, *Curcuma* is a genus of 70 rhizomatous herbs (Amalraj et al., 2017; Carolina Alves et al., 2019). Commercially available *C. amada*, *C. angustifolia*, *C. aromatica*, *C. caesia*, *C. zedoria*. *Longas* are vital. It is the most important because it is used as a spice, condiment, and antiseptic in bruises and sprain treatment (Bhutia et al., 2017). *Curcuma longa* (turmeric) is used as a condiment,

anti-inflammatory, and sprain treatment. It has long been used to dye wool and silk. Nutraceuticals and dietary supplements have become increasingly popular in recent years for their health advantages (Das et al., 2012; Hewlings and Kalman, 2017; Kunnnumakkara et al., 2018; Santini et al., 2017). Curcumin has the potential to treat various diseases as they are less harmful (Goel et al., 2008).

### Ethnomedicinal use of *Curcuma Longa* L

Turmeric, a plant-derived curry spice, is noted for its medicinal uses (Hewlings and Kalman, 2017). As a result of these gains, many yellow nutrients are available on the international market in various forms (support for common relief, mobility and flexibility, cerebral function, and functional cardiac health) (Das et al., 2012; Kunnnumakkara et al., 2018; Santini et al., 2017). Turmeric is a well-known spice used in Indian and other Asian curries for its flavor and color (Araújo and Leon, 2001; Hewlings and Kalman, 2017). Turmeric is primarily produced and distributed in India. Curcumin plants mature in 7–9 months. Soil rhizomes are dried and grind into powder, oleo, curcumin powder, and resin. Turmeric has anti-inflammatory (Aggarwal and Harikumar, 2009), anti-cancer (Willenbacher et al., 2019), anti-platelet, hypoglycemic, hepatoprotective, and antioxidant properties (Perone et al., 2015).

### Antiviral activity of Turmeric

Curcumin has been shown to be antiviral against parainfluenza contamination type 3 (PIV-3), feline overpowering peritonitis virus (FIPV), VSV, HSV, flock house virus (FHV), and respiratory syncytial contamination (Zorofchian Moghadamtousi et al., 2014). This study aimed to examine curcumin's popular counter-parts and secret movement methods. Curcumin anti-viral expertise had been limited to HIV, HSV, HPV, Influenza A (HIAV), and Ebola. Curcumin pleasing effects outperform the powerless outcomes and their condition by relying on various flexible mechanisms inhibiting the blast and pathogen propagation, because new pathogens or variants constantly emerged, making viral disease control difficult. Due to the lack of editing capability, viral RNA polymerase costs more than pre-existing anti-viral tablets (Elena and Sanjua, 2005). It is important to note that the significance, time, and commitment required to expand anti-viral microorganisms caused significant harm (Bolken and Hruby, 2008; Howell and D'Souza, 2013; Lipson et al., 2007).





**Table 5** A summary of various extraction method of phytoconstituents from the above discussed plants

S.N	Plant species	Extraction methods	References
1	<i>T. chebula</i>	Solvent extraction, Maceration, Ultrasound assisted extraction	Dash et al. (2021), Vemuri et al. (2019), Walia et al. (2011)
2	<i>O. sanctum</i>	Soxhlet extraction, Maceration, Supercritical fluid extraction	Rajesh et al. (2013), Garg and Garg (2019), Coelho et al. (2018)
3	<i>W. somnifera</i>	Soxhlet extraction, Conventional refluxing, Supercritical fluid extraction	Dhanani et al. (2017), Karimi and Raofie, (2020), Srivastav and Das, (2014)
4	<i>M. oleifera</i>	Solvent maceration, Soxhlet extraction, Supercritical fluid extraction, Ultrasound assisted extraction	Dadi et al. (2019), Ojewumi et al. (2019), Oladeji et al. (2020), Zhao and Zhang, (2013)
5	<i>A. indica</i>	Soxhlet extraction, Supercritical fluid extraction, Ultrasound assisted extraction, Microwave assisted extraction, Percolation	Adeel et al. (2019), Chaisawangwong and Gritsanapan, (2009), Suttiarporn and Choommongkol (2020), Tyskiewicz et al. (2018)
6	<i>Z. officinale</i>	Soxhlet percolation, Ultrasound assisted extraction, microwave assisted extraction	Vedashree and Naidu, (2018), Saad et al. (2014), Supardan et al. (2012)
7	<i>A. sativum</i>	Solvent maceration, Soxhlet extraction, Ultrasound assisted extraction, Carbon dioxide expanded ethanol method	Chhouk et al. (2017), Fortunata et al. (2019), Mathialagan et al. (2017), Priya Dharshini and Devi, (2017)
8	<i>P. nigrum</i>	Ethanol extraction, Microwave assisted extraction, Supercritical fluid extraction	Mariselvi and Manimegalai (2017), Perakis et al. (2005), Raman and Gaikar, (2002)
9	<i>C. longa</i>	Soxhlet extraction, Ultrasound assisted extraction	Sahne et al. (2016), Shirsath et al. (2017)
10	<i>P. granatum</i>	Soxhlet extraction, Vacuum microwave assisted extraction, Ultrasound assisted extraction	Ali and Kumar (2014), Nag and Sit (2018), Scale (2021)

### Other biological applications

Curcumin is a wonder drug due to its potent anti-insect, anti-parasite, anti-infection, anti-oxidant, anti-tumor properties. Having the ability to influence multiple sub-nuclear targets makes them a potential competitor for disease prediction and possibly therapy. It is now possible to use curcumin-based drugs that are rapidly bioavailable and have a focused effect against contaminations (Mathew and Hsu, 2018) (Table 4).

### *Punica granatum* (Pomegranate)

*Punica granatum* L. (Pomegranate), delicious fruit, is native to China, Iran, Afghanistan and the Indian subcontinent. The old springs of this fruit have connected Iran to Pakistan, China and East India. Pomegranate development extended to the Turkish European outskirts and American southwest, Mexico, and California via. Mediterranean from the west of Persia.

### Ethnomedicinal use of *Punica granatum* L

In Egypt, pomegranate peel extract has been used to treat inflammation, intestinal worms, diarrhea, infertility, and cough. The fruit's high antioxidant activity and other biological/pharmacological applications prompted extensive research in the international clinical community (Celik et al., 2009; Lansky and Newman, 2007).

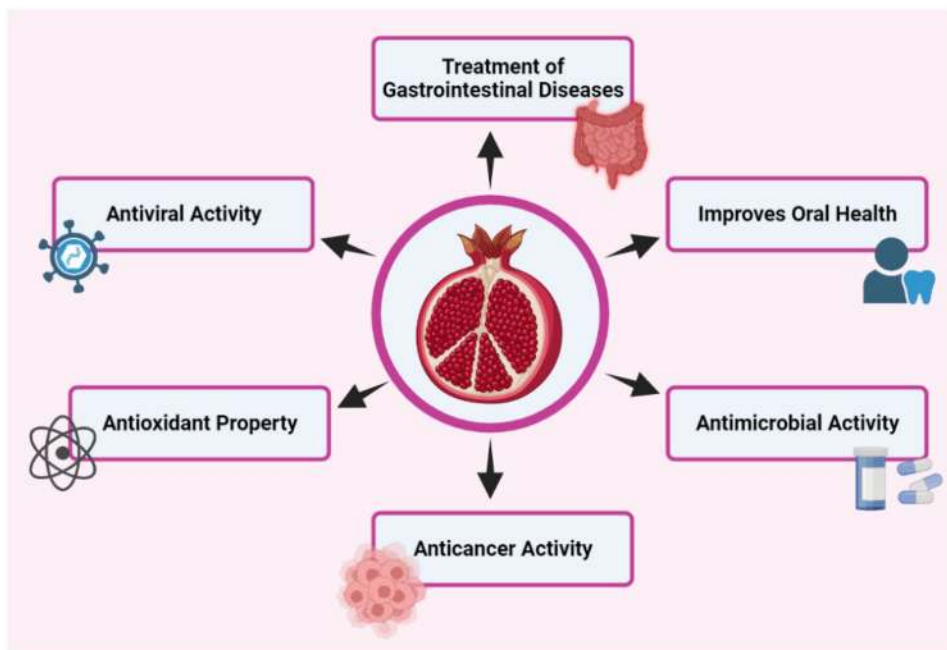
### Antiviral activity of Pomegranate

Pomegranate and its extracts have been shown to have antiviral properties. The methods for the extraction of valuable phytoconstituents from pomegranate has been discussed in Table 5. Many other studies have shown that the fruit extract has antiviral activity against influenza, poxviruses, herpes, and HIV-1 (Howell and Souza, 2017; Kotwal, 2008; Moradi et al., 2019). Tannins and anthocyanins, the hydrolysable principle compounds are responsible for the several pharmacological effects of the fruit extracts (Aviram et al., 2008), including the antimicrobial activity against certain bacteria and viruses. One study found punicalagin to be the most effective of the four flavonoids found in pomegranates, ellagic acid, caffeic acid, luteolin, and punicalagin against influenza virus (Espín et al., 2013) (Fig. 7).

### Other applications

Historically, aqueous fruit extract was used as a douche and enema agent, as well as a home remedy for dysentery, diarrhea, and dental plaque. It has been used to treat intestinal worms, ulcers, and bleeding noses in India. It's also used to treat sore throats and hoarseness. Topical application of ground powder relieves bleeding gums and treats periodontitis (Su et al., 2011) (Table 4).

**Fig. 7** Medicinal effects of *Punica granatum*



## Future prospects and application in bio-nanotechnology

Natural products provide a rich source of biodiversity and provide new insights to combat newly emerged diseases. The pharmacological activity of various medicinal plants and the dietary supplements provided by the fruits, legumes, and vegetable findings prove that they contain useful active ingredients that offer medicinal and nutritional values (Zhu et al., 2018). The biotechnology tools help in breeding different plants to have more dietary outputs in agriculture, and it also strengthened the nutraceutical approaches. It provides the mechanism for breeding techniques to understand the genome-wide sequencing, understanding its metabolomics, secondary metabolite production, bioinformatics (Niazian, 2019). Understanding phytochemicals basic chemical structure and mode of action will help develop new drugs. In the future, more research will be required to determine the chemical compositions' mode of action during metabolism (Subramanian et al., 2016). Solubility, stability, and specific target are all aspects of nanotechnology, which deals with particles ranging in size from 1 to 100 nm. Phytochemicals possess several medicinal properties like antibacterial, anticancer, anti-inflammatory, anti-tumor, anti-viral activities. However, owing to low bioavailability at the target site, nano-size drugs is highly expected to increase the effectiveness of the medication due to strong differential absorption, permeability and retention results, which increases cellular efficiency and reduces systemic toxicity (Srivastava et al., 2016).

## Conclusion

Numerous classes of phytochemicals like tannins, alkaloids, flavonoids, coumarins, terpenes, etc. extracted from medicinal plants have been reported to have antiviral properties. These bioactive compounds inhibit viral infection by targeting different stages of viral infection like inhibiting virus binding to the host cell surface, modulating signaling pathways, and inhibiting viral replication in the host cell. This review enumerated various medicinal plants found predominantly in India namely, *T. chebula*, *O. sanctum*, *W. somnifera*, *M. oleifera*, *A. indica*, *Z. officinale*, *A. sativum*, *P. nigrum*, *C. longa* and *P. granatum*. The taxonomical classification and geographical distribution of these plants were explained. Further, the extraction process for various bioactive constituents from the medicinal plants were enumerated. Finally, detailed information on the specific bioactive component, its target virus, and its mechanism if the antiviral activity were highlighted.

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## Declarations

**Conflict of interest** The authors declare no conflict of interest regarding the publication of the review article.

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