

# Plant-based approach in treatment of hMPV virus

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## Abstract:

To make up for their lack of movement, plants have evolved special defences against the hostile environment. The production of secondary metabolites is an essential component of their coping strategies. They have medicinal qualities against diseases in addition to helping plants defend themselves against infections. Previously, there has been a lot of literature about the usage of medicinal herbs as a natural source of low cost antiviral drugs. Metabolomics is a valuable research method for identifying plant metabolites with antiviral potential. It can be used to isolate molecules in plants that have antiviral properties and investigate the biosynthetic pathways that contribute to the progression of viral diseases. The majority of people worldwide get at least one viral respiratory infection each year, making them one of the most prevalent ailments in the world. In order to treat these illnesses and lessen their symptoms, many plant species are employed in therapeutic systems. Nevertheless, nothing is known about these plants' potential as a treatment for viral respiratory illnesses. One of the primary pathogens that causes acute respiratory infections among children under the age of five is the human metapneumovirus (hMPV), which significantly increases the burden on health. This virus has a huge global economic and social impact that needs to be handled. In the current situation, this hMPV is causing concern. We wish to talk about the without, low cost plant-based strategy and treatments for this hMPV virus in this document.

**Keywords:** hMPV, immune response, anti-hMPV, hMPV.

## 1. Introduction

Today, After 5 years pandemic disease of COVID-19 in 2019, another virus Human metapneumovirus (hMPV) has spread worldwide. hMPV is a novel negative single stranded RNA respiratory syncytial virus (RSV) infection which was first isolated from respiratory of children in 2001. According to the 2016 *Mononegavirales* order classification, HMPV is a member of the *Pneumoviridae* family. Netherlands, European, Asian countries and were the first to identify hMPV. A subtropical region such as Hong Kong has a high rate of hMPV infection in the spring and early summer. In Italy, pestilence peaks arrive during February, and March. Various numerous study reported that, hMPV second or third most cause upper respiratory and lower respiratory tract infections in under 3 years kiddies and Also at risk are adults over 65 aged (Chang *et al.*, 2012; Wang *et al.*, 2013; Geiser *et al.*, 2021). In the period 2006-2009, over 7,000 acute respiratory tract infections (ARTIs) were tested in Soochow University Hospital, Suzhou for hMPV (Wang *et al.*, 2013).

Close contact with infected individuals can spread hMPV, particularly through coughing or sneezing droplets or touching the mouth or shaking hands. HMPV-infection is caused by typical Th17-like immune response, distinguish by emission of TNF- $\alpha$  in the lungs and interleukin (IL)-6. A hMPV infection can cause a variety of symptoms from mild colds to bronchiolitis, pneumonia, and febrile seizures. It is also accompanied by an insufficient Th2-like profile, distinguish by IL-4, 5, 8, & other pro-inflammatory mediators (Chang *et al.*, 2012). PCR-based procedures with virus genome-specific primers failed to detect it, despite immunological tests using virus-specific antibodies (Kahn *et al.*, 2006).

Nature has gifted medicinal plants to us in order for us to live a disease-free and healthy life. Historically, herbal medicine has been used as a form of medicine for thousands of years. Numerous studies on antiviral, antifungal, antibacterial, antiviral, and anthelmintic medicinal herbs and crops have been published in scholarly databases. Recently reported, 9,000 plants have been considered medicinal plants for several medicinal applications worldwide. Plants produced bio chemical compounds that effective against virus. Pharmaceutical intervention is necessary in certain situations, even if immunization is the primary method for controlling and preventing infections caused by hMPV. Additionally, no hMPV vaccines are available on the market. But medicinal plants have advanced attractive properties for boosting urban areas' easy access to healthcare, immunity boost (Alrashedi *et al.*, 2021; Konar *et al.*, 2023; Andrade *et al.*, 2020). However, this study aims to appreciate the anti-hMPV properties of chemical compounds in different native plants.

## 2. History of hMPV

An initial discovery of the hMPV (Human Metapneumovirus) in 2001 occurred when the pathogen was separated from a paediatric patient that had signs and symptoms of infection with the virus. Consequently, The presence of hMPV in ARI patients ranges from 4 to 16%. 6–8. Different regions may experience different hMPV outbreaks each year. hMPV reasons illness principally in kids, However, it can spread in adults and compromised immune system. Acute

bronchiolitis and pneumonia can follow an infection with hMPV and range from mild to potentially fatal (Panda *et al.*, 2014).

The first human member of the Metapneumovirus genus belonging to the *Pneumovirinae* subfamily of the *Paramyxoviridae* family. Single-stranded RNA virus with an enclosed negative sense. There are eight genes in the RNA genome that code for nine distinct proteins. The avian pneumovirus (AMPV), which is likewise a member of the Metapneumovirus genus, shares the same gene order as HMPV (Biacchesi *et al.*, 2003). Two HMPV genotypes, A and B, have been found by phylogenetic analysis. One genotype often predominates during an epidemic, while both genotypes may co-circulate at the same time. A1, A2, and B1 are the clades within each subgroup. The attachment (G) and fusion (F) surface glycoproteins' sequence diversity serves as the primary basis for this classification. In addition to facilitating cross-lineage neutralization, the highly conserved F protein also protects against cross-lineage infection. In 2006, two additional subgroups, A2a & A2b, were characterized. However, this further division was predicated on scant data and has not been validated by other groups. Thereby, there is currently no evidence of these subgroups' clinical importance (Haas *et al.*, 2013).

### 3. Epidemiology

HMPV has been reported in Italy, Canada, France, Spain, Japan, Australia, and Germany since its first discovery by Dutch researchers in 2001. Additionally, the virus has been found in South African children who are HIV-positive and not immunocompromised (Hamelin *et al.*, 2004). Furthermore, research has demonstrated that hMPV is not a novel pathogen, with viral isolation occurring in Europe and Canada during the last 10 to 20 years and serological record of human contamination dating back to 1958 in the Netherlands. Even though hMPV infection is ubiquitous in childhood, instances of serious suppuration in adults and reinfection in immunocompromised individuals suggest that new infections may take place throughout life due to immune responses that are not completely protective or the acquisition of new genotypes (Boivin *et al.*, 2002).

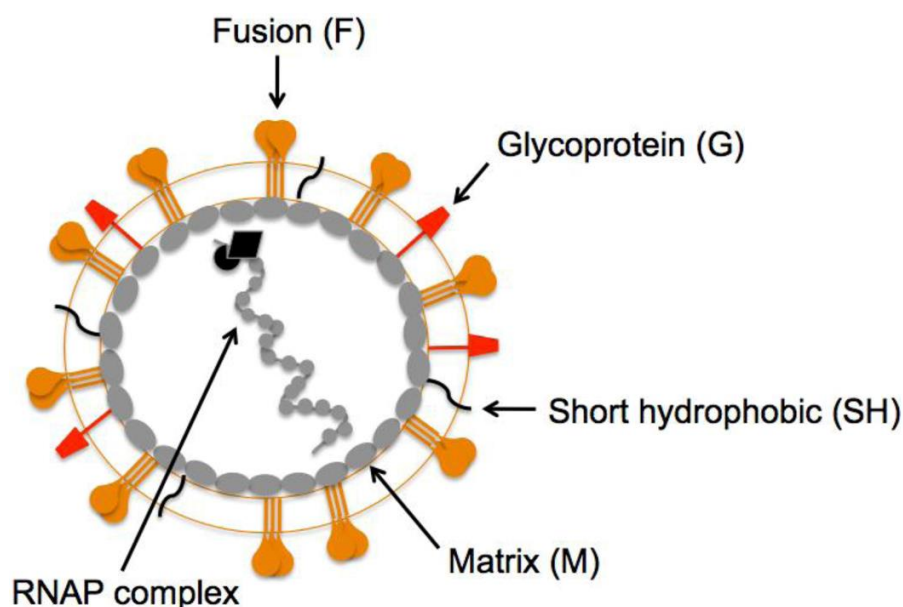
### 4. Viral Genes and Structure

HMPV is a single-stranded RNA virus, its genome is 13.3 kb length, is comprised by eight genes with nine proteins. Genomic sequence is 30'-N-P-M-F-M2-SH-G-L-50', every genes encode by single protein. But M2 gene not encode two special type proteins. All of these genes except for the m2 gene encode a single protein; the m2 gene codes for two distinct proteins, M2-1 and M2-2, due to the overlapping of two ORFs in its mRNA. Surface-located glycoproteins are linked to the matrix protein (M), which helps to attach the inner membrane (Andrade *et al.*, 2020).

Virion lipid bilayers are likely derived from an infected cell's plasma membranes during virus egress. The surface of the hMPV virion is composed of three glycoproteins: the attachment protein (G), small hydrophobic protein and fusion protein (F). The small

hydrophobic (SH) protein reduces gene transcription as it is a type II transmembrane protein that can engage in NF- $\kappa$ B transcriptional activity and utilizes the transcription gene pathway (Masante *et al.*, 2014; Bao *et al.*, 2008; Cox *et al.*, 2013). According to Masante *et al.*, SH protein can play a significant role in virus life cycle by altering the membrane's permeability (Masante *et al.*, 2014). The G protein are found in the cells membranes, encouraging the virus's cellular attachment and that cause hMPV infection. G protein contains a lot of O- and N-linked sugars and is glycosylated (Thammawat *et al.*, 2008). The F protein is a type I fusion protein that is generated as an inactive precursor (F0). The subunits F1 and F2, which are joined by disulphide bonds, must cleave in order for the protein to be biologically activated [8].

The nucleocapsid assembles when hMPV RNA combines with the putative transcription factor (M2-1), large polymerase protein (L), nucleoprotein (N), and RNA synthesis regulatory factor (M2-2) (Andrade *et al.*, 2020). The nucleoprotein (N) that encapsulates the viral RNA genome to shield it from nucleases. The P protein and the N protein interact, ribonucleoprotein (RNP) complex can only be assembled thanks to the P protein [18, (Derdowski *et al.*, 2008; Swagatika Panda *et al.*, 2014).



**Figure 1: Structure of human metapneumovirus (hMPV) virion (Cox *et al.*, 2013).**

## 5. Clinical features

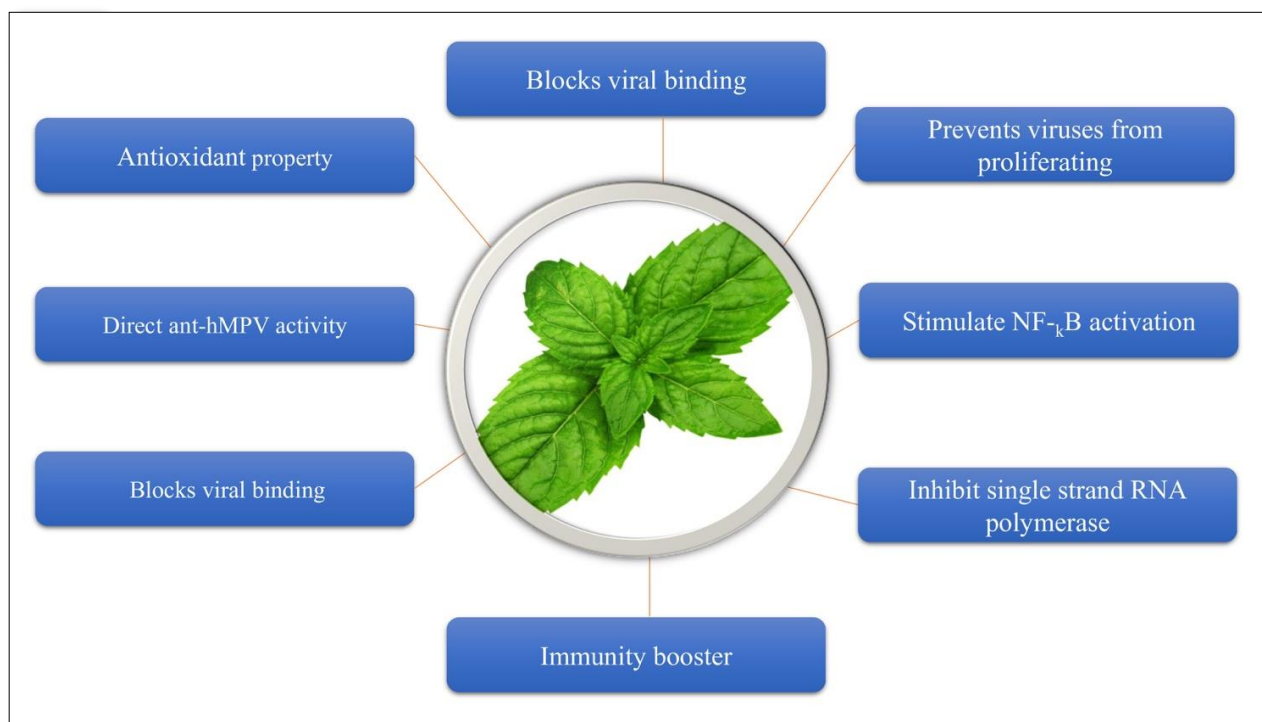
Particularly in young children, the clinical signs of an RSV infection and a hMPV infection are identical. Patients with hMPV are diagnosed with pneumonia, bronchiolitis, and bronchitis. In the course of the infection, common symptoms manifested such as fever, upper respiratory tract infection, lower respiratory tract infection, and wheezing (Panda *et al.*, 2014). According to one study, 50% of young people with hMPV infection were diagnosed with otitis media, while hMPV infection was identified in approximately 8% of children who presented to the hospital with wheezing. Numerous research on children with lower respiratory tract

infections linked to hMPV have found wheezing to be a prevalent clinical sign. In children and adults can lead to asthma exacerbations. COPD is exacerbated by hMPV, and hMPV infection is more common in COPD patients (Williams *et al.*, 2005). A few studies suggest that hMPV infection affects the central nervous system of children and febrile seizures to severe encephalitis and severe encephalitis to feverish seizures (Arnold *et al.*, 2009).

Although asymptomatic children exhibited considerably lower virus loads than symptomatic children, hMPV was nevertheless detected by real-time RT-PCR in these children (Panda *et al.*, 2014). There are several methods for diagnosing hMPV infection. Because hMPV has minor cytotoxic effects and develops slowly in standard cell culture, virus cultivation is comparatively challenging. Shell vial amplification is the name of the quick culture method. Reverse transcriptase-PCR (RT-PCR) assays, which detect viral RNA by NAAT, are the most sensitive way to diagnose hMPV infection (Haas *et al.*, 2013; Broor *et al.*, 2007).

## 6. Phytochemical and remedy

Plants are providers of chemical compounds necessary for their usual metabolic activities (Alrashedi *et al.*, 2021). Plants are wide range essential source of secondary metabolites, which used in pharmaceuticals industry, food additives, fragrances, colours etc (Alrashedi *et al.*, 2021; Konar *et al.*, 2023). Several part or whole parts of plant and herbs are attractive property against hMPV virus (Alrashedi *et al.*, 2021). Numerous active phytochemicals such as flavonoids, terpenoids, vanillic acid, lamiaceae, lignans, apigenin, saponin, Rotenone, tannin and isovanillic acid, have been shown to affect viral replication, cellular processes, membrane permeability (Alrashedi *et al.*, 2021; Konar *et al.*, 2023; Musarra-Pizzo *et al.*, 2021). Plants produce flavonoids, which are extensively dispersed secondary metabolites with antiviral effect, naturally derived from various classes including flavonols, isoflavanoids and anthocyanidins. Moreover, quercetin inhibits NF- $\kappa$ B activity which is essential of hMPV virus gene expression (Musarra-Pizzo *et al.*, 2021). Leaf, Fruit and seeds of *Litchi chinensis*, *Camellia sinensis* and *Phragmanthera capitata* (Green tea) possess antiviral bioactivities (Ghosh *et al.*, 2022; Ibrahim *et al.*, 2015; Kosińska *et al.*, 2014; Konar *et al.*, 2022; Galani *et al.*, 2015). *Eclipta alba* is belong Asteraceae family is used to single inhibited Strand RNA replication of hMPV. Additionally, *Prunus dulcis* has the unique property of blocking viral binding in Vero cells (Musarra-Pizzo *et al.*, 2021). *Cassia fistula* (Golden Shower) and *Azadirachta indica* (neem) plant parts are known to be essential source of secondary metabolites notably Alkaloids, flavonoids, Kaempferol, Steroids and a proanthocyanidin, have several anti-viral activity (Konar *et al.*, 2022; Konar *et al.*, 2023; Duraipandiyan *et al.*, 2007). Several plant antioxidants, including polyphenols, can protect cells from viral damage and mitigate oxidative stress. *Aloe vera* (L.) and *Allium sativum* L. (onions) contain quercetin, an antioxidant that enhances the immune system's function (Srivastava *et al.*, 2024; Azam *et al.*, 2020). Table 1 shows the details of some plant products used to control the ant-hMPV diseases.



**Figure 2: Various mechanisms contribute to the ant-hMPV effects of natural products**

**Table 1: Major Medicinal Plants of Anti-hMPV**

Name	Family	Plant Part	Uses
<i>Acacia nilotica</i>	Fabaceae	Whole Plant	Fruits and leaves contain tannin, which inhibits cold and influenza viruses as well as hMPV virus (Konar <i>et al.</i> , 2023).
<i>Ocimum basilicum</i>	Lamiaceae	Aerial part	It contain sterols, saponins, and flavonoids and phenolics, which inhibits viral replication (Konar <i>et al.</i> , 2023).
<i>Elephantopus scaber</i> L.	Asteraceae	Whole Plant	Contain Syringic acid, Vanillic acid, Isovanillic acid, 3,4-dihydroxy benzaldehyde, Tricin 2-hydroxybenzolate acid (Alrashedi <i>et al.</i> , 2021).
<i>Ocimum sanctum</i>	Lamiaceae	Leaf	Whole Leaf extract contain bioactive compound such as eugenol and apigenin that inhibit hMPV viral activity (Azam <i>et al.</i> , 2020).
<i>Houttuynia cordata</i>	Saururaceae	Whole plant	Quercetin, Capryl aldehyde Blocks viral binding and

			suppresses NF- $\kappa$ B activation (Ghosh <i>et al.</i> , 2022; Azam <i>et al.</i> , 2020)
<i>Prunus dulcis</i>	Rosaceae	Skin	Skin extract rich in polyphenols compounds, almond skin extract rich in polyphenols compounds, that showed anti-binding properties (Musarra-Pizzo <i>et al.</i> , 2021).
<i>Litchi chinensis</i>	Sapindaceae	Fruit	By inhibiting reactive oxygen species, oligonol prevents viruses from proliferating (Musarra-Pizzo <i>et al.</i> , 2021; Ibrahim <i>et al.</i> , 2015).
<i>Camellia sinensis</i>	Theaceae	Leaf	Green tea leaf catechins inhibit RNA polymerase (Musarra-Pizzo <i>et al.</i> , 2021; Konar <i>et al.</i> , 2023).
<i>Solanum xanthocarpum L</i>	Solanaceae	Leaf extract	Flavonoids leaf extract showed anti-virous activity (Konar <i>et al.</i> , 2022).
<i>Phragmanthera capitata</i>	Loranthaceae	Leave extract	Methanol of leaf extracts preventing the entry of viruses (Musarra-Pizzo <i>et al.</i> , 2021; Galani <i>et al.</i> , 2015).
<i>Detarium microcarpum</i>	Caesalpiniaceae	Stem bark extract	Stem bark extract of methanol, inhibits viruses from entering (Musarra-Pizzo <i>et al.</i> , 2021; Galani <i>et al.</i> , 2015).
<i>Azadirachta indica</i>	Meliaceae	Leaf extract	Flavonoids Inhibit first stage of hMPV replication (Konar <i>et al.</i> , 2022).
<i>Eclipta alba</i>	Asteraceae	Whole plant	Extract strongly inhibited RNA replication due to presence of tannins, flavonoids (Musarra-Pizzo <i>et al.</i> , 2021)
<i>Cassia fistula</i>	Leguminosae	Flower	Kaempferol and a proanthocyanidin of flower Suppression of the anti-viral activity (Duraipandiyani <i>et al.</i> , 2007; Konar <i>et al.</i> , 2023).
<i>Hyoscyamus niger</i>	Solanaceae	Whole plant	Various plant part contain alkaloids, flavonoids, tannins, terpenes and anthraquinones that boost immunity and protect the

			body from viral infection (Konar <i>et al.</i> , 2023).
<i>Moringa olifera</i>	Moringaceae	Drumstick	Treatments for viral infections and boosting immunity are available along with HMPV prevention (Konar <i>et al.</i> , 2023).
<i>Syzygium brazzavillense</i> Aubr.	Myrtaceae	Bark, leaves	Aqueous extracts of bark and leaves Inhibit virous replication (Musarra-Pizzo <i>et al.</i> , 2021; Masante <i>et al.</i> , 2014).
<i>Citrus sinensis</i>	Rutaceae	Peels	Flavonoids of peels showed anti viral activity (Kumar <i>et al.</i> , 2022).
<i>Scutellaria baicalensis</i>	Lamiaceae	Dried root	Baicalin and Wogonin both are flavonoids that inhibit viral replication (Srivastava <i>et al.</i> , 2024; ji <i>et al.</i> , 2015).
<i>Lycoris radiate</i> L	Amaryllidaceae	Bulbs	Bulb contain Lycorine compound, stop assembly, inhibit RNA polymerase activity dependent on viral RNA [33, 37]. (Srivastava <i>et al.</i> , 2024).
<i>Allium sativum</i> L	Alliaceae	Bulb and Peels	By inhibiting oxidative stress, viruses can be inhibited [33, 38] (Zhang <i>et al.</i> , 2019; Rouf <i>et al.</i> , 2020).
<i>Aloe vera</i>	Liliaceae	Leaf	Regulate immune system's function (Zhang <i>et al.</i> , 2019; Srivastava <i>et al.</i> , 2024).
<i>Oldenlandia diffusa</i> Roxb	Rubiaceae	Whole Plant	Aqueous extract showed Antiviral activity as well as ant-hMPV activity due to presence of phenolics and flavonoids (Subramaniam <i>et al.</i> , 2012; Kaur <i>et al.</i> , 2023).
<i>Aegle marmelos</i> (L.) corr ex.Roxb.	Rutaceae	Leaf	Leaf extract stimulates immunity and work as hMPV disease resistance (Mondal <i>et al.</i> , 2022).

## Conclusion

Recently medicinal plant derived medicine are receiving increased attention due to the many side effects of chemical and synthetic drugs used for the treatment of respiratory viruses, especially human metapneumovirus. Our study has focused 23 plant species, its bio active



compound such as Kaempferol , flavonoids, alkaloids, rotenone, terpenoids, vanillic acid and phenolic compounds, used to treat hMPV virus that to inhibit RNA polymerase, replication, boost human immunity system and making them useful in fighting hMPV viral infections. It is imperative to screen against hMPV strains due to their prevalence and relatively serious nature. Additionally, the use of plant-extract medicine with anti-hMPV is gaining popularity as an affordable and safe alternative to traditional antiviral medications. This review may highlight the more promising anti-HMPVs for screening.

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## Conflict of interests

The authors state that they have no conflicting interests.

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