



## Original Research Article

## Inhibitory and complementary therapeutic effect of sweet lime (*Citrus limetta*) against RNA-viruses

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## ABSTRACT

Sweet lime (*Citrus limetta*), known as 'Mousambi' or 'Mosambi' in India, is one of the best citrus fruits regarding its nutrient contents. Its bioactive compounds (BAC) are exclusively used for multiple clinical applications considering many therapeutic benefits not only in Asian countries but also in the western world. The fruit pulp and juice are the best sources of ascorbic acid, B-vitamins, amino acids, and other secondary metabolites. Specifically, polyphenols such as flavanones, hesperetin, naringenin, and chlorogenic acid are highly rich in the fruit. The nutrients in sweet lime altogether provide significant anti-inflammatory, antioxidant, anti-cancer, and neuroprotective effects. The purpose of this study is to review and analyze the inhibitory and complementary therapeutic effects of sweet lime's pulp and juices to inhibit the virulence caused by RNA viruses, mainly SARS-CoV-2. This review study was designed based on extensive online searches of relevant open-access literature available in the best quality and reliable databases by using specific keywords and boolean operators. After a rigorous review, we found that flavanones in the fruit can alter or inhibit the polyproteins (pp1a and pp1b) responsible for viral replication. Therefore, sweet lime has potentialities to provide an inhibitory and a complementary therapeutic effect against RNA viruses, mainly SARS-CoV-2. About the antiviral activities, more clinical trials are needed to prove its efficacy; however, reviewing current knowledge, *Citrus limetta* is one of the potent antioxidant, inflammatory fruits available and affordable almost worldwide.

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## 1. Introduction

Citrus fruits are the best sources of ascorbic acid (vitamin C) and secondary metabolites such as phenolic acid, coumarins, carotenoids, flavonoids, alkaloids, limonoids. They are rich in B vitamins, folate, essential minerals, and other bioactive compounds, also. So, the citrus genus is considered one of the best anti-inflammatory, antioxidant, anti-cancer, and neuroprotective agents. In recent days, various citrus fruits are considered for extensive research to determine their effects on complementary medicine and chemotherapy applications. Six Citrus species have already been included in the respective pharmacopeia of many countries, mainly China, Japan, Korea, Indonesia, Nepal, Bhutan, and India.<sup>1</sup>

## 1.1. Properties of citrus fruits

The citrus fruits are popular due to their sensory attributes: taste, color, and astringency. Hence, their organoleptic properties altogether attract many consumers apart from their antioxidant and immuno-protective roles. In general, they can help in cough and cold, indigestion, ringworm infections, controlling blood pressure, skin and hair health, and managing other inflammations, as well.<sup>2,3</sup>

1.2. Sweet lime (*Citrus limetta*)

This review study focused only on sweet lime (*Citrus limetta*), known as 'Mousambi' or 'Mosambi' in India. Its components are exclusively used for multiple clinical applications considering their various therapeutic benefits not only in Asian countries but also in the western

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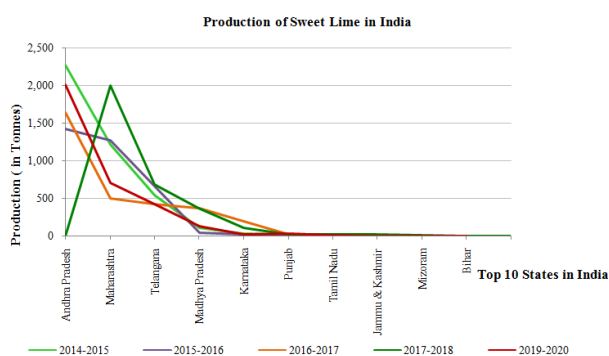
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world. It is regarded as one of the Indian superfoods due to its pharmacological effects. Traditionally, sweet lime has been used to prevent scurvy, skin and hair issues, GI intolerance, constipation, type-II diabetes, ulcers, urinary tract infections, and overall, boosting innate immunity. Earlier studies have shown that there are many effective compounds present in Sweet lime pulp, are responsible for its antioxidant and anti-inflammatory functions. d-limonene is one of these bioactive compounds (BAC) available in sweet lime. It is the principal constituent of Citrus limetta that offers pharmacokinetic and pharmacodynamics properties. Phytochemical analyses show that there are so many essential phytoconstituents like tannins, alkaloids, flavonoids, glycosides, anthraquinones, phenolic, terpenes, saponins, essential oils present in Citrus limetta; around 30 bioactive compounds are identified with the help of mass spectrophotometry, which are available in fruit pulp, juice even in the peel, as per various studies. The main component, limonene in the citrus peel oils, constitutes about 45%-94.6% in concentration out of the total fruit portion.<sup>4-6</sup>

### 1.3. Production of sweet lime

Among all the continents, Europe did the highest business on lemons and limes during 2019, with the shipment value at \$1.5 billion, i.e., 42% of the total in the world market. India and China contribute majorly to lime production worldwide. Andhra Pradesh (~1800 tonnes), Maharashtra (~500 tonnes), and Telangana (~300 tonnes) are the top three sweet lime-producing states in India, sustainable for the last five years in India.<sup>7</sup>

The graphical presentation of the production of Mosambi in India has been showing in Figure 1. India is gradually progressing the production of this fruit due to its high demand.



**Fig. 1:** Production of Sweet Lime based on top 10 states in India since 2014 till 2020. (financial year).

Source: National Horticulture Board (NHB)-Government of India; <https://agriexchange.apeda.gov.in/>

## 2. Materials and Methods

This review study is primarily focused to review and analyze the inhibitory and complementary therapeutic effects of sweet lime's pulp and juice with respect to the RNA virus-neutralizing properties, mainly of SARS-CoV-2. This study was designed and based on rigorous online searches of relevant open-access literature available in best quality and reliable databases such as the National Center for Biotechnology Information (NCBI), mainly Pubmed, Biomed (BMC), Directory of Open Access Journals (DOAJ), and Google Scholar. Keywords and phrases used for online searches: 'virucidal effect of sweet lime (*Citrus limetta*),' 'role of mosambi on RNA viruses,' 'therapeutic action of sweet lime,' 'inhibitory effect of sweet lime.' Other relevant keywords were also applied along with boolean operators OR, AND, NOT.<sup>8-10</sup>

## 3. Discussions

### 3.1. Nutrients and Bioactive components

Sweet lime (*Citrus limetta*) as a citrus fruit is rich in vitamin C and other minerals and plenty of other adequate nutrients that all together provide an inhibitory, complementary therapeutic effect. As per the Indian Food Composition Table-2017 (ICMR-NIN), the fruit's 100 g edible portion contains a good amount of water content (moisture 92 g), both soluble and insoluble fiber (total 2.07 g), and total free sugar 3.42 g. Further, it has a significant amount of folate (15.38 mcg), biotin (2.23 mcg), and Phylloquinone (K1-26 mg). In the categories of vitamins and minerals, almost all the B-vitamins in proportionate quantities, 47 mg ascorbic acid, 26 mg calcium, and a very high amount of potassium, i.e., 202 mg in 100 g edible fruit. As per IFCT-2017, Citrus limetta also rich in good numbers of fatty acids: total PUFA 86 mg, total SFA 78 mg, 68 mg linoleic acid, and 66 mg palmitic acid. Similarly, aspartic acid 20 g, glutamic acid (5.5 g), proline (6.9 g), amino acids are found remarkable. Above all, total polyphenols 117 (+/-12 mg) is highest amongst all the citrus fruits available in tropical countries like India.<sup>11-13</sup>

Table 1 Refers to nutrients and bioactive components (BAC) of sweet lime (*Citrus limetta*).<sup>13</sup>

### 3.2. Indian diets and sweet lime

Indian sweet lime (Mosambi) is under the Rutaceae family is one of the best rich sources of vitamin C, naringin, hesperidin, flavanones, anthocyanins, and other polyphenols that altogether boost immunity, antioxidant, anti-inflammatory, and total health benefits effects. There are various diet patterns across the world, out of which vegetarian, non-vegetarian, and Mediterranean diets are becoming popular in addition to typical Ketogenic, Paleolithic, Atkin, Dukan diets. In India, large numbers of

**Table 1:** Nutrients and bioactive components (BAC) of sweetlime (Citrus limetta)<sup>14</sup>

Nutrients	gram	Nutrients	mg	Nutrients	mg	Nutrients	mg
Energy	28.0	Thiamine	0.06	Ergocalciferol	0.30 mcg	Magnesium	16.0
Protein	0.77	Riboflavin	0.01	Tocopherols (Alpha)	0.07	Manganese	0.04
Ash	0.48	Niacin	0.17	Vitamin -E	0.07	Molybdenum; and Nickel	0.001
Total Fat	0.21	Pantothenic Acid	0.25	Phylloquinone (K1)	2.20 mcg	Zinc	0.05
Total Fibre	2.07	Total B6	0.05	Calcium	26.0	Phosphorus	21.0
Carbohydrate	5.20	Biotin	2.23 mcg	Chromium	0.017	Potassium	202.0
Moisture	92.0	Total Foliates	15.38 mcg	Copper	0.03	Selenium	0.72 mcg
Total CHO	3.95	Total Ascorbic Acid	47.0	Iron	0.11	Sodium	1.17
Total Starch	0.52	Palmitic Acid	66.0	Amino Acids	gram	Amino Acids	gram
Fructose	0.70	Stearic Acid	11.0	Methionine	0.97	Alanine	3.39
Glucose	2.60	Palmitoleic Acid	8.40	Cystine	1.33	Arginine	1.30
Sucrose	0.12	Oleic Acid	27.0	Phenylalanine	1.32	Aspartic Acid	20.0
Total Free Sugar	3.42	Linoleic Acid	68.0	Threonine	1.29	Glutamic Acid	5.5
Histidine	3.40	Alpha Linolenic Acid	17.0	Thryptophan	0.48	Glycine	5.5
Isoleucine	2.12	Total SFA*	78.0	Valine	1.73	Proline	6.9
Leucine	2.66	Total MUFA*	37.0	Serine	3.40	Tyrosine	0.80
Lysine	2.31	Total PUFA*	86.0	Chlorogenic Acid	1.48 mg	Ferulic Acid	0.02 mg
Hesperetin	22.17 mg	Naringenin	1.64 mg	Hesperdin	13.45 mg	Total Polyphenols	117+/-12 mg

[#All values are based on 100 g edible portion of asweet lime]; [gram, milligram, microgram indicated as g, mg, and mcgrespectively]. [\*SFA-saturated fatty acid,\*MUFA-monounsaturated fatty acid, \*PUFA-polyunsaturated fatty acid][Source: Indian Food CompositionTables 2017.National Institute of Nutrition (ICMR). Department of HealthResearch, MoHFW, Government of India]

the population are eithervegetarian or vegan. People from the north and west, and middle parts of India, thoroughly practice vegetarian diet patterns, while Jain people are typically vegan. In the same way, people from the east, north-east, south usually choose a non-vegetarian or ovo-vegetarian diet.<sup>30-32</sup> Whatever the reasons behind diet practice, seasonal Indian fruits effectively combatdifferent lifestyle disorders like obesity, diabetes, and skin or hair issues. Vegetables, fruits, and citrus fruits are rich in bioactive substances such as minerals, polyphenols, and vitamins, including vitamins A, C, D, E. Hence, sweet lime can be named one of the best Indian superfoods due to its all-out potentialities.<sup>33-36</sup>

### 3.3. Pathophysiology of SARS-CoV-2

#### 3.3.1. Structure of SARS-CoV-2

The main focus of this review study is the most concerned RNA virus, SARS-CoV-2, which belongs to Betacoronavirus (genus), Sarbecovirus (subgenus), and Coronaviridae (family). SARS-CoV-2 is the virus that causes COVID-19 (the disease), usually spread by droplets during coughing or sneezing of an infected

person. The COVID-19 or Coronaviruses are enveloped, positive-stranded RNA viruses with spike-like glycoprotein projections on their surface that look like a crown. Several structural and non-structural proteins are encoded in the coronavirus genome. The structural proteins are membrane (M), the envelope (E), and the spike protein (S) in charge of host infection, membrane fusion, viral assembly, morphogenesis, and virus particle release. The non-structural proteins (nsps; 3, 5, 11, 14, and 15) make viral replication and transcription easier.<sup>37-40</sup>

#### 3.3.2. Life cycle of the virus

Attachment, penetration, biosynthesis, maturity, and release are the five processes in the virus's life cycle with its host. Viruses bind to the host receptor by attachment, followed by penetration through membrane fusion or endocytosis. Viral RNA reaches the nucleus for replication when the viral contents are released into the host cells. Similarly, viral proteins are made from viral mRNA, called biosynthesis. As a functional receptor, Angiotensin-converting enzyme 2 (ACE2) was found in various tissues, including lung cells, gastrointestinal tissue, and even the brain. The virus's spike

**Table 2:** A list of all RNA viruses with their structure and tentative role of BioActive Compounds present in sweet Lime. <sup>15-21 22-29</sup>

Family of virus	Names of virus	Layer & symmetry of capsid structure	Type of nucleic acid	Effective BAC	Functions
<i>Arenaviridae</i>	Lymphocytic choriomeningitis virus, Lassa fever	Shape-Enveloped-;Complex	single-stranded (-)	Phylloquinone(K1);- VitaminC	Thrombocytopenia and coagulation defects can be observed. Sweet lime has a good role in this[57-70] virus
<i>Arteriviridae</i>	Arterivirus, equine arteritis virus	Shape-Enveloped-;Icosahedral	single-stranded (+)	Zinc, Vitamin C	Sweet lime can help due to the presence of zinc and vitamin c as immunity-boosting action[56-58]
<i>Astroviridae</i>	Astrovirus	Shape-Naked; Icosahedral	single-stranded (+)	Oral Rehydration Solution, Vitamin C	In diarrhea issue, need ORS, probiotics, and polyphenols including sweet lime juice for hydration and GUT health[59-61]
<i>Bornaviridae</i>	Borna disease virus	Shape-Enveloped; Helix shape	single-stranded (-)	B-Vitamins, mainly B6, Methylcobalamine,	Citrus fruits, pulps, and juices can help Alzheimer's disease due to water-soluble vitamins and other polyphenols[62-69]
<i>Bunyaviridae</i>	Sin-Nombre virus and California encephalitis virus	Enveloped; Helix shape	single-stranded (-)	All vitamins and Polyphenols	Avoidance of animal meats but more fruits and vegetables needed. All phytochemicals & polyphenols are helpful [56-65]
<i>Caliciviridae</i>	Norwalk virus	Shape-Enveloped ;Icosahedral	single-stranded (+)	Enough electrolytes	Stomach Flu condition may affect G.I. Hence, all minerals and polyphenols[62-64].
<i>Coronaviridae</i>	Human Coronavirus: OC43, HKU1, 229E, -NL63, SARS CoV1, and SARS coV2, Middle East Respiratory Syndrome-CoV	Helix shape;- Enveloped	single stranded (+)	Hesperidin,- Hesperetin,- Naringin and other BACs	Helps in immunity-boosting, glucose, and other hormonal functions by vitamin C and polyphenols as available in sweet limes[9-65]
<i>Filoviridae</i>	Marburg virus, Ebola virus,	Helix shape;Enveloped	single-stranded (-)	Potassium, ordinary traditional fortified- foods/Micro-nutrient powder	Requirement of immunity; to avoid hypokalemia, need potassium, and other polyphenols, probiotics. Sweet lime can play a good role as an antioxidant[63-70]
<i>Flaviviridae</i>	Hepatitis C virus, Dengue virus, Yellow fever virus, Zika virus	Shape-Enveloped-;Icosahedral	single-stranded (+)	Electrolytes, Vitamin C, Polyphenols Delphinidin,- Epigallocatechingallate	Apart from enough water, sweet lime and other citrus fruits juices are helpful due to the high amount of polyphenols 56,65
<i>Hepeviridae</i>	Hepatitis E virus	Shape-Naked; Icosahedral	single-stranded (+)	Adding more vitaminD, avoiding red meats, high fat	All vegetables, fruits including sweet lime, are helpful but not excess iron foods 64-66
<i>Orthomyxoviridae</i>	Influenzavirus A, Influenzavirus B, Influenzavirus C, Isavirus, Thogotovirus	Helix shape;Enveloped	single-stranded (-)	High protein foods rich in essential amino acids	All good quality protein, vegetables, fruits rich in polyphenols, including sweet lime having antioxidant effects.66,68
<i>Paramyxoviridae</i>	Canine distemper virus (CDV), Respiratory syncytial virus (RSV), Measles and Mumps virus, and Rinderpest virus (RV.)	Helix shape;Enveloped	single-stranded (-)	Vitamin C, All polyphenols like Resveratrol, - Quercetin- Hesperidin,- Hesperetin, Naringin	Need of good innate immunity and healthy dietary habits. Plenty of water, electrolytes, citrus juices, including sweet lime helpful. Milk, good quality ghee, butter may help at home dietary management 64-68
<i>Picornaviridae</i>	Enterovirus, Rhinovirus, Hepatovirus, Cardiovirus, Aphthovirus, Poliovirus, Parechovirus, Erbovirus, Kobuvirus, Teschovirus, Coxsackie-	Shape-Naked; Icosahedral	single-stranded (+)	Fresh foods and hygiene mandatory	Polyphenols, fresh boil vegetables rich in B Vitamins. Home-made food is recommended 65-69

<i>Reoviridae</i>	Rotavirus and Reovirus	Shape-Naked; Icosahedral	double-stranded	A low casein diet is recommended	Avoidance of bovine milk for high Casein protein due to intolerance. However, citrus fruits are not having issues 62,71
<i>Rhabdoviridae</i>	Vesicular stomatitis (VSV), Rabies virus (RV.)	Helix shape; Enveloped	single-stranded (-)	Cutellarein, Silvestrol, Tryptanthrin, Caffeic acid, Quercetin, Myricetin,	These polyphenols provide antiviral activity by maintaining concentrations below the toxic plasma level 65-72
<i>Togaviridae</i>	(EEEV) - Eastern Equine encephalitis	Icosahedral; -Shape -Enveloped	single-stranded(+)	B-Vitamin and proper hygiene, drinking water	Best nutritional recommendation for brain health through vitamins, protein, and fruit juices is needed for polyphenols and phytochemicals. 65-70

glycoprotein mediates SARS-CoV-2 internalization to its receptor (ACE2) on cell membranes of the organs in the human body.<sup>41-45</sup>

### 3.3.3. COVID-19 Inflammatory markers

Gao et al., 2020 discussed in their paper that COVID-19 is dependent on inflammatory mediators. Its replication causes inflammatory responses in cells, macrophages, and the release of cytokines. Several inflammatory markers can be used to identify and detect disease specificity. Inflammatory markers like procalcitonin (PCT), serum ferritin, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), interleukin-6 (IL-6), and serum amyloid A (SAA) have been correlated to a higher risk of COVID-19.<sup>45-49</sup>

### 3.3.4. Phospholipid and functional enzymes

Abdalla et al. 2020 reviewed in their article that the primary components of the pulmonary surfactant are phospholipids, with phosphatidylcholines (PCs) being the most common. COVID-19 infection caused an increase in cytosolic phospholipase A2 (cPLA2) expression, resulting in phosphatidylglycerol depletion and cleavage of esterified fatty acids. It also increases inflammation and lung damage. Secretory phospholipase A2 (sPLA2) is another enzyme involved in eicosanoid synthesis. Monocytes, macrophages, neutrophils, and eosinophils increase and produce inflammatory substances like cytokines and chemokines.<sup>47-51</sup>

### 3.3.5. RNA mechanism and infection process

The viral particle gets entered into a small structure outside or inside a cell of the human body. The vesicle's envelope is removed due to the viral particle and welcomes the genomic RNA that usually gets released into the cytoplasm. The two types of Open Reading Frame, also called ORF1a and ORF1b RNAs, are produced by the genomic RNA, followed by the translation into polyproteins of the virus (pp1a and pp1b). After this stage, a proteolytic process operated by viral enzymes breaks down the pp1a and pp1b proteins. The action results in a total of 16 non-structural proteins. In contrast, some non-structural proteins form a

transcription or replication complex (RNA-dependent RNA polymerase) that uses genomic RNA positive (a typical model). Subgenomic RNAs produced through transcription are structural proteins after translation, will form new viral particles.<sup>43</sup> When the viral load is high, cell is infected with many viral particles. As a result, the cell's entire protein synthesis machinery is devoted to viral replication before the cell dies. The final step may be triggered by the "apoptosis" process (if death is slow and controlled) or by "energetic-metabolic chaos," which results in the breakdown of cell membranes, including lysosomes, and a complete loss of structural integrity. T-lymphocytes and antibodies may strike the infected cell and autoimmune phenomena.<sup>52-55</sup>

### 3.4. Role of bioactive compounds in sweet lime towards RNA viruses<sup>56-62</sup>

This short review draws attention to some constituents of sweet lime (*Citrus limetta*) for their multivitamin and flavonoid content. Among the flavonoids, hesperidin has the most crucial role.

#### 3.4.1. Hesperidin

Hesperidin is a plant-sourced pigment, a flavanone glycoside found in almost all citrus fruits, and plays a tremendous antioxidant activity. Out of total polyphenols, its contribution is maximum (13.45 mg) in 100 g edible mosambifruit pulp or fruit juices. This compound so far has attracted the attention of many researchers because of its binding capacity to the spike protein and protease of the RNA viruses, including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It alters the polyproteins of the virus (pp1a and pp1b) into the complex genomic structure responsible for viral replication. A study showed that hesperidin and ascorbic acid inhibit or slow down the formation of free radicals and reduce infections and inflammation. Hence, it is one of the best components in the fruit.<sup>57-60</sup>

In COVID-19 patients, there is a possible chance that hesperidin interacts better with the SARS-CoV-2 protease. However, other lime flavonoids with lower binding

energy (compared to the reference ligands, lopinavir, and nafamostat) to the three essential proteins, such as tangerine, naringenin, and nobiletin, also have low binding. However, considering the mode of action of this BAC, mosambi whole fruit or juice may be helpful towards RNA virus infections.<sup>55-59</sup>

#### 3.4.2. Naringenin and naringin

Naringenin is the metabolite of naringin and anaglycone. Naringenin is present in pure juice, whereas naringin is in citrus juices. Naringin is a glycoside under the flavanone group. It contributes in mosambi 1.64 mg in 100 g edible fruit pulp or fruit juice out of total polyphenols. There is a difference between these two flavanones that the sugar moiety in naringin induces steric hindrance of the scavenging community, making it less potent than naringenin. The water solubility of naringin is mild, so in the intestine, the gut microflora converts naringin to its aglycon naringenin, which is better absorbed. Naringin in sweet lime (*Citrus limetta*) is metabolized in the proximal colon by GUT microbiota as good bacteria with the production of their hesperetin, aglycones, other phenolic compounds. Studies have also shown that intestinal flavonoids and their metabolites regulate the constituents and activity of the intestinal bacteria, which ultimately results in sound physiological effects in the GI tract. Overall the compounds have a highly decisive inhibitory role against RNA virus infections.<sup>61-64</sup>

#### 3.4.3. Hesperetin

Hesperetin is the flavanone group found abundantly in all citrus, including sweet lime. The fruit's 100 g edible portion contains 22.17 mg of this flavanone, one of the best bioactive compounds responsible in mosambi fruit or juice for its potent antioxidant activities. Hesperetin and its metabolites play a critical role in reducing inflammatory conditions through various anti-inflammatory pathways in the human body. Glycosidic hesperetin, also called hesperidin, provides significant responses to the anticarcinogenic effect. Further, hesperetin administration resulted in higher expression of various detoxifying enzymes in rat models of chemically induced colon cancer and rat models of lung cancer. In rat hepatocytes, hesperetin prevented bile acid-induced apoptosis and cytokine-induced inflammation. TUNEL assay and serum AST and ALT levels revealed that hesperetin improved liver histology and protected against hepatocyte injury.<sup>65,66</sup>

#### 3.4.4. Chlorogenic acid

CGA is a group of phenolic secondary metabolites formed by some plant species and is an essential component of coffee. It is one of the most abundant polyphenol compounds in the human diet. Antibacterial, antioxidant, and anticarcinogenic effects are just some

of the biological properties of CGA. Its functions and applications, especially about glucose and lipid metabolism, have recently received increased attention. CGA inhibits the activity of  $\alpha$ -glucosidase, G-6-pase expression, and HMG COA reductase. Hence, its various essential functions may help COVID-19 and its comorbid patients. The most crucial parts are lipid profile alterations by balancing lipoproteins, enzymes involved in lipid metabolism, fat absorption inhibition, and activation of fat metabolism in the liver. Further, it plays a significant role in reducing the susceptibility of LDL oxidation and decreasing LDL cholesterol. Well-controlled secretion of insulin, improving glucose tolerance and resistance. Hence, it has one of the best practical hypoglycemic and antidiabetic effects through mosambi or other citrus fruits for any RNA virus-infected patients.<sup>65-67</sup>

#### 3.4.5. Ferulic acid

Out of total polyphenols in sweet lime, although ferulic acid is found (0.02 mg) in minimal quantities, it also plays remarkable inhibitory and anti-inflammatory roles against viral diseases. It acts inside the fruit as a potent antioxidant, antimicrobial, antiallergic, hepatoprotective, anticarcinogenic, antithrombotic, increases sperm viability, antiviral, and vasodilatory actions, metal chelation, regulation of enzyme activity, activation of transcriptional factors, gene expression, and signal transduction are just some of the biological activities.<sup>65-69</sup>

#### 3.4.6. Zinc

Zinc is an essential element for all people of different ages. Although it is deficient in sweet lime, it still helps in cognitive impairment, growth, neurosensory disorders, hyperammonemia, and immunity. A study showed that zinc enhances serum testosterone level, oligospermia by improving T-cells function.<sup>69-72</sup>

## 4. Conclusions

Sweet lime (*Citrus limetta*) is one of the best citrus fruits having almost all vitamins, minerals, amino acids, fatty acids, and polyphenols. It has the 2<sup>nd</sup> highest total polyphenols, with a high amount of potassium among citrus groups. Hence, considering multiple nutrients and plenty of bioactive compounds, it is usually a potent antioxidant. In general, sweet lime pulp and juice can be consumed regularly for their inhibitory and complementary therapeutic effect against RNA viruses, including SARS-CoV-2, except for chronic kidney diseases or other critical health issues. More clinical trials are needed to prove its efficacy; however, reviewing current knowledge, it is one of the potent antioxidant, inflammatory super food available and affordable almost worldwide.

## 5. Source of Funding

None.

## 6. Conflict of Interest

None.

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