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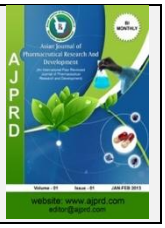

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Review Article

Phyllanthus Emblica as A Preventive Supplement for Viral Pandemic: From Traditional Use to Clinical Research

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A B S T R A C T

Phyllanthus emblica Linn., commonly known as Indian gooseberry or Amla, is one of the most valued medicinal plants in traditional Indian medicine systems such as Ayurveda, Unani, and Siddha. It is rich in vitamin C, polyphenols, alkaloids, and tannins, which contribute to its diverse pharmacological properties including antioxidant, immunomodulatory, anti-inflammatory, antiviral, hepatoprotective, cardioprotective, and antidiabetic activities. Recent studies have demonstrated that bioactive compounds such as phyllaemblicin B, phyllaemblinol, and phyllaemblicin G7 exhibit strong binding affinities to key SARS-CoV-2 proteins, suggesting potential therapeutic value in viral infections. Traditional and modern pharmacological evidence highlights Amla efficacy in enhancing immunity and managing disorders like respiratory infections, diabetes, cardiovascular disease, and oxidative stress-related conditions. A randomized controlled clinical trial in COVID-19 patients revealed that adjunct therapy with Amla significantly reduced hospital stay, improved oxygen saturation, and alleviated symptoms such as fever, cough, and shortness of breath, without adverse effects. These findings substantiate its role as a safe and effective preventive supplement during viral pandemics. However, larger multicentric trials and mechanistic studies are needed to validate its clinical efficacy and establish dosage guidelines. This review compiles traditional knowledge, phytochemical composition, pharmacological activities, and clinical research evidence on Phyllanthus emblica to explore its potential as a preventive and therapeutic supplement for viral pandemics.

KEYWORDS: Phyllanthus emblica, Amla, Fruit, COVID-19, SARS-CoV-2, Herbal medicine.

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INTRODUCTION:

Mother Nature has given humans amazing medicinal herbs to help them live healthy, disease-free lives. Indian gooseberry, or Amla, also known as Phyllanthus Emblica Linn, is one of the many therapeutic plants utilized in traditional Indian medical systems (such as Ayurveda, Unani, and Siddha). In Ayurvedic and Unani medicine, (Syn. Emblica officinalis Gaertn.) is a significant medicinal herb that is a member of the Euphorbiaceous family. It is widely used as a tonic to replenish the body depleted vitality and energy. Growing in South East Asia, China, India, Pakistan, Uzbekistan, and Malaysia, amla is a small to medium-sized deciduous tree. Its thin, light grey bark increases its height by 8 to 18 meters. Its simple, light green, sub-sessile leaves, which are closely spaced along the branchlets and resemble pinnate leaves, have greenish yellow flowers. Its globose, meaty, pale-yellow fruits have six vertical furrows that are buried and contain six trigonous seeds in crustaceous cocci that have two or three seeds. A very nutrient-dense food, amla is one of the best providers of minerals, amino acids, and vitamin C.Numerous chemical components, including phenols, alkaloids, and tannins, are present. The hydrolysable tannins that are thought to have biological activity are gallic acid, ellagic acid, and emblicanin A and B. Particularly, the fruit has therapeutic properties and has been used to treat diarrhoea, jaundice, inflammation, and a variety of other ailments in traditional medicine and Ayurveda as a strong rasayana.Amla fruit is widely used as a diuretic, laxative, liver tonic, refrigerant, stomachic, restorative, and hair tonic in the four

Indian medicinal systems. It can be taken either by itself or in combination with other herbs to avoid ulcers and dyspepsia, treat fever and the common cold, and more. In addition to Pharmacological research on Amla shows that it contains analgesic, anti-tussive, anti-atherogenic, and adaptogenic qualities in addition to its cardio, gastro, nephro, and neuro qualities. Twelve preventive and thirteen anti-cancer properties. Also, it has been observed that amla has immunomodulatory, chemopreventive, radio, chemo, antioxidant, anti-inflammatory,and anti-mutagenic properties. These qualities work well to prevent and treat a number of illnesses, including cancer, heart disease, liver disease, atherosclerosis, diabetes, peptic ulcers, anaemia, and many more. Byfocussing on the processes behind the activities and illuminating the therapeutic applications and clinical studies, the current work aims to comprehend the nutritional value, traditional usage, biochemical ingredients, and significant medicinal qualities of amla. Additionally, it summarises the findings of the last five yearsworth of study on amla and identifies the areas that need more investigation to determine its efficacy and application in a number of illnesses(1).Through the droplets released during coughing, sneezing, or talking, the new coronavirus transmits from person to person. New infections are brought on by sick individuals exhaled droplets entering the lungs of others. If people touch the contaminated surfaces with unwashed hands and then touch their faces, the droplets can spread the infection. Even though sputum and saliva are important viral carriers, new research indicates that the disease may spread through the mouth and faeces.Additionally, the aerosol-generating processes (AGPs) make virus transmission easier than usual (2). It is a common medicinal plant in Ayurvedic, Unani, and folk medicine. Additionally, the Rigveda, which is said to be the oldest collection of human knowledge, makes reference to it. It boosts immunity against illnesses, according to the Ayurvedic medical system. When taken in dietary forms, Indian gooseberry appears to be safe for the majority of individuals. It can also be used as a supplement to support immunity and prevent viral illnesses (3).Herbal Ayurvedic medications may be useful in both preventative and therapeutic therapy of the SARS CoV-2 (Covid-19) coronavirus. In addition to pneumonia, disseminated intravascular coagulation (thrombosis) may also be a cause of COVID-19; as a result of this thrombosis, the lungs are most affected because they are the most inflamed, but there are also heart attacks, strokes, and numerous other thromboembolic diseases that may primarily cause pulmonary thrombosis or thromboembolism (4).After acute pneumonia cases were recorded in Wuhan, China, in 2019, the cause was identified as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), a novel enveloped RNA beta coronavirus. COVID-19 rapidly became a deadly pandemic that killed a lot of people between December 2019 and August 2020. The WHO announced a Public Health Emergency of International Concern in January 2020. A zoonotic origin in the Huanan seafood market was suggested by the 96.2% similarity between bat-CoV and SARS-CoV-2 found in genome sequencing, with pangolins and civets thought to be potential intermediate hosts. While control techniques decreased R0 below 1, human-to-human transmission, which had a R0 of 2.20 to 3.70, was a major factor in the virus proliferation. On March 11,2020, the WHO declared COVID-19 a pandemic following reports from over 200 countries (5).

Figure 1: Phyllanthus Emblica.

HISTORY:

For centuries, Amla has been employed to treat and cure various diseases. It is considered as a precious gift of nature and one of the best herbal medicines in traditional medicine. Minerals, vitamins, and other organic substances. The process of producing Emblica was recorded in Sanskrit during the 1st century AD. Arabic, Tibetan, and Egyptian books, the Siddha (Indian), Ayurvedic, and Unani systems of medicine, all mention the use of Emblica for remedy. Fresh and dried fruit, seeds, leaves, and roots, bark, and flowers of the plant are used. The amla fruit is praised for its cooling and dry, light nature according to the Ayurvedic system of medicine. In India, the fruit is generally eaten the pickled way (6).

CLASSIFICATION:

TAXONOMICAL CLASSIFICATION:

Table 1: TaxonomicalClassification of Phyllanthus emblica (7), (8),(9)

Kingdom	Plantae
Division	Angiospermae
Class	Dicotyledons
Subclass	Rosidae
Order	Geraniales
Family	Euphorbiaceae
Genus	Emblica
Species	Officinalis Gaertn

VERNACULAR NAMES:

Table 2: Vernacular Names of Phyllanthus emblica (7), (8)

English	Indian Gooseberry
Marathi	Anvala
Sanskrit	Amalaki
Hindi	Amla
Gujarati	Ambala

MORPHOLOGY:

The amla tree is a deciduous tree that is small to medium in size and usually reaches a height of 8 to 18 meters. Its younger, lighter-colored surface is exposed beneath the older bark when its thin, light-grey bark exfoliates in tiny, irregular flakes. About 70 cm is the diameter of the primary stem. There are usually two to seven sections to the main trunk.scaffolds towards the bottom. The pinnate faishonleaves are densely packed and measure 10–13 mm in length by 3 mm in width, giving the branches a fluffy appearance. After the fruits set, leaves appear. Clusters of six to ten flowers are produced on the leaf axils, and the flowers are unisexual, 4 to 5 mm long, and pale green in colour. Fruits weigh 5.3–5.7 g, with a volume of 4.5–5.0 mL, a diameter of 2.1–2.4 cm, and a juicy, almost globose form. Each of the three segments that make up the fruit six-ribbed stone typically contains two seeds that are 4-5 mm long, 2-3 mm wide, and weigh between 572 and 590 mg (7).

PLANTING AND DESCRIPTION:

Amla is often grown from seeds, however trees produced from seeds have a lengthy gestation time and produce lower-quality fruits. Budding of shields is done on large fruits are produced by one-year-old seedlings whose buds were taken from superior strains. By top working, older trees of lower kinds can be revitalised and readily transformed into excellent varieties. In May and June 1 m^3 trenches are constructed

with a 4.5 m spacing between them, and they should be kept in the sun for 15 to 20 days. Before planting the grafted seedling, fill each hole with surface soil that has been combined with one kilogramme of superphosphate and fifteen kilogrammes of farm yardmanure (10). Tree with alternating, bifurcated, pinnate leaves that produce flowers;leaflets that are whole, alternating, linear-obtuse, and abundant; spherical, striated petioles; 6-parted calyx; blossoms in the Males are more prevalent in the lower leaflet axils and around the common petiole underneath the leaflets, whereas females are scarce, solitary, sessile, and occasionally combined with males in the outermost floriferous axils; Three stigmas; a globular, fleshy, smooth, six-striated drupe; an obvate-triangular, three-celled nut; two seeds per cell; and tiny, greenish-yellow flowers. In October, flowers bloom (10).

GEOGRAPHICAL DISTRIBUTION:

India, China, Indonesia, Burma, and the Malay Peninsula are among the many tropical and subtropical nations where Phyllanthus emblica is frequently found. Tropical regions are where it originated. Southeast Asia, specifically the Malaccane Islands, Bangladesh, Bhutan, Pakistan, Nepal, central and southern India, and Sri Lanka. It is widely distributed in Madhya Pradesh deciduous woodlands. Madascar was the original location of its cultivation. Pakistan, Sri Lanka, Uzbekistan, Malaysia, Ceylon, Indonesia, and a few more nations throughout the world are other places where it flourishes. Amla can be found growing in plains, on hill slopes up to 200 meters, and in coastal locations. It is a potential crop which grows in the marginal soils andVarious kinds degraded lands such as salt affected soils, Salines and dry and semi-dry regions. An acre can also support roughly 200 trees when growing an orchard (11).

PHYTOCHEMISTRY:

It has been discovered that Amla has a rich phytochemistry that is dispersed throughout the plant- fruits, leaves, and roots. The main class of secondary metabolites consists of polyphenols, from which several substances of phenolic acids, flavonoids, tannins, other phenolics, and their derivatives were identified in different studies. Regarding phenolic acids, hydroxybenzoic acids (4-hydroxybenzoic acid, coumaric acid, gallic acid, protocatechuic acid, syringic acid, and vanillic acid) were identified in fresh fruit and commercial products obtained from the fruits. Gallic acid is the only hydroxybenzoic acid found in leaves and branches. Hydroxycinnamic acids were identified as caffeic acid and chlorogenic acid and found to be present only in amla fruits. Flavonoids represent another chemical class present in amla plants. In more detail, the classes of flavonols, flavones, flavanones, and flavan-3-ols have been identified in various parts of the amla plant. Flavonols are extensively distributed in the different parts of the amla plant. Kampferol and its derivatives such as dihydrokaempferol, kaempferol 3-b-dglucopyranoside, kaempferol 3-o-rhamnoside, kaempferol-3-o-α-l-(6-ethyl)-rhamnopyranoside, and kaempferol-3-o-α-l-(6-methyl)-rhamnopyranoside, have been identified in the fruits, leaves, branches, and shoots. Similarly, quercetin and its derivatives, as quercetin 3-b-D-glucopyranoside, quercetin 3-O-glucoside, quercetin 3-O-rhamnoside, and rutin, have shown the same distribution in fruits, leaves, and branches. Fresh fruits and fruit commercial products contain the flavones apigenin, luteolin, and myricetin. Myricetin 3-O-rhamnoside was identified only in leaves and branches of the amla tree. Interestingly, flavanones and flavan-3-ols were found only in leaves and branches. The flavanones that have been identified included eriodictyol and naringenin along with their derivatives ((S)-eriodictyol Amla leaves and branches are the primary source of hydrolysable tannins (1,2,3,4,6-penta-O-galloyl-β-D-glucose, 1,2,3,6-tetra-O-galloyl-β-D-glucose, and 1,2,4,6-tetra-O-galloyl-β-D-glucose) and phlorotannins (2-(2-methylbutyryl) phloroglucinol 1-O-(6-O-β-D-apiofuranosyl)-β-D-glucopyranoside).Tannic acid, which was found in amla fruit, is an exception. Furthermore, reports of other phenolics in amla fruit included 2,4-di-tert-butylphenol and Phenol, 3,5-bis (1,1-dimethylethyl)). Furthermore, amla was found to contain alkaloids, namely phyllantine and phyllantidine (12).

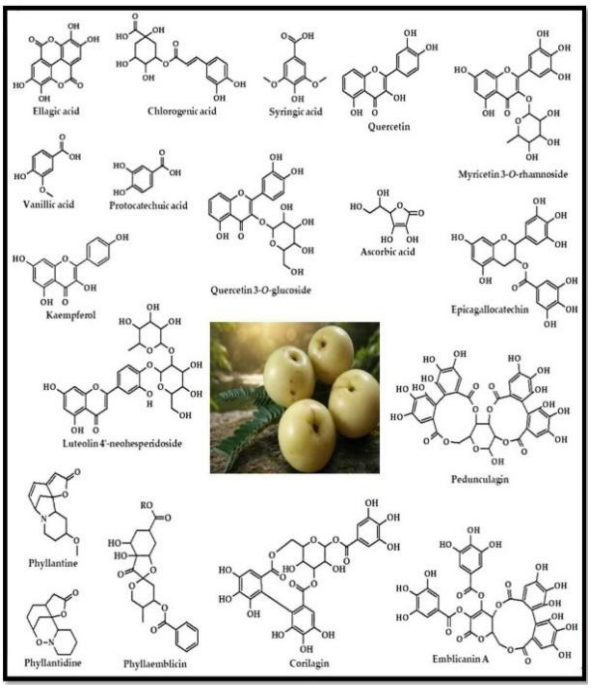

Figure 2: Main phytochemical components in Phyllanthus emblica

CHEMICAL CONSTITUENTS:

One of the most researched plants is amla. It is said to include phenols, alkaloids, and tannins. Of the tannins found throughout the plant, 28% are found in the fruits. The fruit contains two hydrolysable tannins, Emblicanin A and B, which have antioxidant qualities. Gallic acid, ellagic acid, and glucose are produced when one of the tannins is hydrolysed, while the other yields ellagic acid and glucose. There is also Phyllemblin in the fruit. Activity-directed fractionation identified a number of phytochemicals, including geraniin, furosin, corilagin, and gallic acid. Alkaloids like phyllantine and phyllantidine are present, as are flavonoids like quercetin. Its fruit juice has the greatest vitamin-C concentration. More vitamin C is present than in oranges, tangerines, and lemons (1).

Table 3: Amla Fruit (Phyllanthus emblica) Chemical Constituents (1)

Type	Chemical Constituents
Hydrolysable Tannins	Emblicanin A and B, Punigluconin, Pedunculagin, Chebulinic acid (Ellagitannin), Chebulagic acid (Benzopyran tannin), Corilagin (Ellagitannin), Geraniin (Dehydroellagitannin), Ellagotannin
Alkaloids	Phyllantine, Phyllembein, Phyllantidine
Amino acids	Glutamic acid, Proline, Aspartic acid, Alanine, Cystine, Lysine
Phenolic compound	Gallic acid, Methyl gallate, Ellagic acid, Trigallayl glucose
Vitamins	Ascorbic acid
Carbohydrates	Pectin
Flavonoids	Quercetin, Kaempferol
Organic acids	Citric acid

ECHANISM OF ACTION:

Phyllanthus emblica with its immunomodulatory qualities, Phyllanthus emblica may also help the community immunity and general health in the fight against SARS-CoV-2 infection. High binding affinities were demonstrated by Phyllaemblicin-B and Phyllaemblinol from Phyllanthus emblica to the helicase protein, one of the main targets of COVID-19. Phyllaemblicin G7 from Phyllanthus emblica shown a strong affinity for the COVID-19 Spike Protein. For Phyllanthus emblica to have a therapeutic effect, its anti-inflammatory and anti-oxidative qualities are essential (13).

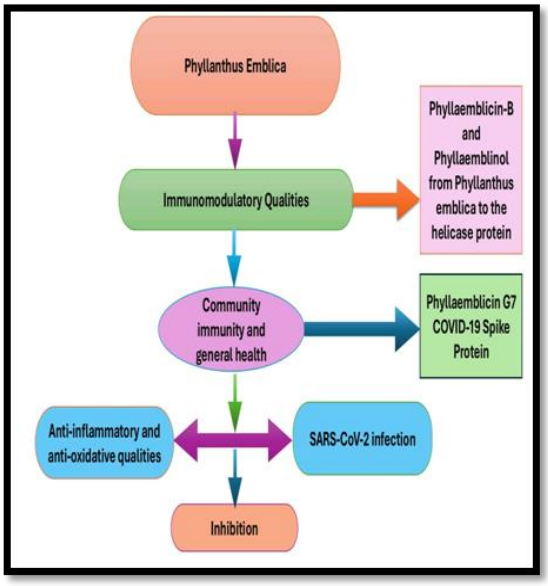

Figure 3: Mechanism of action of Phyllanthus emblica

PHARMACOLOGICAL ACTIVITY:

Immunomodulatory Activity & Immunity Enhancer:

A component that has the ability to alter both innate and adaptive immune responses is known as an immunomodulator. Bioactive chemicals from medicinal plants have garnered increasing attention recently for their potential to modulate the immune system. A natural immunological reaction to infections, inflammation promotes tissue healing and repair. However, pain, tissue damage, and functional impairment can result from severe inflammation. Because it raises blood levels of CD4, CD8, CD16, CD19, IgM, IgG, albumin, and globulin, Phyllanthus emblica improves the efficacy of the immune system. The greatest notable immunological improvement was observed in the experimental groups treated with P. emblica at 250 mg/kg b.wt. Its aqueous fruit extract dramatically increased the antibody titer, leukocyte count, lymphocyte percentage, and delayed hypersensitivity in mice, demonstrating dose-dependent immunomodulatory effects in albino rats (100–200 mg/kg for 19 days) (14). Because of its exceptional antibacterial strength, P. emblica can be used to combat infections, causing resistance to pathogens and boosting immunity. Chromium (VI) was employed as an immune suppressor to assess P. emblica immuno-modulatory characteristicsThefindings demonstrated that P. Emblica not only reduces the inhibitory effect of chromium (VI) on lymphocyte proliferation, but also prevents apoptosis and DNA fragmentation (15).

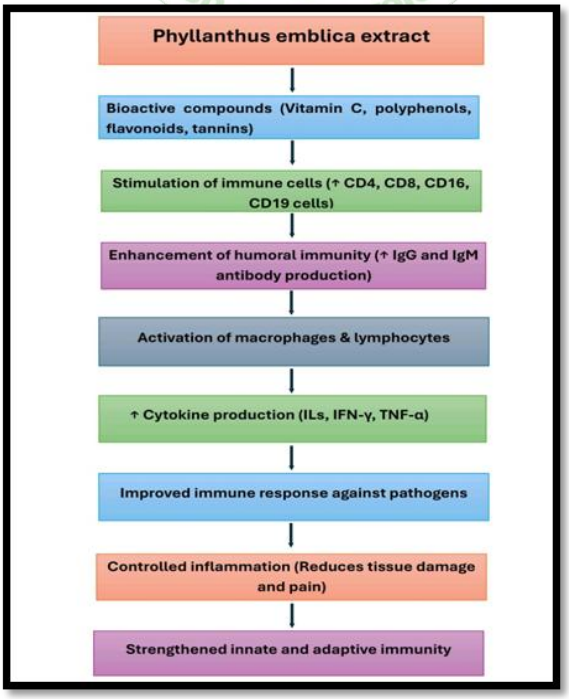

Figure 4: Immunomodulator Activity of Phyllanthus emblica

ANTIVIRALACTIVITY:

Phyllanthus emblica with its immunomodulatory qualities, Phyllanthus emblica may also help the community immunity and general health in the fight against SARS-CoV-2 infection. High binding affinities were demonstrated by Phyllaemblicin-B and Phyllaemblinol from Phyllanthus emblica to the helicase protein, one of the main targets of COVID-19. Phyllaemblicin G7 from Phyllanthus emblica shown a strong affinity for the COVID-19 Spike Protein. For Phyllanthus emblica to have a therapeutic effect, its anti-inflammatory and anti-oxidative qualities are essential (13). It has been shown that P. emblica prevents herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) infection in vitro by directly blocking HSV-1 particle entry using viral attachment and penetration at an earlier stage. Additionally, it suppresses HSV-1 intracellular proliferation for a considerable amount of time after infection. Chemical components that were separated from P. Emblica root demonstrated potent anti-coxsackie virus action in an in vitro investigation. P. emblica sesquiterpenoid glycoside has possible anti-hepatitis B virus (HBV) properties, particularly against the HBV surface antigen (HBsAg) and HBV excretion antigen (HBeAg) secretion. P. Emblica shown antiviral efficacy against EV71 and H3N2 in addition to these viruses (16).

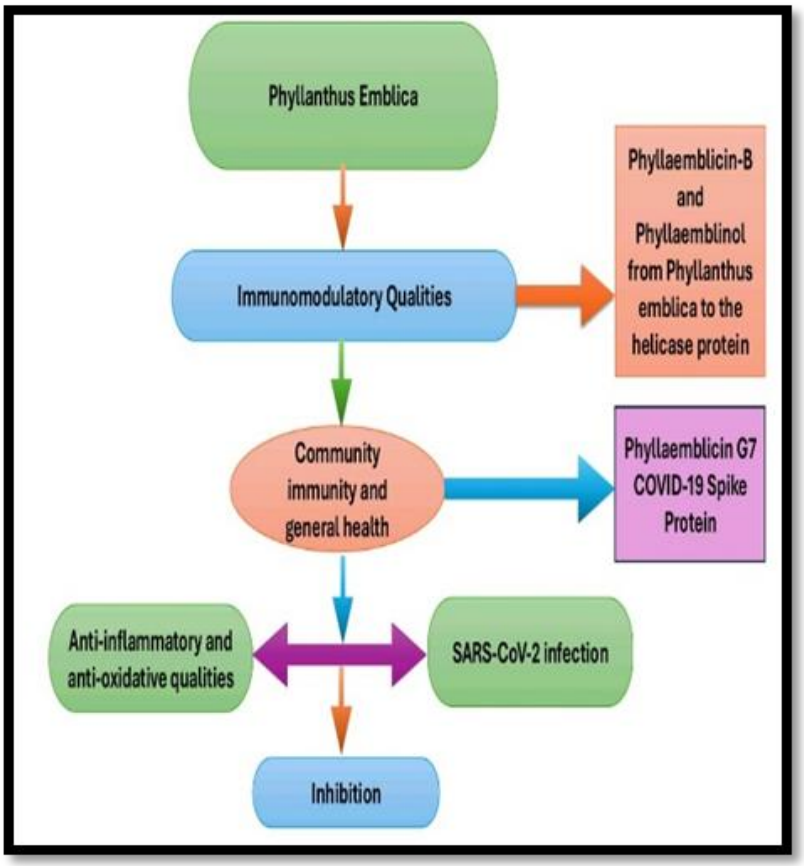

Figure 5: Antiviral Activity of Phyllanthus emblica

ANTI-INFLAMMATORY ACTIVITY:

The body essential innate immunological reaction to outside stimuli, such damage or pathogen infection, is inflammation.This vital immunological function aids in the bodyability to heal from injury. Inflammation is thought to be advantageous since it aids in recovery, repair, and protection against stress brought on by infections and dangerous situations. Acute and chronic inflammation are two categories for the intricate biological reactions involved. The body is protected by acute inflammation, which repairs wounds and stops microbes from invading, but chronic inflammation harms essential cells, molecules, and organs, which leads to conditions like cancer, diabetes, inflammatory bowel disease, neurological issues, cardiovascular disorders, and muscle inflammation. Moreover, chronic inflammation hastens the ageing process. Nitric Oxide and COX-2 are strongly and dose-dependently inhibited by fruit extracts from Phyllanthus emblica. Oxidative stress, inflammation, and cardiovascular damage can result from the overproduction of NO, a crucial immunological signalling molecule. P. emblica ethanolic extract (95%) showed greater NO inhibition (49.1%) at 50 and 100 µg/mL than commercial extracts and hot water in LPS-stimulated RAW264.7 cells. Additionally, the COX-2 inhibition was stronger, peaking at 46.4% at 10 µg/mL. Inhibiting COX-2 aids in managing inflammation in a number of illnesses. By decreasing the activity of the COX-2 enzyme and preventing macrophages from producing NO, P. emblica reduces inflammation. Its anti-inflammatory activity is mediated by the inhibition of important inflammatory enzymes, including COX-1, COX-2, and 5-LOX, which are essential for thesynthesis of proinflammatory mediators. P. emblica has the potential to be used therapeutically to manage inflammatory diseases since it suppresses them, which lowers inflammation (14).

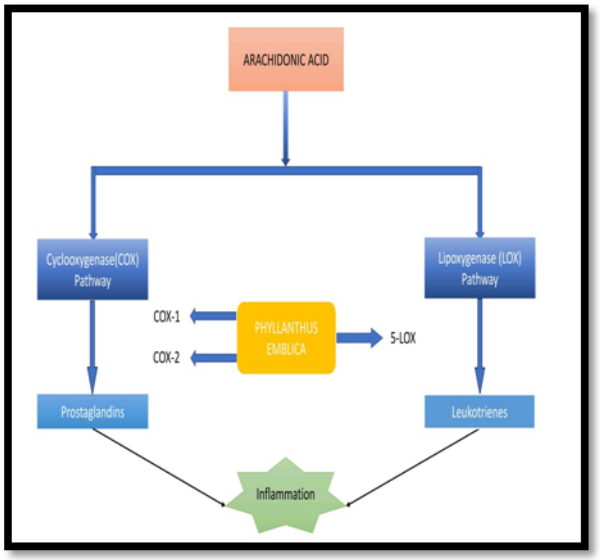

Figure 6: Anti-inflammatory Activity of Phyllanthus emblica

HEPATOPROTECTIVE ACTIVITY:

The accumulation of hepatic steatosis that is not caused by excessive alcohol intake is known as non-alcoholic fatty liver disease (NAFLD), one of the most common chronic liver illnesses. It is closely linked to metabolic syndrome. A rich source of gallic acid and numerous other well-known medicinal phytochemicals and acids is Phyllanthus emblica. In vitro, Phyllanthus emblica fruit has the ability to reduce liver fibrosis and hepatic steatosis. Additionally, it has been demonstrated in vivo that the gallic acid content improves oxidative stress, hepatosteatosis, and dyslipidaemia brought on by a high-fat diet (HFD). A study was started by Huang et al. with the goal of assessing the hepatoprotective impact of P. emblica L. fruit aqueous extract (WEPE) on NAFLD in an animal model. In rats given a high-fat diet, WEPE was found to dramatically lower body weight, peritoneal fat, and epididymal fat. It also increased antioxidant enzyme activities and improved steatosis by raising adiponectin in adipocytes, PPAR-α in the liver, and SREBP-1c in the liver. WEPE may be able to lessen hepatic fat deposition because of this. These results demonstrated that WEPE might be useful in the treatment of steatosis brought on by an HFD(14).

CARDIOPROTECTIVE ACTIVITY:

The antioxidant impact of bioactive tannoid principles of E. officinalis was investigated in a study on oxidative stress in the rat heart caused by cardiac ischemic reperfusion. Using an aqueous methanol fraction, an emblicanin A and emblicanin B enriched fraction of fresh juice of E. officinalis fruits was extracted and employed for testing in this investigation. During the 14 days leading up to the perfusion tests, the extract of E. officinalis and vitamin E were taken orally twice a day. According to the findings, E. officinalis significantly counteracted the effects of ischemia-reperfusion on the activity of key antioxidant enzymes, including glutathione peroxidase (GPX), catalase (CAT), superoxide dismutase (SOD), and lipid peroxidation (LPO). According to this study, E. officinalis antioxidants may have cardioprotective properties (17).

RADIOPROTECTIVE ACTIVITY:

Emblica officinalis extract has been shown to lessen radiation sickness symptoms and death in mice given it prior to exposure to varying gamma radiation dosages. When comparing subsequent triphala-treated mice prior to irradiation to the non-drug-treated irradiated controls, a similar delayed onset of mortality and decrease in radiation sickness symptoms were observed(18). In animal models, P. emblica radioprotective properties have been studied. Investigated how well Swiss albino mice were protected from sublethal gamma radiation (9 Gy) by an aqueous preparation of P. emblica fruit. After 30 days, the fruit pulp extract dose that proved to be the most effective against radiation was 100 mg kg-1 BW, with an 87.5% survival rate. Discovered that Swiss albino miceexposure to radiation was much lessened by P. emblica fruit pulp, indicating that P. emblica extract could be helpful in lowering radiation therapy adverse effects. Revealed that in mice exposed to γ-radiation, triphala is also an effective radioprotective agent(19).

NEUROPROTECTIVE ACTIVITY:

Impact on Neuroprotection Pretreatment with 500 and 700 mg/kg of hydroalcoholic extract of E. officinalis fruit significantly ($P<0.001$) enhanced the delay of seizures in comparison to the group that received vehicle treatment. Additionally, it mitigated the decline in glutathione and significantly stopped the rise in thiobarbituric acid-reactive chemical levels. Additionally, as demonstrated by increased latency in the passive avoidance task, E. officinalis significantly corrected cognitive deficit and dose-dependently moderated the kainic acid-induced rise in TNF-α levels in the brain (17).

ANTICANCER AND ANTIPROLIFERATIVE ACTIVITY:

E. officinalis has the potential to be effective in treating cervical malignancies caused by the human papillomavirus because it inhibits activator protein-1 and targets the production of viral oncogenes that cause cervical cancer. The ethanolic whole plant extract of E. officinalis was used at a

concentration of 100µg/ml to conduct an in vitro cytotoxicity test against five human cancer cell lines. Plant extract exhibited 82% growth inhibition against the lung (A-549) cell line. The plant extract demonstrated the highest level of activity in the colon 502713 cell line, while it showed no activity in the liver cell line (Hep-2). There was 97% and 98% activity of the plant extract in the IMR-32 neuroblastima cell line and the HT-29 liver human cancer line, respectively. A549 (lung), HepG2 (liver), HeLa (cervical), MDA-MB-231 (breast), SK-OV3 (ovarian), and SW620 (colorectal) are the six human cancer cell lines whose cell growth can be markedly inhibited by E. officinalis fruit extract at 50–100µg/mL. The effects of P. emblica and T. bellerica extracts, either alone or in conjunction with doxorubicin or cisplatin, on the proliferation of HepG2 and A549 cells were assessed using the sulforhodamine B (SRB) assay. Both plant extracts showed growth-inhibiting properties against the two tested cancer cell lines. Research has also shown that amla extracts are cytotoxic and inhibit the growth of certain tumour cell lines, including B16F10 (murine melanoma) and MK-1 (human gastric adenocarcinoma), in vitro (18).

ANTITUSSIVE ACTIVITY:

E. officinalis antitussive properties were evaluated in awake cats by mechanically stimulating the tracheobronchial and laryngopharyngeal mucous membranes. Although only at higher doses (200 mg/kg body weight) does the ethanol extract of E. officinalis fruits appear to have a good ability to inhibit mechanically provoked cough, this suggests that E. officinalis has antitussive activity in conscious cats that is dose-dependent but greater than that of dropropizine, a common non-narcotic antitussive medication. The dry extract of E. officinalis is thought to have antitussive properties in addition to its antiphlogistic, antispasmolytic, and antioxidant actions. It also has an impact on mucus secretion in the airways (17).

ANTIOXIDANTS AND ANTI-AGING:

The use of amla as an antioxidant has been studied by number of scholars. Research indicated that experimental individuals had elevated levels of the free-radical scavenger superoxide dismutase (SOD) in amla preparations. Emblica officinalis (Eo) demonstrated MMP-1 and MMP-3 inhibitory efficacy, iron and copper chelating ability, and free radical quenching ability in addition to reducing UV-induced erythema. Amla was evaluated against behavioural and biochemical abnormalities brought on by cold stress in a different study. Oral administration of triphala (1 g/kg body weight) for 48 days effectively inhibited these changes in albino rats. Empiricanin A (2,3-di-O-galloyl-4,6-(S)-hexahydroxydiphenoyl-2-keto-glucono-D-lactone) and emblicanin B (2,3,4,6-bis-(S)-hexahydroxydiphenoyl-2-keto-glucono-D-lactone), both hydrolysable tannins, demonstrated potent antioxidant properties. Because asbestos produces superoxide radicals, both emblicanins A and B protected erythrocytes against oxidative stress. When exposed to asbestos, emblicanin A oxidises to emblicanin B, which works in concert to protect erythrocytes more effectively than vitamin C. Additionally, they improve vitamin C ability to convert dehydroascorbic acid to ascorbic acid. A comparable recycling process was noted in the combination of vitamin C and rutin (10).

ANTI-DIARRHEAL AND ANTI-DYSENTERIC ACTIVITY:

Patients with diarrhoea are treated with P. emblica fruits, while those with dysenteritis benefit from a fruit mixture with sour milk. Additionally, P. emblica has been studied on the ileum of guinea pigs and rabbits to examine castor oil-induced diarrhoea. The combined blocking of muscarinic receptors and Ca2+ channels demonstrated antidiarrheal activity, according to the results (15).

ANTIPYRETIC AND ANALGESIC ACTIVITY:

The purpose of the study was to investigate the antipyretic and analgesic properties of ethanol EO (EEO) and AEO extracts of EO fruits in many experimental units. Brewer's yeast-induced hyperthermia in rats was significantly reduced by a single oral dosage of EEO and AEO (500 mg/kg, i.p.). In the analgesic test, mice writhing response to acetic acid was further markedly inhibited by EEO and AEO. In the tail-immersion scan, neither AEO nor EEO displayed any huge analgesic pastime. These results support the strong analgesic and antipyretic properties of EO fruit extracts. Alkaloids, tannins, phenolic compounds, carbohydrates, and amino acids were found in the extracts according to preliminary phytochemical screening; these substances may also be in charge of the extractsanalgesic and antipyretic effects (20).

ANTIULCER ACTIVITY:

Anti-ulcer characteristics in rats, the anti-ulcer and antioxidant properties of Pepticare, a herbomineral Ayurvedic formulation made of EO, Tinospora cordifolia, and Glycyrrhiza glabra, have been examined.Peptic anti-ulcer sentiments stem from its antioxidant qualities. To cure ulcers, EO extract (EOE) was studied. EOE can influence both defensive and offensive mucosal variables, and it has strong curative and therapeutic effects on ulcers (21).

ANTIDIABETIC ACTIVITY:

E. officinalis is useful in managing diabetes because of its high vitamin C concentration. When eaten every day for two months, a tablespoon of its juice combined with a cup of bitter gourd juice encourages the pancreas to release insulin, which lowers blood sugar levels in diabetics. When using this medication, dietary restrictions should be closely followed. It also keeps diabetes-related eye problems at bay. Regardless of coronary artery disease, diabetes mellitus raises the risk of cardiomyopathy and heart failure due to reduced insulin sensitivity, autonomic dysfunction, hypertension, and left ventricular hypertrophy. Fruit juice has been reported to be helpful for cardiac damage in type 1 diabetes mellitus; increased oxidative stress is a contributing factor to morphological and functional abnormalities in diabetic cardiomyopathy. A reduction in blood glucose and triglycerides, as well as an improvement in liver function with normalisation of alanine transaminase activity, were noted in alloxan-induced diabetic rats treated with aqueous amla fruitextract.In streptozotocin-induced diabetes, the hydro-methanolic extract of E. officinalis leaves restored impaired antioxidant status in a dose-dependent manner more effectively than rats treated with glibenclamide. By scavenging free radicals and lowering diabetic complications, the extract also had protective effects against lipid peroxidation. Aldose reductase (AR) is implicated in diabetic

problems, such as cataracts, and E. officinalis has been shown to be a significant inhibitor of AR. Investigating natural components that can be used in everyday life could aid in the management of diabetes complications (10).

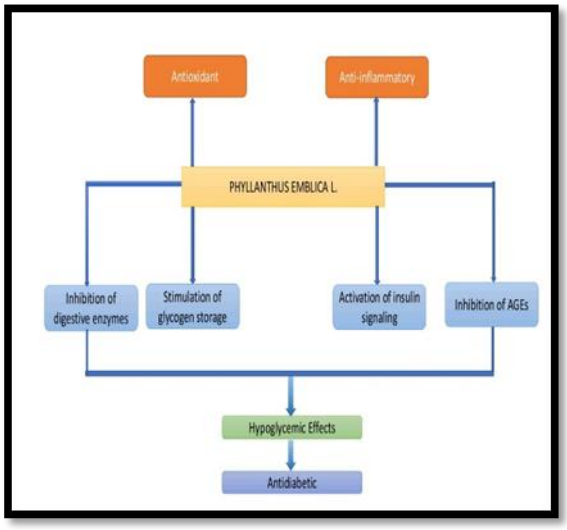

Figure 7: Anti-diabetic Activity of Phyllanthus emblica

ANTIMICROBIAL AND ANTIMUTAGENICITY ACTIVITY:

Amla antimicrobial properties have also been documented. Fruits acidified with hydrochloric acid showed antibacterial action in both their ether and 80 percent alcoholic extracts. The growth of M. pyogenes var. S.typhosa and S. paratyphi was inhibited at a concentration of 0.21 mg/ml by the other extract of acidified alcoholic extract, whereas that of M. pyogenes var. albus, S. schottmmellari, and S. dysenteriae was inhibited at a concentration of 0.42 mg/ml. Escherichia coli, K. ozaenae, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, S. paratyphi A, S. paratyphi B, and Serratia marcescens were all found to be susceptible to the strong antibacterial activity. Both direct and S9-dependent mutagen-induced mutagenicity was inhibited by triphala extracts in acetone and chloroform.Emblica officinalis fungal endophytes exhibited antioxidant and antibacterial properties(10).

LAXATIVE ACTIVITY:

P. emblica fruit or fresh fruit preserved in sugar or pickled can be used as a laxative on a daily basis. This relieves constipation. Introducing a drink made from amla juice combined with honey or lemon can help treat diarrhoeal illnesses and dysentery. It also helps to get rid of burning while you urinate. Sometimes, Indian gooseberry is used to treat stomach hyperacidity and constipation. Dysentery and chronic diarrhoea are two gastrointestinal conditions that have historically been treated using Phyllanthus emblica. Milk-based carriers are commonly combined with amla decoctions in Ayurvedic and traditional practices. Its high fibre content minimises constipation by encouraging intestinal regularity. Traditional doses can vary, while clinical preparations often consider standardised quantities based on therapeutic need (22).

ANTIBACTERIAL ACTIVITY:

The antibacterial qualities of the fruits of the Phyllanthus emblica L plant are investigated. The fruits are extracted with distilled water, and their antibacterial qualities are then assessed. Bacillus cereus, Shigella species, Salmonella typhi, Vibrio cholerae, Staphylococcus aureus, Salmonella paratyphi A, and Salmonella paratyphi B are all checked for. The major antibacterial activity of the aqueous Phyllanthus emblica fruit extract (APE) was screened using Mueller-Hinton (MH) agar and the agar well diffusion method. By creating holes and putting test medications at 25%, 50%, 75%, and 100% v/v concentrations in contrast to the conventional drug amikacin (30µg/ml), one may see areas where bacterial growth is inhibited. There was a pattern of growth inhibition zones that varied with dose. There is theoretical evidence for the antibacterial properties of flavonoids, triterpenoids, glycosides, tannins, and anthraquinones (23).

ANTIHYPERLIPIDEMIC ACTIVITY:

The fruit juice and gallic acid of P. emblica were tested for their hyperlipidaemic potential in a variety of experimental animal models. The administration of tyloxapol supplements, a high-fat diet, and poloxamer-407 caused hyperlipidaemia in the rat model. The rat model showed a decrease in plasma cholesterol and a slowed rate of oil filtration in the liver and aorta after being treated with gallic acid and P. Emblica fruit juice. Furthermore, the plant extract increased the degree of lipid oxidation via carnitine palmitoyl transferase (CPT) and increased the expression of peroxisome proliferator-activated receptors-alpha (PPARα) while lowering the activity of hepatic lipogenic enzymes. Along with a lower rate of LDL-receptor degradation caused by a decrease in proprotein convertase subtilisin/Kexin type 9 (PCSK9), hepatocytes were shown to have increased cholesterol absorption through enhanced LDL-receptor expressions. Furthermore, P. emblica restored glucose homeostasis by upregulating the expression of the Glut4 and PPARϒ proteins in adipose tissue. As a result, it showed significant hyperlipidaemic activity by upregulating PPARs, lipogenic enzymes, and Glut4 and downregulating PCSK9 and lipogenic enzymes (24).

EYE DISORDER MODULATOR:

Studies have shown that a mixture of honey and P. Emblica can enhance vision. Opium juice is combined with Trifala and Opium poppies to create tablets of this type of traditional medication. The eyes are bandaged and these tablets are kept over them. This combination has been shown to alleviate eye pain in this way. To create a herbal eye drop composition, a variety of plants were used in another ophthalmic study. Among the plants that were employed were Terminalia belerica, Rosa damascene, P. emblica, Carumcopticum, Ocimum sanctum, Meldespumapum, Cinnamomum camphora, and Curcuma longa. This research design looked at a variety of ocular conditions. Acute dacryocystitis, conjunctivitis, surgical cataract, xerosis, and conjunctival degenerative diseases were among them. Improvement without adverse consequences was observed. By producing an effective nontoxic formulation that may aid in the treatment of inflammatory, infectious, and degenerative diseases, this research helped Opthacare (15). The juice of Indian gooseberries and triphala powder (which is formed by combining hirda, behde, and amla powder) with honey helps to retain vision, treat glaucoma and conjunctivitis, and significantly lower intraocular tension in traditional medicine, amla is used to treat a variety of eye conditions, including redness, lacrimation, eye irritation, and burning. Because E. officinalis inhibits aldose reductase, its tannin-rich fractions have been demonstrated to have protective effects against diabetic cataract. Another method of treatment involves applying a collyrium created from an infusion of fruit seeds and exudate obtained from fruit incisions to conjunctival inflammations and other eye conditions (25).

PULMONARY ACTIVITY:

Disorder of the respiratory system When the system is impacted, Amla has been shown to be able to restore regular breathing. Ten grammes of Phyllanthus emblica leaves, five Terminalia chebula fruits, nine Piper nigrum seeds, and one garlic are crushed to make the paste, which is then combined with 25 millilitres of cow's milk and clove ghee. Asthma, cough, and other respiratory conditions can be best treated with fresh Amla juice combined with honey (26).

MEMORY ENHANCING ABILITY:

Amla powder improved the memory scores of both young and old mice75 in a dose-dependent manner. When Amla powder was administered for 15 days, brain cholinesterase activity and total cholesterol levels were likewise decreased, and the amnesia caused by scopolamine (0.4 mg/kg, i.p.)and diazepam (1 mg/kg, i.p.) was reversed. Their research showed that Amla many positive effects, including its ability to improve memory, lower cholesterol, and inhibit the activity of the enzyme cholinesterase, may make it a viable treatment for Alzheimer's disease (27).

SNAKE VENOM NEUTRALIZER:

The antisnake venom action of EO and Vitex negundo was Initially investigated. The plant extracts considerably reduced the venom of Viperarussellii and Naja kaouthia in both in vitro and in vivo experiments. Thecoagulant, hemorrhage-defibrinogenating, and inflammatory effects of V. russellii venom were considerably reduced by both plant extracts. Plant extracts have a strong ability to neutralise snake venom and require more research, as evidenced by the absence of precipitating bands between the extract and snake venom (28).

TRADITIONAL USES:

A variety of illnesses are treated with amla in the Tibetan, Sri Lankan, Chinese, and Indian medical systems, as well as in the Ayurvedic, Siddha, and Unani systems. Known as a rasayana, it is used to delay senescent and degenerative developments. The fruits are sour, astringent, bitter, acrid, sweet, and anodyne in traditional medicine. It has cooling, ophthalmic, carminative, digestive, stomachic, laxative, dyspepsia, rejuvenating, diuretic, antipyretic, and tonic properties, among other beneficial effects. They are helpful for vitiated conditions like tridosha, diabetes, cough, asthma, bronchitis, cephalalgia, ophthalmopathy, dyspepsia, colic, flatulence, hyperacidity, peptic ulcer, erysipelas, skin diseases, leprosy, haematogenesis, inflammations, anaemia, emaciation, hepatopathy, jaundice, diarrhoea, dysentery, haemorrhages, leucorrhoea, menorrhagia, cardiac conditions, intermittent fevers, and premature grey.Amla has also been linked tohepato, cardiac, nephro, and neuroprotective benefits, as well as antioxidant, anti-inflammatory, analgesic, antipyretic, and restorative capabilities(1).

CLINICAL RESEARCH:

A randomized, double-blind, placebo-controlled clinical trial was conducted at Razi and Sina Hospitals, affiliated with Ahvaz Jundishapur University of Medical Sciences, Iran, between May and June 2020. A total of 61 COVID-19 positive patients were enrolled and randomly assigned to two arms: intervention (n = 31) and control (n = 30).

Intervention protocol:

Patients in the intervention arm received 2 g sachet powder of Phyllanthus emblica (Amla) every 12 hours for 10 days in addition to standard COVID-19 therapy (hydroxychloroquine + lopinavir/ritonavir). The control group received placebo sachets along with routine treatment.

Primary outcomes:

RT-PCR results between the first and last days of the trial.

Secondary outcomes:

Length of hospital stay (LOS), clinical symptoms (fever, cough, shortness of breath, weakness, sore throat, chills, myalgia, respiratory rate), laboratory markers (Hb, lymphocytes, PMN count, platelets, ESR, CRP, SpO2), and lung involvement on CT scans.Results:

Baseline demographics were similar across both groups. At study completion:RT-PCR results showed no significant difference (P = 0.07).Mean LOS was significantly shorter in the intervention group (4.44 days) compared with the control(7.1days, P < 0.001).

Significant clinical improvement was observed in fever (P = 0.004), cough (P = 0.001), shortnessof breath(P = 0.004), and myalgia (P = 0.005).

Oxygen saturation improved significantly in the intervention arm (P < 0.001).

CRP levels and lung CT involvement showed greater reduction in the Amla group.

No adverse events were reported.

Conclusion:

Although Amla did not significantly influence RT-PCR results or lung involvement, it improved clinical symptoms, shortened recovery time and hospital stay, and reduced CRP levels without side effects (29).

CASE STUDY:

A randomized controlled trial involving 61 hospitalized patients with confirmed COVID-19 was conducted in Iran to evaluate the efficacy of Phyllanthus emblica (Amla) as an adjunct therapy. Thirty-one patients received 2 g of Amla sachet powder twice daily for 10 days, while thirty patients received placebo, both groups continuing standard antiviral therapy.

The study revealed that patients in the Amla group had a significantly shorter hospital stay (mean 4.44 days) compared to the control group (7.18 days). Clinical outcomes showed marked improvement in fever, cough, shortness of breath, and myalgia among patients treated with Amla. Furthermore, oxygen saturation levels and CRP values improved significantly in the intervention arm. Despite these benefits, RT-PCR conversion rates and lung CT involvement did not differ significantly between the two groups. Importantly, no adverse effects were reported.

This case study suggests that Amla, when used as an add-on therapy, can reduce disease severity and hasten recovery in COVID-19 patients, though larger and longer trials are warranted to confirm these findings (29).

WORLD RESPONSE TO COVID-19:

CountriesCOVID-19 policy responses may differ because to a lack of expertise controlling pandemics. The outbreak inspired a variety of non-pharmaceutical efforts to reduce population risk.Beyond medical treatments and immunisations, NPIs effectively reduced virus transmission and mortality while harming economies and delaying recovery. Face covers, particularly nasal masks, were strongly recommended as the most cost-effective NPI. Face masks reduced COVID-19 cases in Germany by 45% in 20 days with little economic impact when compared to closures or contact prohibitions. Diagnostic testing for respiratory symptoms was prioritised due to virus transmission caused by delayed restrictions, noncompliance, and poor contact tracking.Limiting contact lowered interactions and viral replication, hence lowering R0.Global variations in lockdown time and duration made it difficult to analyse the impact of restrictions.Lockdowns resulted in economic losses, unemployment, and mental health difficulties, confounding cost-benefit analysis(5).

SAFETY AND TOXICITY STUDIES:

Safety and toxicity Humans have been treated with plants, particularly medicinal ones. In vitro and in vivo research have demonstrated the efficacy of Phyllanthus emblica in inhibiting certain pathologies, and its raw parts or extract have been utilised to cure a variety of ailments since the prehistoric age. Oral dosages of P. emblica at 300, 600, and 1,200 mg/kg were administered for 270 days in chronic toxicity trials; no pathological alterations were observed in the treated animals. The fruit extract of P. emblica was found to be non-toxic at 200, 400, 300, and 500 mg/kg in earlier investigations. Additionally, it was observed that rats can safely receive doses of up to 2000 mg/kg b.w. of Phyllanthus emblica ethanolic extract. The biochemical test, behavioural observation, and haematological analysis of P. emblica showed no harmful effect. Found that both male and female rats can safely consume up to 9 mL/kg/day of fermented P. emblica fruit juice mediated by Lactobacillus sp. For 60 days, and that no rat showed any appreciable changes in body weights, internal organs, haematology, or biochemical markers (14).

FUTURE RESEARCH SCOPE AND POLICY IMPLICATIONS:

Future Research scope and policy implications for the future according to this study, drug use, sales, and purchases increased significantly in the local environment during the COVID-19 pandemic. There is a dearth of effective monitoring and evaluation of over-the-counter medications, according to the Bangladesh NDP 2016 [24]. But both drug dealers and consumers favoured using antibiotics that were bought without a prescription from a doctor. Understanding the buying, stockpiling, and prescription usage patterns in the event of a pandemic or other public health emergency is crucial. For the purpose of improving drug distribution and promoting the sensible use of medications, drug regulatory authorities and legislators must take into account the panic-style drug sales, storage, and consumption during the pandemic. For primary care, the drug administrators can use a qualified chemist to prescribe and dispense medications. It's necessary to start research on public awareness campaigns and promote the results on social media, in print, and online to encourage people to see a doctor and increase knowledge of the potential risks of using unnecessary medications and unprescription drugs. The studies conclusions provide insightful information on the local context of medical behaviour during the COVID-19 pandemic. To make their health system more resilient, policymakers can apply these lessons learnt in each local outbreak or impending pandemic (30).

LIMITATIONS AND STRENGTHS:

The current study has a number of limitations, such as 1) not evaluating adherence and specific clinical findings, such as the patients smoking status and disease complications; 2) not documenting long-term follow-up outcomes following treatment cessation; and 3) having a small sample size for this clinical trial. The following are the studies strengths: First, in comparison to previous investigations, this RCT study has provided more thorough data. Second, this study was a double-blind randomised controlled trial (RCT), one of the most dependable study designs for COVID-19. To provide more accurate information about the plants therapeutic effects on COVID-19, however, results, follow-up findings, and laboratory or immunological investigations with immunomodulatory properties. The repeated chest imaging for all participants should be assessed for at least a few months after treatment termination. We would also

advise evaluating each of these characteristics in various age groups. Lastly, although though this study only looked at one region, more nationwide multicenter studies are advised to evaluate other unknown characteristics that could impact Amla safety and effectiveness, like race, geography, and climate (29).

ACKNOWLEDGEMENT:

This review highlights the powerful role of Phyllanthus emblica (Amla) as a natural preventive supplement against viral pandemics. The authors—Ms. Nikita S. Wable and Dr. Sachin B. Somwanshi from Pravara Rural Education Society's College of Pharmacy (For Women), Chincholi, Nashik—present how this ancient herbal fruit, known for its healing and immune-boosting properties, continues to inspire modern clinical research. This work beautifully connects traditional wisdom with modern science to promote health and wellness for future generations.

CONCLUSION:

Phyllanthus emblica (Indian gooseberry or Amla) has been a cornerstone of traditional medicine in India for centuries, revered for its potent rejuvenating, antioxidant, and immunomodulatory properties. The comprehensive review highlights that its rich phytochemical profileparticularly compounds such as emblicanin A and B, gallic acid, ellagic acid, flavonoids, and alkaloidscontributes to its wide range of pharmacological actions, including antiviral, anti-inflammatory, hepatoprotective, cardioprotective, antidiabetic, and anticancer effects.In the context of viral pandemics such as COVID-19, both experimental and clinical findings suggest that Phyllanthus emblica enhances immune function, reduces inflammation, and mitigates disease severity. Its bioactive compounds demonstrate high binding affinities to SARS-CoV-2 target proteins such as the spike and helicase enzymes, supporting its therapeutic potential. The clinical trial evidence reviewed indicates that Amla supplementation improved clinical symptoms, reduced hospital stay duration, and lowered CRP levels in COVID-19 patients without adverse effects, confirming its safety and efficacy as an adjunct therapy.However, limitations such as small sample sizes, lack of long-term follow-up, and regional constraints highlight the need for further multicentric, large-scale clinical investigations. Standardisation of extract formulation, dosage, and administration protocols is also essential to ensure reproducibility and global acceptance.Overall, Phyllanthus emblica stands out as a promising natural preventive and therapeutic supplement, bridging the gap between traditional knowledge and modern clinical research. Its inclusion in integrative health approaches may strengthen global preparedness and resilience against present and future viral pandemics.

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