



Review Article

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Triphala: An Indian Ayurvedic herbal formulation for coronavirus (SARS-CoV-2) disease (Covid-19)

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Article Info

Abstract

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This review paper updated the significance and pharmaceutical effects of Triphala as an alternative traditional herbal Indian folk medicine used as a immunity booster during the recent outbreak of coronavirus-2 (SARS-CoV-2) mutants, Delta (B.1.617.2) and Delta Plus (AY.1). The current outbreak of coronavirus-2 mutants, Delta (B.1.617.2) and Delta Plus (AY.1) is wreaking havoc in India. The new epicentre of the highest number of corona viral mutant infection cases and death rate has been recorded in Indonesia. The hallmark of the coronavirus disease is the cytokine storm, a massive cytokine and chemokine release due to an uncontrolled dysregulation of the host immune defence that causes loss of function of multiple organs and leading to death. One of the evidence to support Triphala alone inhibited the RNA viruses including human coronavirus. Triphala herbal formulation can reduce the production of progeny of human coronavirus, HCoV-NL63 particles and have an antiviral effect under in vitro conditions. In India, Triphala herbal formulation with an additional supplementation of pumpkin seeds, coconut water, sugar cane juice, *Aloe vera* juice, neem (*Azadirachta indica*) leaf juice, and melatonin rich diet has played an important role in controlling coronavirus disease than Triphala alone. However, clinical trials of Triphala with new additional supplementations is lacking for the scientific validation. On the basis literature survey, there is a ray of hope for the Triphala with additional supplementation as a new therapeutic drug for combating Covid-19 viral infections.

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Introduction

The outbreak of second wave of coronavirus (SARS-CoV-2) mutants, Delta (B.1.617.2) and Delta Plus (AY.1) with mucormycosis has devastated India by more number of hospitalizations and increased death

rates (Mlcochova et al., 2021; Malabadi et al., 2021a, 2021b, 2021c, 2021d, 2021e, 2021f, 2021g, 2021h; Yang, 2021). Therefore, the outbreak of Delta (B.1.617.2) and Delta Plus (AY.1) mutants pandemic has created a global health crisis posing an unprecedented public health emergency. The Delta plus

variant (AY.1) is related to the Delta strains, an existing variant of concern thought to have driven the deadly second wave of infections on 11th April month of 2021 in India (Malabadi et al., 2021g). This second wave of mutant, Delta (B.1.617.2) and Delta Plus (AY.1) outbreak in India has created lot of problems, viral infections were out of control, shortage of oxygen supply and bed facilities in the hospitals with highest number of deaths, and becomes challenge to the Indian health care system (Mlcochova et al., 2021; Malabadi et al., 2021g, 2021f). At this critical situation in India, health care workers have exhausted, medical facilities are not enough due to the shortage of supply, hospitals are over-crowded, and many people are infected due to cross contamination of the virus. Social media is full of desperate people (doctors, nurses, health care workers and the public) seeking medical oxygen, hospital beds, and other necessities (Malabadi et al., 2021f). Therefore, Government of India has put strict lock down measures to curb the growth curve of the virus. This has ruined the economy of India on one side and on the other side Covid-19 control measures were effective. This Delta plus variant (AY.1) has also been found in nine other countries like in USA, UK, Portugal, Switzerland, Japan, Spain, Poland, Nepal, Russia and China as compared to the original highly contagious Delta strain, which has now spread to 80 countries throughout globe (Mlcochova et al., 2021; Malabadi et al., 2021g, 2021f). According to WHO report, everybody is vulnerable and people should continue to using masks and to avoid crowds, even if they're fully vaccinated.

Indonesia has become the new epicentre of the pandemic, surpassing India and Brazil to become the country with the world's highest count of new viral infections in non-vaccinated people. Every infected person, anywhere in the world, offers the coronavirus another opportunity to morph into a new variant. The more infections there are globally, the more likely new variants will arise. Therefore, unvaccinated people are not protected and will set the country on fire over and over again. Vaccinated people will be protected from severe illness and death, but there may be other consequences. There are also concern about fully vaccinated people might become infected. Breakthrough infections were expected to be vanishingly rare with the original virus. However, recent data suggested that they may be less so with the delta variant. It is roughly twice as contagious as the original coronavirus, and some early evidence hints that people infected with the corona

virus variant carry the virus in much higher amounts. "The larger the force of infection that comes from the pandemic in unvaccinated populations.

The Delta variant of coronavirus (SARS-CoV-2) is becoming the globally dominant version of the disease (Mlcochova et al., 2021; Malabadi et al., 2021f, 2021g). India's first wave of SARS-CoV-2 infections has started in March 2020 was relatively mild and was controlled by a nationwide lockdown (Mlcochova et al., 2021). Delta variant's (B.1.617.2) of concern increased transmissibility has enhanced spike proteins attachment to the lung epithelial cells, which provided a much higher capacity to infect many more people than the original Wuhan strain (Wu et al., 2020a, 2020b; Zhou et al., 2020a, 2020b; Mlcochova et al., 2021; Malabadi et al., 2021g). The SARS-CoV-2 Delta mutant, B.1.617.2 variant was first identified in the state of Maharashtra, India and has spread throughout India, displacing the B.1.1.7 (Alpha) variant and other pre-existing lineages (Mlcochova et al., 2021; Malabadi et al., 2021g, 2021f). According to the study reported by Mlcochova et al., (2021), the Delta variant (B.1.617.2) showed 8 fold approximately reduced sensitivity to vaccine-elicited antibodies compared to wild type Wuhan-1 bearing D614G (Mlcochova et al., 2021). These combined epidemiological and *in vitro* data indicated that the dominance of the Delta variant (B.1.617.2) in India has been most likely driven by a combination of evasion of neutralising antibodies in previously infected individuals and increased virus infectivity (Mlcochova et al., 2021). The breakthrough transmission clusters in hospitals associated with the Delta variant (B.1.617.2) are concerning and indicated that infection control measures need to continue in the post-vaccination era (Mlcochova et al., 2021).

The outbreak of Delta Plus (AY.1) variant which is more infectious than previous mutated strains of covid-19 (Mlcochova et al., 2021; Malabadi et al., 2021a; Yang, 2021; Wu et al., 2020a, 2020b; Zhou et al., 2020a, 2020b). The delta Plus (AY.1) strain is characterised by K417N mutation in the spike protein of the SARS-CoV2 virus that causes the Covid-19 disease (Mlcochova et al., 2021; Wu et al., 2020a, 2020b; Zhou et al., 2020a, 2020b). The K417N mutation has been associated with "immune escape" phenomenon, which means that the virus is less susceptible to available vaccines or less responsive to any drug therapy (Mlcochova et al., 2021). Delta Plus (AY.1) variant of corona virus (SARS-CoV-2) is

spreading more easily, binds more easily with ACE2 receptors of lung or respiratory epithelial cells and is potentially resistant to monoclonal antibody therapy, a potent intravenous infusion of antibodies to neutralise the virus (Mlcochova et al., 2021).

India is one the leading country in the world possessing very good Eco-climatic conditions housing wide range of medicinal plants (Malabadi et al., 2007). India is known for the rich biodiversity of several medicinal plants (Malabadi and Nataraja, 2002a, 2002b ; Malabadi et al., 2021a, 2021e, 2021f; Kulkarni et al., 2020; Swamy et al., 2016; Malabadi, 2008; Laddimath and Rao, 2016; Malabadi and Vijayakumar, 2005, 2007 2008; Malabadi et al., 2009, 2010a, 2010b, 2011a, 2011b; Malabadi et al., 2012a, 2012b, 2012c, 2012d; Kambhar et al., 2020; Kawalekar, 2011, 2012; Malabadi et al., 2016a, 2016c, 2016d; Malabadi et al., 2017a, 2017b; Malabadi et al., 2018). Traditional herbal plants have been used as a source of medicine from ancient times (Malabadi et al., 2007, 2021a; Kawalekar, 2011, 2012; Kambhar et al., 2020; Laddimath and Rao, 2016). Crude plant extracts or isolated secondary metabolites have been observed in phytotherapeutic treatment of various ailments (Malabadi et al., 2007; Malabadi et al., 2021a; Laddimath and Rao, 2016; Kawalekar, 2011, 2012; Sharma, 2009; Kambhar et al., 2020). There are two types of traditional herbal medicinal plant systems, one is codified that is organized Indian system of medicines under the umbrella of Ayurveda, Siddha and Unani (Upadhyaya et al., 2014). The second one is non-codified that is nothing but local or folk medicine practiced by traditional healers (Malabadi et al., 2007; Upadhyaya et al., 2014; Laddimath and Rao, 2016; Kambhar et al., 2020; Kawalekar, 2011, 2012).

There are some traditional herbal medicine remedies from *Ayush* systems which provide relief and alleviate some of the symptoms of Covid-19 (Ministry of Ayush, Government of India, 2020). The medicines selected in the protocol have immuno-modulatory effect i.e. they tend to strengthen the immunity of a person in a natural way. *Ayush* systems follow a holistic approach towards disease management and maintaining health of a healthy person. It provides detailed advocacy and interventions for disease prevention (Ministry of Ayush, Government of India, 2020). There are various interventions in *Ayush* systems which are presently being used in prophylactic approaches as well as in the management of Covid-19, and are providing good results (Ministry of Ayush, Government of India, 2020). The fusion of

knowledge of medicinal plants with modern scientific and bio-medical applications can give us the cost effective and potential new drugs (Sharma, 2009). As such, traditional medicine is of contemporary relevance in India to achieve self reliance in primary health care needs. The survival of age old traditional Folk systems of medicine in India is based on strong belief in the efficacy and success story of herbal medicines (Sharma, 2009). Medicinal plants play an important role in drug development, as these are the source of majority of ingredients in Ayurvedic as well as Modern medicine. Medico-Ethno botanical survey programme has played a pivotal role in the medicinal plant research programmes by the Ministry of Ayush, Government of India, New Delhi, India. These botanical survey programmes are conducted by the Central Council for Research in Ayurvedic Sciences, Ministry of AYUSH, Government of India, New Delhi, India. It is an apex organization for undertaking, coordinating, formulating, developing and promoting research in *Ayurvedic* sciences on scientific lines.

This review paper highlights about one of the traditional herbal medicine, Triphala used as an alternative approach for controlling coronavirus (SARS-CoV-2) mutants Delta (B.1.617.2) and Delta plus (AY.1). Triphala has been used as an immunity booster with proven biological properties as per the literature survey might play an important role for combating viral outbreaks. However, more clinical trials should be needed for this valuable medicine for the scientific validation. Pharmaceutical properties of Triphala have been discussed.

Triphala: An Indian *Ayurvedic* formulation

Triphala (Sanskrit; Tri = three and Phala = fruits) is defined as a well known tri-herbal Indian *Ayurvedic* formulation consisting of dried fruits of the three plant species, *Emblica officinalis* (Amalaki or the Indian Gooseberry) (Family-*Euphorbiaceae*), *Terminalia bellirica* (Bibhitaki or Karitaki) (Family-*Combretaceae*), and *Terminalia chebula* (Haritaki) (Family-*Combretaceae*) that are native to the Indian subcontinent (Ozah, 2020; Saxena et al., 2017; Dhanalakshmi et al., 2007; Mukherjee et al., 2006; Baliga et al., 2012, 2013; Baliga, 2010; Peterson et al., 2017; Malabadi et al., 2021a; Rasool and Sabina, 2007; Kumari et al., 2009; Ozah, 2020). In India, this tri-herbal combination of dried fruits, Triphala is very famous and used as a traditional home remedy for

combating common cold, throat infections, antimicrobial, antiviral, antibacterial and antifungal infections (Malabadi et al., 2021a; Shanbag, 2015; Pradeep et al., 2016; Peterson et al., 2017; Mamgain et al., 2016; Bhattacharjee et al., 2015). In Karnataka state of India, plants are commonly called as Aalalekai or a Aalale mara in Kannada language for *Terminalia bellirica* and *Terminalia chebula* (Malabadi et al., 2021a). Both *Terminalia bellirica* and *Terminalia chebula* trees were found abundant in Western Ghats forests of Karnataka, Maharashtra, Goa, Kerala, Tamil Nadu, and Andhra Pradesh. In India, the *Terminalia bellirica* and *Terminalia chebula* trees were widely spread and commonly grown in gardens, and roadside as a shade trees. Medicinal plants still play a significant role in primary health care in many developing countries, since natural products constitute a key source of drugs in medicine (Malabadi et al., 2021a; Tarasiuk et al., 2018).

Triphala is one of the oldest (1000 year) herbal medicine well documented in the Indian *Ayurveda* called the Charaka Samhita (Bhishagratna, 1963; Agnives'a et al., 1976; Baliga et al., 2012; Peterson et al., 2017). According to Charak Samhita (Indian *Ayurveda*), the daily oral consumption of *Triphala Rasayana* (Triphala with honey and ghee) has the potential to make a person live for one hundred years devoid of old age and diseases (Bhishagratna, 1963; Agnives'a et al., 1976; Baliga et al., 2012; Biradar et al., 2007; Peterson et al., 2017). Therefore, Triphala is called as the King of *Ayurvedic* herbal medicine which has been well documented in Sushruta Samhita text book in India formulated for many human health disorders (Bhishagratna, 1963; Agnives'a et al., 1976; Biradar et al., 2007; Biradar et al., 2007; Baliga et al., 2012; Verma et al., 2016; Peterson et al., 2017; Malabadi et al., 2021a). Therefore, Triphala is considered as a multipurpose therapeutic drug for many health disorders. Triphala is classified as a Tridoshic Rasayana, meaning as Energy and Immunity booster and appropriate for Vata, Pitta, and Kapha or all types of patients (Peterson et al., 2017; Baliga et al., 2012; Biradar et al., 2007; Shanbag, 2015; Pradeep et al., 2016; Peterson et al., 2017; Mamgain et al., 2016; Bhattacharjee R, et al., 2015; Shanbag, 2015; Pradeep et al., 2016; Peterson et al., 2017; Mamgain et al., 2016; Bhattacharjee R, et al., 2015). Triphala is also digestive, laxative at normal doses, bowel tonic at low dose, purgative at high doses, carminative, expectorant, antispasmodic, and bronchodilator (Baliga et al., 2012;

Biradar et al., 2007; Peterson et al., 2017; Belapurkar et al., 2014; Nariya et al., 2009; Rayudu and Raju, 2014).

According to *Ayurvedic* Rasayana, the taste of Triphala is defined as sweet, sour, pungent, bitter, and astringent but not salty with special mode of action or trophism for all doshas (energy, and immunity booster; mind and body types; for all ages, for all the disease) (Dhanalakshmi et al., 2007; Ozah, 2020; Mukherjee et al., 2006; Baliga et al., 2012; Peterson et al., 2017). Triphala extract exerted highly protective anti-aging effects on human skin cells in vitro. Therefore, potential dermal anti-aging effects of Triphala, such as increasing collagen and elastin, increasing cellular antioxidants, and decreasing hyper-pigmentation (Peterson et al., 2017; Verma et al., 2016; Baliga et al., 2012; Biradar et al., 2007; Shanbag, 2015; Pradeep et al., 2016; Peterson et al., 2017; Mamgain et al., 2016; Bhattacharjee R, et al., 2015). Triphala-derived polyphenols such as chebulinic acid are transformed by the human gut microbiota into metabolites such as urolithins which have the potential to prevent the oxidative damage (Baliga et al., 2012; Biradar et al., 2007; Peterson et al., 2017; Verma et al., 2016).

Triphala: Pharmacology

Triphala in *Ayurvedic* Rasayana formulation is used as a rejuvenative herbs, for the treatment of gastrointestinal tract disorders, prevents diarrhea, hypolipidemic effect, and reduces stress related problems, reducing the total cholesterol levels, and low-density lipoprotein (Tarasiuk et al., 2018; Srikumar et al., 2006; Saravanan et al., 2007; Maruthappan et al., 2010; Nariya et al., 2009, 2011; Peterson et al., 2017; Dhanalakshmi et al., 2007; Mukherjee et al., 2006; Baliga et al., 2012; Belapurkar et al., 2014; Kumari et al., 2009; Dhanalakshmi et al., 2007; Rasool and Sabina, 2007; Kumari et al., 2009). Triphala exerts hypoglycemic effects and showed antidiabetic activity by inhibiting the activity of pancreatic glycolytic enzymes, namely alpha-amylase and alpha-glucosidase, which break down larger polysaccharides into glucose molecules that enter the blood stream, thereby reducing blood glucose levels (Rajan and Antony, 2008; Yang et al., 2013; Ganeshpurkar et al., 2015; Peterson et al., 2017; Gurjar et al., 2012; Patel et al., 2012). Triphala also induces enteroprotective effects, due to the high antioxidant content. In addition to this, Triphala may also promote the proper digestion and absorption of food, reduce serum cholesterol levels, improve

circulation, relax bile ducts, prevent immunosenescence, maintain homeostasis of the endocrine system, and increase the production of red blood cells and hemoglobin content (Baliga et al., 2012; Peterson et al., 2017; Belapurkar et al., 2014; Rasool and Sabina, 2007; Kumari et al., 2009; Mukherjee et al., 2006).

The other potential medicinal uses of Triphala, which include free radical scavenging, antioxidant, antifungal, antibacterial, antiviral, hypolipidemic effects, antimicrobial, antiallergic, anti-inflammatory, immunomodulating, appetite stimulation, gastric hyperacidity reduction, dental caries prevention, antipyretic, analgesic, antimutagenic, wound healing, anticariogenic, antistress, adaptogenic, hypoglycemic, anticancer, hepatoprotective, chemoprotective, radioprotective, and chemopreventive effects (Baliga et al., 2012; Zhang et al., 2021; Phetkate et al., 2012; Naik et al., 2005; Jagetia et al., 2002, 2004; Reddy et al., 2009; Gautam et al., 2012; Biradar et al., 2007, 2008; Peterson et al., 2017; Belapurkar et al., 2014; Nariya et al., 2009; Rayudu and Raju, 2014; Dhanalakshmi et al., 2007; Kalaiselvan and Rasool, 2016; Mukherjee et al., 2006; Rasool and Sabina, 2007; Kumari et al., 2009; Saxena et al., 2017). Triphala has been reported as a potential antineoplastic agent and Triphala exerts an antineoplastic effect on many cancer cell lines, including those of the breast, prostate, colon, and pancreas (Baliga, 2010, 2013; Kaur et al., 2005; Peterson et al., 2017; Vadde et al., 2015; Sandhya et al., 2006; Deshpande et al., 2014). Therefore, Triphala could be used as a potential adjunct therapy in the management of colon and other cancers.

Triphala is a rich source of vitamin C, flavonoids and showed anti-cataract potential which helps in maintaining eye good health (Gupta et al., 2010; Peterson et al., 2017). Triphala also plays an important protective role in dentistry and used as a mouth rinse (Prakash and Shelke, 2014; Srinagesh et al., 2012; Shanbag, 2015; Pradeep et al., 2016; Peterson et al., 2017; Mamgain et al., 2016; Bhattacharjee R, et al., 2015; Prabhakar et al., 2014; Tandon et al., 2010). The fruits of *Terminalia chebula* has anti-asthma, anti-tumor, stomach strengthening, expectorant, sore throat, and dyspnea effects and it is usually used to treat infectious diseases (Zhang et al., 2021). *Terminalia bellirica* fruits have the function of convergence, digestion, defecation, deworming, treatment of bronchitis, asthma, and ophthalmopathy (Zhang et al., 2021).

Triphala: Biochemistry

The major constituents of the Triphala formulations are the tannins, gallic acid, ellagic acid, and chebulinic acid, chebulagic acid which are potent antioxidants and therefore, resulted in the immunomodulatory activity without any side effects (Belapurkar et al., 2014; Baliga et al., 2012; Biradar et al., 2007; Peterson et al., 2017; Mukherjee et al., 2006; Rasool and Sabina, 2007; Kumari et al., 2009; Zhang et al., 2021). Gallic acid is a natural phenolic compound with various biological activities such as antioxidant, anti-inflammatory, antibacterial, anticancer, antiviral and cardiovascular protection (Zhang et al., 2021; Shanbag, 2015; Pradeep et al., 2016; Peterson et al., 2017; Mamgain et al., 2016; Bhattacharjee R, et al., 2015). Gallic acid not only destroys virus particles against A and B Influenza virus but also showed broad-spectrum antiviral activity. Therefore, gallic acid is a promising drug source for targeting viral particles. It exhibits concentration-dependent inhibition at higher concentrations. Moreover, gallic acid, methyl gallate and pentagalloyl glucose can inhibit the replication of IAV in MDCK cells, which may be a sensitive agent for inhibiting influenza A H1N1 influenza virus infection (Zhang et al., 2021). Triphala also contains other bioactive compounds such as flavonoids (e.g., quercetin and luteolin), saponins, anthraquinones, amino acids, fatty acids, and various carbohydrates. In addition, Triphala-derived polyphenols such as chebulinic acid are also transformed by the human gut microbiota into bioactive metabolites to prevent oxidative damage (Belapurkar et al., 2014; Baliga et al., 2012; Biradar et al., 2007; Peterson et al., 2017; Mukherjee et al., 2005; Rasool and Sabina, 2007; Kumari et al., 2009). Further, 1,2,3,4,6-penta-O-galloyl- β -D-glucopyranose (PGG) is a more common tannin compound in Triphala which exhibit antiviral effects. Excoecariphenol D, corilagin, geraniin and chebulagic acid also showed potential inhibitory effects on HCV NS3-4A protease (Zhang et al., 2021). The 1,2,3,4,6-penta-O-galloyl- β -D-glucopyranose (PGG) antiviral mechanisms include direct inactivation, inhibition of virus adsorption on host cells and expression of viral genes, and protein translation inhibition of replicated viral genomes (Zhang et al., 2021). Triphala contains a variety of acyl-glucose and has a variety of antiviral effects, such as HIV, and antiviral drugs for severe acute respiratory syndrome coronavirus (SARS-CoV) (Zhang et al., 2021). The 1,2,6-Trigalloyl- α -D-glucose and 1,2,3,6-tetra-O-galloyl- α -D-glucose have a significant inhibitory effect

on HCV NS3 protease (Zhang et al., 2021). The fruit of *Emblica officinalis* has the functions of diuresis, invigorating stomach, and can be used for diarrhea. In addition, *Emblica officinalis* has many pharmacological activities, namely, anti-diabetic, antioxidant, anti-microbial, anti-fungal, anti-allergic, anti-viral and anti-cancer properties (Zhang et al., 2021).

Triphala: Coronavirus

Clinical settings and regulations of research on Covid-19 through Ayurveda, Unani, Siddha, and Homeopathy systems have already been published by the Indian Ministry of Ayush, Government of India, New Delhi, India (INDIA, 2020; Silveira et al., 2020; Malabadi et al., 2021; Rastogi et al., 2020; Ozah, 2020). Triphala with main components and common phenolic tannin compounds have different degrees of antiviral effects, which can inhibit DNA viruses, such as Herpes simplex virus type-1 (HBV) and simplex virus type (HSV). Furthermore, Triphala have inhibitory effects on many RNA viruses, such as human immunodeficiency virus type 1 (HIV-1), RSV, hepatitis C virus (HCV), rabies virus (RABV), human rhinovirus (HRV), influenza A virus (IAV) and human coronavirus (Zhang et al., 2021). Moreover, Triphala has obvious antioxidative stress and antiviral immunity, and promoted hypoxia tolerance and lung injury repair (Zhang et al., 2021). In an *in vitro* experiments, gallic acid, caffeic acid and chlorogenic acid of Triphala herbal formulation can reduce the production of progeny of human coronavirus, HCoV-NL63 particles and have an antiviral effect (Zhang et al., 2021).

Terminalia bellirica is effective against all three HIV-1 pseudoviruses with the least cytotoxicity and the greatest antiviral potential (Zhang et al., 2021). The compounds extracted from *Terminalia bellirica* can be used as HIV reverse transcriptase and have anti-HIV-1, antimalarial and antifungal activities (Zhang et al., 2021).

Ellagic acid has antiviral activity against human rhinovirus (HRV) and Ebola virus (EV) (Zhang et al., 2021). Ellagic acid has different inhibitory effects on a variety of viruses (Zhang et al., 2021). Further, both chebulagic acid and chebulinic acid also showed an *in vitro* antiviral activity (Zhang et al., 2021). In one of the study, chebulagic acid treatment of lethal human enterovirus 71 (EV71)-attacking mice can effectively reduced the mortality and relieved the symptoms by

inhibiting virus replication. Therefore, chebulagic acid may be a potential therapeutic agent for EV71 infection (Zhang et al., 2021).

Corilagin inhibits Herpes simplex virus type-1 (HSV), reduces the cytotoxicity of EV71 or Coxsackie virus A16 to Vero cells has a protective effect against Japanese encephalitis virus (JEV)-induced Parkinson's disease, and HIV viral infection showed high antiviral activity (Zhang et al., 2021). In addition, gallic acid is also resistant to dengue virus (DENV), HBV, EV71 and EV (Zhang et al., 2021).

The compounds extracted from *Emblica officinalis* also have antiviral functions (Baliga, 2010; Baliga et al., 2012, 2013; Zhang et al., 2021; Malabadi et al., 2021). One of the study found that 1,2,4,6-tetra-O-galloyl- α -D-glucose (1246-TGG) extracted from *Emblica officinalis* can significantly resist the infection with herpes simplex virus type-1 (HSV-1) and herpes simplex virus type-2 (HSV-2) at nontoxic concentrations (Zhang et al., 2021). The sesquiterpene glycosides extracted from *Emblica lanceolata* and the main tannin compound Phyllaemblicin B, Euglycoside B has a strong activity against Cox sackie virus B3 (CVB3) (Zhang et al., 2021). Pharmacological studies have shown that *Terminalia chebula* has an inhibitory effect on viral infections such as human immunodeficiency virus type 1 (HIV-1), herpes simplex virus type 1 (HSV-1) cytomegalovirus (CMV) and influenza A virus (IAV) (Zhang et al., 2021). *Terminalia chebula* are rich in hydrolyzable tannins with good antiviral activity (Zhang et al., 2021).

In India, Triphala is commercially available in local market under different brand names, 1) Himalaya Herbal drugs- Triphala powder and in the form of tablets, 2) Dabur-Triphala Churna powder, 3) Zandu-Triphala Churna powder, 4) Pure Indian Foods-Triphala in Ghee, 5) Baidynath-Triphala juice; Triphala Churna powder, 6) JIVA Organic Triphala powder, 7) Organic India- Triphala Herbal Supplement- Triphala powder, 8) SEWANTH'S-Triphala supplemented with *Phyllanthus niruri* and *Glycyrrhiza glabra*, 9) KAPIVA Ayurveda-Triphala natural herbal juice, 10) Gopala Ayurveda.com-Triphala capsules.

In India, during the recent outbreak of coronavirus, SARS-CoV-2 with mutated strains, Delta (B.1.617.2) and Delta Plus (AY.1), the products of Triphala have reached very high demand and there was a shortage of

supply, selling at high price, and people were struggling to get Triphala. Therefore, most of local people in the rural areas of Karnataka state, India including traditional herbal healers were helping Covid-19 patients with Triphala, an alternative herbal medicine as a immunity booster. In addition to this, the local traditional healers in Karnataka, Tamil Nadu, Kerala, Goa, Andhra Pradesh, Telangana, Maharashtra states, India have also helped Covid-19 patients with Triphala and additional supplementation. Triphala is consumed with coconut water as an additional supplementation. Triphala powder is also mixed with sugar cane juice which is rich in mineral nutrients, sweet in taste for the oral consumption for children's and elderly people. Some of the traditional healers were also practicing the consumption of Triphala with diluted *Azadirachta indica* (Neem) juice with strong antiviral properties. In addition to this, Triphala with Aloe vera (*Aloe barbadensis*) juice is also used as an additional supplementation. Triphala is also consumed with fruit juice containing melatonin rich drink (Malabadi et al., 2021c).

Among all these additional supplementations, one of the interesting herbal formulation is Triphala is consumed with pumpkin seeds. The rationale behind the use of pumpkin (*Cucurbita pepo*) or *Cucurbita moschata* seeds belongs to the family *Cucurbitaceae* (Fu et al., 2006; Meru et al., 2017) is an important nutritious diet rich in antioxidants and zinc. Pumpkin seed contains significant levels of antioxidants (tocopherols and tocotrienols) and zinc. The high levels of unsaturated fatty acids (oleic and linoleic acids) in pumpkin seed oil provide health benefits that reduces the risks of arteriosclerosis and heart-related ailments (Stevenson et al., 2007; Fu et al., 2006; Meru et al., 2017). The pumpkin seeds are rich in zinc, protein, fibers, minerals like iron, zinc, calcium, magnesium, manganese, copper, sodium, and PUFA (polyunsaturated fatty acids), phytosterol, vitamins and antioxidants (Muscogiuri et al., 2020). Antioxidant and zinc rich in pumpkin seeds inhibit the coronavirus (SARS) activity (Velthuis et al., 2010; Muscogiuri et al., 2020). Antioxidants increase the number of T-cell subsets, enhance lymphocyte response, increased interleukin-2 production, potentiated natural killer cell activity, and increased response to influenza virus vaccine compared with placebo (Muscogiuri et al., 2020).

In general, Covid-19 patients admitted in hospital are suffering from malnutrition. Therefore, dietary therapy

with Triphala plays an important role as a immunity booster. Covid-19 patient diet should contain source of vitamin E, vitamin D, antioxidants, Beta Carotene and zinc (Muscogiuri et al., 2020). The major dietary sources of vitamin E are vegetable oils (soybean, sunflower, corn, wheat germ, and walnut), nuts, seeds, spinach, and broccoli (Muscogiuri et al., 2020). Vitamin D deficiency has been associated to viral epidemics and significantly higher risk of death from respiratory tract infections (Chandra, 1992; Muscogiuri et al., 2020). Further, vitamin D protects respiratory tract preserving tight junctions, killing enveloped viruses through induction of cathelicidin and defences, and decreasing production of pro-inflammatory cytokines by the innate immune system, therefore reducing the risk of a cytokine storm leading to pneumonia (Muscogiuri et al., 2020). Therefore Covid-19 patients are encouraged to get more vitamin D from diet (Muscogiuri et al., 2020). Foods containing vitamin D include fish, liver, egg yolk and foods (e.g., milk, yogurt) with added vitamin D (Muscogiuri et al., 2020). Beta Carotene is the most abundant in sweet potatoes, carrots, and green leafy vegetables while sources of vitamins C include red peppers, oranges, strawberries, broccoli, mangoes, lemons, and other fruits and vegetables (Muscogiuri et al., 2020).

Another essential trace element that is crucial for the maintenance of immune function is zinc. It has been reported that zinc inhibited severe acute respiratory syndrome (SARS) coronavirus RNA-dependent RNA polymerase (RdRp) template binding and elongation in Vero-E6 cells (Velthuis et al., 2010; Muscogiuri et al., 2020). Although oysters contain the most of the zinc per serving, the most common food to get zinc are represented from poultry, red meat, nuts, pumpkin seeds, sesame seeds, beans, lentils, olive oil, fresh fruits and vegetables, protein-rich legumes, and fish (Muscogiuri et al., 2020).

Conclusions

This review paper has presented some of the interesting and important medicinal properties of Triphala, which is one of the age old Indian folk medicine. Triphala has been used for combating many human health disorders including viral diseases. On the basis of literature survey, there are few reports of Triphala inhibiting coronavirus activity. During the recent outbreak of coronavirus mutants, Delta (B.1.617.2) and Delta Plus (AY.1), Triphala with additional supplementation of

pumpkin seeds, sugar cane juice, Aloe vera juice, neem juice, and melatonin was more effective in boosting the immunity in Covid-19 patients than Triphala alone. However, there are no proven Covid-19 clinical trials for the scientific validation of Triphala. Therefore, clinical trials particularly with Covid-19 could be the new ray of hope in dealing with viral infections. One of the author Silveira et al., (2020) recently coated that herbal medicines are not a magic bullet” to solve the problems related to flu - let alone Covid-19 or any other coronavirus (Silveira et al., 2020). Herbal folk medicines neither can avoid the virus infection but may alleviate symptoms and potentially improve the general wellbeing of patients. It requires a careful assessment of whether such Triphala adjuvant therapies are justified or not. Triphala can only be a suitable therapy at a stage when the severity of the disease is minor For an herbal medicine to be a medicine of high quality, chemically well-characterized, and pharmacologically well-studied preparations are acceptable only. For successful and effective development of a drug, the basic requirement is the correct identification of the source of biologically active compound, its availability and processing. Therefore, a rigorous and evidence-based Triphala with additional supplementations approach will have a balanced assessment of such medicines.

Conflict of interest statement

Authors declare that they have no conflict of interest.

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