



## **Nutraceutical and Pharmacological Appraisal of Āmla (*Emblica officinalis* Gaertn.): A Review**

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### **ABSTRACT**

*Āmla* (*Emblica officinalis* Gaertn, Family: Euphorbiaceae) is a medicinally important plant indigenous to tropical and sub-tropical regions of South-east Asia. The tree is 5-25 metres tall, deciduous, having deltoid-squamiform leaves and bears pale-green globose fruits 2-4 cm in diameter. In Unani medicine, it is widely used in compound formulations or in raw form in many disorders of central nervous system, gastro-intestinal system, skin, hair, general debility etc. In Ayurveda, it is classified as a rasayana, i.e., drugs which promote longevity and delay ageing. *Āmla* fruit is one of the richest sources of Vitamin C (478.56 mg/ 100 ml), alongwith important constituents such as gallic acid, ellagic acid, iron, magnesium, phosphorous, potassium etc. recent researches on *Āmla* have revealed the presence of several biologically active substances with scientifically proven effects as anti-oxidant, anti-ageing, immunomodulatory, memory enhancing, protective towards vital organs such as liver, heart kidneys; anti-depressant, anti-cancer and many more beneficial effects. Most of the experiments have been carried out on *Āmla* fruit and are dose-

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dependent. Moreover, no toxic effects have been reported in any of the studies. This review focuses on the various biologically active components of *Āmla* and its relevance in modern pharmacology.

**Keywords:** *Āmla*; *Emblīca*; *nootropic*; *anti-oxidant*; *neuroprotective*.

## 1. INTRODUCTION

*Āmla*, commonly known as Indian Gooseberry is the fruit of *Emblīca officinalis* Gaertn. (Syn.: *Phyllanthus emblica* Linn.), an important medicinal plant belonging to the family Euphorbiaceae/ Phyllanthaceae [1]. *Āmla* occupies a significant place in traditional and folk medicine, and also a religious significance. In Indian mythology, it is believed to be the first tree to be created in the universe, and known as the 'fruit of heaven' or 'nectar fruit'. Its Sanskrit name *Āmlakī* translates into 'The Fruit where the Goddess of Prosperity Resides' and the tree is worshipped in Hindu religion for the numerous benefits it provides [2]. The tree also has an ornamental value, especially when it bears the pale green berries [3]. In Unani medicine, *Āmla* has an immense importance as a nutraceutical as well as for its pharmacological applications [4]. It is described as having a *bārid* (cold) and *yābis* (dry) temperament, and used in a wide variety of disorders including skin diseases, gastro-intestinal ailments, cardiac conditions, cerebral weakness, weakness of other vital organs and general debility etc. In fact, it is one of the most frequently used drugs, as a compulsory part of all *īṭrīfālāt* (a type of oral semi-solid preparation in Unani medicine, usually used for central nervous system and gastro-intestinal problems), and other compound formulations such as *Jawāriṣh Āmla*, *Anūshdarū*, *Safūf-i-Hāḍim* etc [5,6,7].

## 2. METHOD OF DATA COLLECTION

Extensive review of Unani literature was conducted initially to identify the main clinical uses and benefits of *Āmla*. In the next step, major scientific search engines (Pubmed, Science Direct, Web of Science) were searched for studies regarding the nutraceutical and pharmacological uses of *Āmla*. The search was restricted to articles published within last 10 years. Keywords used for the search were '*Emblīca officinalis*', '*Phyllanthus emblica*', 'uses', 'antioxidant', 'chemical constituents', 'nutraceutical' etc. in various combinations. The studies which provided information regarding action mechanism were preferred, preferably

where the whole *Āmla* fruit had been used in raw form. Poorly designed studies were excluded. Preference was also given to clinical studies so that the article may be useful for practical application and further clinical studies. The overall aim was to elaborate health benefits of *Āmla* and validate its clinical uses as described in Unani medicine, as well as to present the contemporary knowledge.

## 3. TAXONOMY AND DISTRIBUTION

The Taxonomical classification of *Āmla* is given in Table 1.

**Table 1. Taxonomical classification of Āmla**

Kingdom	Plantae (Plants)
Subkingdom	Tracheobionta (Vascular plants)
Superdivision	Spermatophyta (Seed plants)
Division	Angiospermae (Flowering plants)
Class	Dicotyledonae (Dicotyledons)
Subclass	Rosidae
Order	Geraniales
Family	Euphorbiaceae
Genus	<i>Emblīca</i>
Species	<i>officinalis</i> Gaertn.

**Synonyms:** *Phyllanthus emblica* L., *Cicca emblica* Kurz, *Diasperus emblica* (L.) Kuntze, *Dichelactina nodocolis* Hance, *Emblīca arborea* Raf., *Mirobalanus emblica* Burm., *Phyllanthus glomeratus* Roxb. ex. Wall., *Phyllanthus mairei* H. Lev., *Phyllanthus mimosifolius* Salisb [8]. A variety of the plant, *Emblīca fischeri* Gamble, also known as *Myrobalan emblic* is a small tree distributed in South India and bears edible fruits [9].

*Āmla* is indigenous to the tropical and subtropical regions of South-East Asia, particularly central and south India, Bangladesh, Pakistan, Sri Lanka, Uzbekistan, Malaysia, southern China and Mauritius from near sea-level upto an altitude of 1500 metres. It is also cultivated for its fruits in West Indies, Central America, Japan and Madagascar. The tree is commonly domesticated for its nutritional and ornamental value in India, Malaysia, China and Singapore. It flourishes best in deep fertile soil. However, it has a good

draught resistance and may thrive in dry, arid soil which is inadequate for most trees. It is observed that the nutritional content of *Āmla* fruit declines in highly alkaline soil (pH 8.0). The tree is fire resistant to a great extent and one of the first trees to recover after a fire. However, it is slow growing and bears fruit after 5-8 years [8]. When grown in alkaline soil, *Āmla* is known to reduce the pH of the soil, making it suitable for other crops [9]. Fresh *Āmla* fruits resemble green sour plums and are about the size of a walnut, having important nutraceutical and therapeutic benefits [10].

#### 4. BOTANICAL DESCRIPTION

**Tree:** *Āmla* tree is 5-25 metres tall deciduous tree with a canopy spread of approximately 30 feet [9]. It has a crooked and knarled trunk upto 35 cm in diameter with a thin, smooth, grey bark peeling in patches. The main branches are angular and densely pubescent. The branchlets are glabrous or finely pubescent, 10-20 cm long.

**Leaves:** Leaves on the main branches are deltoid-squamiform, resembling stipules. Those on the branchlets are biseriolate, alternate, thin, sessile, narrowly oblong, 5-25 mm in length resembling pinnate leaves.

**Flowers:** Flowers are greenish-yellow in colour, fascicled in the axils of leaves. The male flowers are more concentrated at the base of young twigs; the female flowers are solitary and higher up the twig.

**Fruit:** *Āmla* fruit is depressed, globose, 2-4 cm in diameter, having six vertical striations over the surface, pale green in colour which turns to yellow with maturation. The fruit epicarp is thin, translucent, and strongly adhered to the crisp and juicy mesocarp. A hexagonal stone is embedded in the centre of mesocarp which has three slightly dehiscent compartments, each usually containing two trigonous, 4-5 mm x 2-3 mm seeds [8].

**Flowering and fruiting:** Pale green coloured flowers grow in small dense clusters between the months of March-May in northern regions of India. However, the flowering pattern is altered in southern states [8]. In Tamil Nadu, *Āmla* flowers in the months of June-July and again in February-March [9].

#### 5. NUTRITIVE AND MEDICINAL CONSTITUENTS

*Āmla* is the richest source of Vitamin C. the fruit juice contains the highest amount of Vitamin C (478.56 mg/ 100 ml) as compared to other fruits such as lime, grapes, pomegranate and apples. In addition, the nutritional constituents of the fruit (per 100 gm of *E. officinalis* fruit) include carbohydrates (82.91 gm), protein (6.04 gm), fat (0.51 gm), fibre (2.78 gm), Iron (11 mg), magesuim (46 mg), zinc (0.23 mg), chromium (0.82 mg), phosphorous (159 mg), potassium (2.54 gm), calcium (129 mg), copper (0.22 mg) and nicotinic acid (0.2 mg) [11,12]. The setials of some pharmacologically active constituents of *Āmla* are given in Table 2.

**Table 2. Some pharmacologically active constituents of *E. officinalis***

S. no.	Name of constituent	Molecular formula	Biological activity
1.	Chebulinic acid	C <sub>41</sub> H <sub>32</sub> O <sub>27</sub>	Antioxidant activity, anti-secretory and cryo-protective activity
2.	Chebulagic Acid	C <sub>41</sub> H <sub>30</sub> O <sub>27</sub>	Antispasmodic action
3.	Emblicanin-A	C <sub>34</sub> H <sub>22</sub> O <sub>22</sub>	Antioxidant activity
4.	Emblicanin-B	C <sub>34</sub> H <sub>22</sub> O <sub>22</sub>	Antioxidant activity
5.	Gallic acid	C <sub>7</sub> H <sub>6</sub> O <sub>5</sub>	Radioprotective effect, hemopreventive effect, anti-carcinogenic, antioxidative, anti-mutagenic, antiallergic and anti-inflammatory activities.
6.	Ellagic acid	C <sub>14</sub> H <sub>6</sub> O <sub>8</sub>	Radioprotective and chemopreventive effect, antityrosinase Activity, antioxidant, antiproliferative, and antiatherogenic Properties, estrogenic/antiestrogenic Activity
7.	Quercetin	C <sub>15</sub> H <sub>10</sub> O <sub>7</sub>	Radioprotective, chemopreventive, hepato protective effect
8.	Phyllantine	C <sub>14</sub> H <sub>17</sub> NO <sub>3</sub>	Anti-bacterial activity
9.	Phyllantidine	C <sub>13</sub> H <sub>15</sub> NO <sub>3</sub>	Neuropharmacological activity (CNS activity)
10.	Punigluconin	C <sub>34</sub> H <sub>26</sub> O <sub>23</sub>	Antioxidant activity
11.	Pedunculagin	C <sub>34</sub> H <sub>24</sub> O <sub>22</sub>	Antitumor activity, Antioxidant activity

## 6. TRADITIONAL USES

*Is'hāl* (Diarrhoea): Take dried *Āmla* fruit and soak it in water. When it softens, grind it into a pulp and add a little salt. Make pills of the size of a gram seed and use in a dose of two pills twice a day. Alternately, soak *Āmla* fruit overnight in water and decant the water in morning, this may also be used as a remedy for diarrhoea.

*Kathrat-i-'Atash* (Excessive thirst): For quenching thirst, decant of *Āmla* prepared as described above is prescribed orally.

*Khafqān-i-qalb* (Palpitation): *Murabba Āmla* (preserve/ jam made with *Āmla* fruit), preferably covered with silver foil is effective in palpitation. Best used during the evening.

*Do'f-i-baṣr* (weakness of vision): Crush fresh *Āmla* fruits and express the juice. Apply it with a suitable applicator in the eyes.

*Do'f-i-dimāgh* (weakness of brain) and *Do'f-i-rahim* (weakness of uterus): *Murabba Āmla* is effective in both conditions. Oil made with *Āmla* fruit should be applied on the scalp for weakness of brain.

*Intishār-i-sha'r* (falling of hair): Crush fresh *Āmla* and apply on hair roots. Also, soak *Āmla* in water and rinse hair with the water. Application of *Āmla* oil is also beneficial for hairfall [13].

## 7. PHARMACOLOGICAL USES

### 7.1 Antioxidant Activity

*Āmla* contains a number of biologically active compounds having an antioxidant activity like tannins (ellagitannins and gallotannins), flavonoids, flavonols, anthocyanins and phenolic acids [14]. In a recent study, *Āmla* fruit extract was found to improve mitochondrial dysfunction in skeletal muscles. It was also found to have cyto-protective effects and lowered the reactive oxygen species level induced by oxidative stress [15]. The fruit extract also demonstrated a dose-dependent protective effect on plasma proteins and red blood cells; and also restored the membrane integrity at higher levels, mainly due to the presence of gallic acid, quinic acid, and quercetin [16]. Gastroprotective effects of fruit extract of *Phyllanthus emblica* Linn. were also evaluated in a standard-controlled clinical study. In addition to clinical improvement, *Āmla* fruit extract also caused the healing of damaged

mucosa and inhibition of *H. pylori* after 14 days of the therapy [17].

### 7.2 Cardio-protective Activity

*Āmla* is one of the fruits described as having a cardioprotective effect by Ibn Sina in his famous treatise '*Kitab al-Advia al-Qalbia*' (the book on drugs for cardiac diseases) [18]. According to Ibn Sina, it is a cardiotonic drug and also protects the heart by virtue of correcting the diseases in surrounding organs such as gastro-oesophageal reflux disease and dys-temperament of the surrounding organs etc. Recent studies have shown that *Āmla* has a number of cardiovascular effects including antiatherogenic, vasodilatory, anticoagulant, antioxidant, anti-inflammatory, antiplatelet, antidyslipidemic, antihypertensive, and lipid deposition inhibitory effects. It also improves vascular endothelial function and protects against certain drug toxicities (e.g. isoproterenol) as well as ischemia-reperfusion injury [10] *P. emblica* extract caused a dose-dependent decrease in platelet aggregation; and also enhanced the activity of standard anti-coagulant drugs (clopidogrel and ecosprin) [19]. In a recent animal study, *E. emblica* ethanolic extract showed a protective effect against high-fat diet-induced oxidative stress on coronary arteries [20]. The effects are attributed to the emblicanin, tannins, flavonoids, polyphenols, gallic acid and ascorbic acid present in the fruit [21].

### 7.3 Hypolipidemic Activity

*Āmla* is thought to interfere with cholesterol absorption and protein metabolism leading to weight loss in animal models of hyperlipidemia. The presence of flavonoids helps in lowering lipid level by inhibition of 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase (HMG CO-A) pathway. *Āmla* also induces reverse cholesterol transport by increasing lipoprotein lipase activity which in turn enhances the oxidation of fatty acids from VLDL (very low density lipids) and TG (triglycerides) [21]. Supplementation of *P. emblica* extract caused significant improvement in the lipid profile and oxidative stress in two recent clinical studies in a 12-week period. A decrease in *hs*-CRP (high sensitivity C-reactive protein) and improvement in endothelial dysfunction was also observed [22,23]. In another interesting study, one-month supplementation of 50 gm of *Āmla* in raw form effectively decreased the cholesterol levels and LDL in 35 male patients [24]. There is also

evidence that the Indian gooseberry may prevent hyperlipidemia of old age by diminishing the oxidative damage in old age [25].

In a recent important study, 500 mg *Āmla* extract twice a day caused extremely significant reduction in atherogenic index of the plasma, triglycerides and total cholesterol in a multi-centric placebo-controlled trial in South India in a 12-week study. There was no reduction in coenzyme Q10 (Co Q10) which is seen with statins. Reduction of Co Q10 is associated with numerous neurological and myopathic abnormalities, as well as increased risk of diabetes [26].

#### 7.4 Neuro-protective and Memory Enhancing Activity

There is convincing evidence that *Āmla* has a multifaceted effect on neurological tissues. In a recent *in vitro* study, it was observed that the chebulagic acid present in *Āmla* enhances autophagy in intracellular proteins and organelles and also protects against neuronal toxin 1-methyl-4-phenylpyridinium (MPP+) which mimics the pathology of Parkinson's Disease. Hence leading to preservation of dopaminergic neurons involved in the disease process [27]. In another study, *E. officinalis* aqueous and methanolic extract was found to protect neuronal cells from oxidative damage caused by hydrogen peroxide. The intensity of DNA damage was markedly attenuated, and recovery from damage was also enhanced [28]. *E. officinalis* extract also decreases the nitrite levels, inflammatory cytokines and oxidative stress in patients at high risk of diabetic neuropathy, HIV-induced dementia, haloperidol-induced tardive dyskinesia and other CNS maladies. A dose-dependent attenuation of kainic acid and pentylentetrazole was observed by a hydroalcoholic extract of *E. officinalis* which could completely eradicate the generalized seizures and status epilepticus, while also enhancing the cognitive function. Methanolic extract of *E. officinalis* fruit also showed a significant inhibitory effect on acetylcholinesterase which is one of the key targets of Alzheimer's Disease [11].

*Āmla* is also one of the best known nootropic drugs. In a recent controlled study on fluoride-exposed rats, dried *Āmla* powder (100 mg/day) caused restoration of damage caused by fluoride reflected by normalized protein levels and acetylcholinesterase [29]. A reversal of diazepam and scopolamine induced amnesia is also

observed [11]. A protective effect on the DNA fragmentation and apoptosis induced by a high fat and salt diet has also been observed by the tannoid fractions of *E. officinalis*. In addition to reducing the oxidative stress, the fractions also led to activation of nuclear erythroid 2-related factor (Nrf2) which regulates expression of various anti-oxidative and cytoprotective genes. A stabilizing effect on mitochondrial membrane potential (MMP) and mitochondrial ATP on neuronal cells was also observed which can control cell death [30].

#### 7.5 Anti-depressant Activity

Aqueous extract of *E. officinalis* was found to have a positive anti-depressant effect at 200 mg/kg in a recent controlled animal study. The effect was thought to be caused by interaction with  $\alpha$ 1-adrenoceptors, and decreasing the levels of GABA (Gamma-Aminobutyric Acid) in brain, the target molecule of anti-depressants. The extract also lowered the levels of MOA (Monoamine oxidase) which causes degradation of endogenous CNS enzymes. The effects were reversed by pretreatment with  $\alpha$ 1-adrenoceptor antagonist drugs, which confirmed the mechanism of action. Since the effect was primarily seen on the monoaminergic system, it was hypothesized that ascorbic acid, flavonoids and tannoid principles may be responsible for the action, supported by the anti-oxidant effect [31]. However, there is still a dearth of information on the anti-depressant effects of *Āmla*, and only few researches have been done, while no clinical studies were available in the past ten years which could provide conclusive evidence.

#### 7.6 Anti-diabetic Activity

Experimental research on *Āmla* have demonstrated its effects as a potent drug which targets many of the pathological changes in both type-1 and type-2 diabetes and exerts a multitude of actions including prevention of diabetes complications. Oral treatment with 100 mg/kg/day of hydroalcoholic extract *E. officinalis* in STZ (streptozotocin) induced diabetic rats showed a glucose-lowering activity after a four-week study, which was strongly correlated with the polyphenol content of the extract. There was also a decrease in concentration of lipids which has been deranged by STZ injection, along with an increase in anti-oxidant enzymes. It was suggested that the hydroalcoholic extract increases peripheral uptake of insulin as well as having an insulin-like effect, without increasing

adiposity [32]. However, the intake of powdered raw fruit of *Āmla* is also known to have a direct insulin-like action in alloxan-induced diabetic rats whose  $\beta$ -cells did not produce any insulin, the effect was missing in the hydroalcoholic extract. In a clinical study, 3 gm/ day of *E. officinalis* fruit powder significantly ( $p < 0.05$ ) reduced the blood glucose and cholesterol levels in normal and diabetic subjects in three weeks. However, the values remained within the normal limits for both groups [33]. Recently, 1-O-galloyl- $\beta$ -D-glucose ( $\beta$ -glucogallin) has been identified in *Āmla* fruit which prevents hyperglycemia-induced sorbitol accumulation in lens which causes cataract and other complications [34]. In addition, the gallic acid component of *Āmla* also stimulates pancreatic insulin secretion, restores  $\beta$ -cell structure and prevents apoptosis of  $\beta$ -cells. Intake of *Āmla* also decreases the advanced glycation end-products associated with oxidative damage. In most of the studies, the effects have been compared to standard drugs [35].

### 7.7 Anti-cancer and Anti-mutagenic Activity

Several studies strongly advocate the preventive effect of *Āmla* against initiation, promotion and progression in several types of human cancers. Tannins present in *Āmla* are also known to have specific cytotoxic effect on human oral squamous cell carcinoma cells. *Āmla* extract has been found to possess anti-proliferative activity on solid tumors and also reduced their size through inhibition of cell cycle-regulating enzyme, Cdc25 phosphatase in a dose-dependent manner. Anti-proliferative activity has been attributed to 18 phytochemicals (norsesquiterpenoids, phenolic compounds, proanthocyanidin polymers and gallic acid) of *Āmla* [36]. *P. emblica* extract was observed to potentiate the action of chemotherapeutic drugs while preventing adverse effects on normal cells and reducing the risk of secondary chemotherapy-induced tumors [37]. The flavonoid quercetin is being studied as an specific anti-cancer molecule. However, the activity cannot be attributed to a single compound and is probably caused by a complex interaction of the various phytochemical present in the berry [38]. *Āmla* extract also increased the expression of autophagic proteins and reduced the expression of angiogenic genes in human ovarian cancer cells. It also acted in synergism with cisplatin and reduced cell proliferation in the cancer cells [39]. In another animal study, *P. emblica* extract down-regulated the interleukin 1 $\beta$

and prevented precancerous lung lesions induced induced by benzopyrene [40].

### 7.8 Anti-microbial Activity

Anti-microbial activity of *Āmla* has been a topic of research interest in the past few decades. In an interesting study, the aqueous infusion and aqueous extract of *E. officinalis* exhibited potent antibacterial activity against 345 bacterial isolates including *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhi* and *S. paratyphi* A & B [41]. More recently, anti-bacterial (both gram negative and positive), anti-viral and anti-fungal activity has also been identified in the extracts of *P. emblica*, with specified MIC (minimum inhibitory concentration) values. Essential oils of emblica obtained by hydrodistillation and supercritical fluid extraction showed good anti-microbial activity in an *in vitro* study, attributed mainly to  $\beta$ -caryophyllene,  $\beta$ -bourbonene, 1-octen-3-ol, thymol, and methyl eugenol components in the oils. The effects are also thought to be mediated through flavonoids (by disrupting DNA replication), tannins (inhibition of extracellular enzymes or direct effect on bacterial metabolism) and phenolics (antioxidant and radical scavengers, cause disruption of electron transport chain, membrane destabilization, disruption of membrane transport) [42]. *E. officinalis* gel was tested in patients of periodontitis as an adjunctive to scaling and root planning. There was a significant decrease in inflammation and periodontal destruction with 10% sustained-release gel [43]. Glochicoccinoside D isolated from *P. emblica* roots displayed strong activity against influenza A virus H3N2 and EV71 virus (hand, foot and mouth virus) [44]. A recent study has reported the presence of eight bisabolane sesquiterpenoid glycoside phyllaemblicins G1–G8, alongwith phyllaemblicin F, phyllaemblic acid and glochicoccin with potential anti-HBV (Hepatitis-B virus) activity [45]. In a recent development, magnesium oxide nanoparticles have been prepared from *E. officinalis* fruit extract which are used to treat cotton fabric to be used as anti-bacterial dressing [46].

### 7.9 Hepato-protective Activity

*Āmla* provides protective effects on liver function against several toxic agents and also chemical-induced carcinogenesis. In a recent animal study, aqueous extract of *P. emblica* had a protective effect on hepatic cells against Non-

Alcoholic Fatty Liver Disease. Steatosis was also improved by increase of adiponectin in adipocytes and PPAR- $\alpha$  in liver tissues, alongwith a decrease in peritoneal and epididymal fat mass [47]. Quercetin present in *Āmla* fruit has protective effect in alcohol-induced liver damage. Animal studies have demonstrated that emblicanin A and emblicanin B protect against hepatotoxicity caused by iron overload. *Āmla* also has a protective effect against paracetamol, arsenic, cadmium, carbon-tetrachloride and ochratoxin induced liver toxicity. It offers specific protection against anti-tubercular drugs isoniazid, rifampicin and pyrazinamide through antioxidant and membrane stabilizing effects [48]. Aqueous extract of *E. officinalis* (100  $\mu$ g/ml) was reported to modulate the anti-oxidant defense system and hence provide protection against hepatocellular cancers. There was no adverse effect noted at this high dose, so the extract was considered non-toxic to hepatic cells [49].

### 7.10 Nephro-protective Activity

There is a potential protective effect of *Āmla* on renal tissues as suggested in recent studies. However, only two studies could be located in the past ten years, hence the mechanisms have not been explored in detail. In an animal study, aqueous extract of *E. officinalis* (2 mg/day) caused a significant reduction in lipid peroxidation induced by ochratoxin in liver and kidneys. The effects were attributed to Emblicanin A and B antioxidants and associated with a significant increase in the activity of the activity of hepatic antioxidants [50]. In another controlled study, a herbal *Āmla*-containing preparation normalized the anti-oxidant enzymes, serum creatinine, urea and uric acid levels in animal models of bromobenzene toxicity ( $p < 0.05$ ) at a dose of 250 and 500 mg/kg [51].

### 7.11 Gastro-protective Activity

The protective effects of *Āmla* on the gastric epithelium have been studied in the recent past. Crude ethanolic extract of *P. emblica* showed a dose-dependent biphasic effect on NSAID (non-steroidal anti-inflammatory drugs) induced ulcers in a standard-controlled study on swiss albino mice. The extract was effective in healing the ulcers from third day at a dose of 60 mg/ kg, but the effects were reversed at 120 mg/kg. However, the extract showed no toxic effects at upto 300 mg/ kg. An immunomodulatory role was also observed, evidenced by reduced pro-

inflammatory cytokine (TNF- $\alpha$  and IL-1 $\beta$ ) levels and up-regulation of anti-inflammatory cytokine (IL-10) concentration [52]. Ethanolic extract of *Āmla* in a dose of 500 mg/kg was evaluated for its gastro-protective effects in a standard controlled clinical study. The extract showed significant improvement in pain, vomiting, sleep disturbances and other associated problems. Healing effect on the gastric mucosa was also observed on biopsy. In other studies, *P. emblica* ethanolic extract showed inhibitory effect on *H. pylori* with minimum inhibitory concentration values ranging from 0.91 to 1.87  $\mu$ g/ $\mu$ l [17].

In an important placebo-controlled trial, *P. emblica* fruit powder significantly reduced regurgitation, heartburn and epigastralgia in patients of gastro-esophageal reflux disease. The reduction of symptoms was close to 50%, which was clinically significant. Based on observations, it was also suggested that in addition to the anti-oxidant effect, *Āmla* suppresses the brain-gut interaction, stress and promotes sleep, which also contributes to the improvement of symptoms [53].

### 7.12 Wound Healing Activity

Freeze-dried extract of *P. emblica* extract at a dose of 0.1  $\mu$ g/ml accelerated endothelial wound closure, promoted endothelial sprouting and nitric oxide production in cells exposed to oxidative damage. However, it was cytotoxic at doses of 50–200  $\mu$ g/mL. The effects were similar to ascorbic acid used in similar concentration as the extract; hence the wound healing activity was attributed to the anti-oxidant effect of ascorbic acid [54]. In another study, alcoholic extract of *E. officinalis* accelerated wound closure and healing in full-thickness wounds in animal models. An increase in collagen fibres, aldehyde content, and tensile strength was observed. There was an increase concentration of anti-oxidants mainly ascorbic acid, superoxide dismutase, glutathione peroxidase and catalase at the site of wound indicating an anti-oxidant effect. Interestingly, the extract maintained its efficacy after being stored for one year [55].

### 7.13 Anti-HIV Activity

There is preliminary evidence that *Āmla* fruit may have beneficial effects for HIV/ AIDS patients. In a recent study, a herbal formulation containing *E. emblica* was tested as an adjuvant therapy in AIDS patients on ART (anti-retroviral therapy) against a control group (only ART). The test

group showed better symptom improvement and better increase in CD4 helper cells without causing increase in SGOT, SGPT, Alkaline Phosphatase, Urea and Creatinine, hence, better tolerance to ART. It was concluded that the herbal formulation decreases the resistance to ART and improves the outcome of therapy. The results were attributed to the presence of high concentration ascorbic acid which is a strong immunomodulator [56]. In another study, a polyherbal gel formulation containing *P. emblica* fruit extract showed potent in vitro anti-HIV-1 and anti-HSV-2 activities at lower IC values as compared to acyclovir. There were no adverse effects on the survival of lactobacilli, breach of epithelial monolayer or increase in pro-inflammatory cytokines, and could prove to be effective in the prevention of sexually transmitted HIV-1 and HSV-2. Anti-HIV-1 activity was attributed to gallic acid, ellagic acid, tannins and catechins present in the formulation, which are present in abundant amounts in *Āmla*. It was also postulated that catechins and polyphenols stimulated the growth of lactobacilli [57].

#### 7.14 Anti-ageing Activity

In ayurveda, *Āmla* is classified as a *rasayana*, that is, the drugs which promote longevity, prevent illness and ameliorate symptoms of old age. In a recent study, *Āmla* formulation prepared by traditional Ayurvedic method was given in a dose of 45 gm/ day to healthy volunteers. After 45 days of treatment, there was an increase in telomerase activity and telomere length as compared to age-matched placebo controls. The increase of telomerase activity may delay the onset of ageing process by marking critical upper limit of telomere length. No adverse effects were noted during the study in any age group [58]. In an *in vivo* model of Alzheimer's Disease, the tannoid principles of *E. officinalis* demonstrated neuroprotective effects against memory loss through attenuation of acetylcholinesterase, oxidative stress, apoptosis and amyloid toxicity [59]. *E. officinalis* extract also showed protective effects against collagen degradation and benefitted collagen synthesis in an animal study, providing evidence of its anti-ageing activity [60]. Intake of fresh fruits of *E. officinalis* increased the lifespan in *Drosophila melanogaster* by scavenging of reactive oxygen species [61]. Topical application of cream containing *E. officinalis* have also demonstrated protective effects against ultraviolet radiation-induced aging process, attributed to the presence of phenolic acids and flavonoids [62].

#### 7.15 Radio-protective Activity

*E. officinalis* extract effectively inhibited UVB (ultraviolet-B) radiation induced photo-aging in human fibroblasts by restoration of disturbed cell cycle, inhibition of hyaluronidase and scavenging of reactive oxygen species ( $p > 0.001$ ) [63]. In another similar study, freeze-dried juice of *P. emblica* fruit (0.5 mg/ml) inhibited the induction of reactive oxygen species and restored the collagen-damage in ultraviolet radiation-exposed fibroblasts ( $9.5 \pm 0.28$ -fold protection) as compared to ascorbic acid ( $3.7 \pm 0.07$ -fold protection). The extract was also more stable under UV exposure and since it contained only trace amount of ascorbic acid, the effect was probably mediated by several components like gallic acid, mucic acid in addition to ascorbic acid [64]. In an important study, mice exposed to 700 rads (7000 mSv) of radiation for 10 days were treated with fruit pulp of *E. officinalis* at a dose of 2.5 gm/ kg. The acceptable safe upper limit of radiation exposure for humans is 1.67 mSv per month. The extract significantly attenuated the biological effects of radiation evidenced by lowering of lipid peroxides, glutathione and other antioxidant enzymes. It was concluded that *E. officinalis* could be useful in reducing the adverse effects of therapeutic radiation [65,66].

#### 7.16 Anti-amnesic Activity

Various extracts of *Āmla* have been demonstrated to have protective and curative activity against age and toxicity induced amnesia. Alcoholic fruit extract of *Āmla* improved cognitive functions, brain antioxidant enzymes, and acetylcholinesterase (AChE) activity in animal models of Alzheimer's disease. Among the various extracts tested, the one derived from the unripe fruit of *Āmla* gave the best results (100 and 200 mg/kg;  $p < 0.01$ ,  $p < 0.001$  respectively) [67,68]. In another standard-controlled study, *Āmla* extract reversed amnesia produced by Scopolamine, Diazepam and Cyclosporine comparable to standard drugs [69]. In another study, scopolamine-induced cholinergic dysfunction was corrected by *E. officinalis* extract (600 mg/kg) [70]. In another study, 100 mg/day of dried fruit of *Āmla* helped in overcoming neuronal toxicity caused by fluoride reflected by decrease in malanoaldehyde levels which were increased by fluoride exposure [71]. Tannoid principles of *E. officinalis* (200 mg/kg) significantly ameliorated the aluminium concentration, acetylcholinesterase activity, and A-beta synthesis-related molecules in brain of



mice exposed to aluminium chloride. The locomotor, memory and spatial learning impairments were significantly improved [72].

## 8. CONCLUSION AND RECOMMENDATIONS

*Āmla* has the potential to be called 'the sustainer' of humans considering the wide range of its beneficial effects. The humble berry contains a remarkable cocktail of vitamins, minerals and anti-oxidants in the right proportion which have miraculous effects as preventive and therapeutic, packed by nature in a way that cause practically no adverse effects and endow with health and longevity. Modern scientific studies have validated the traditional knowledge about the medicinal effects of *Āmla*. Interestingly, many studies on raw fruit have provided exceptional results in many disease conditions such as diabetes and as an anti-oxidant which advocates for its use as a nutraceutical. It is also imperative to note that most of the scientific studies have focused on a particular extract of the plant in a single disease condition, with the target of extracting the active component. However, on an extensive review of literature, it is observed that the fruit provides beneficial effects to several bodily systems without harming any, even when used at higher doses [49]. Also, there may be synergistic action between various components, not explored yet. Hence, it seems more pertinent that the fruit should be used whole as prescribed in traditional systems of medicine.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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