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A Review on *Phyllanthus emblica*: Anti-inflamatory and Antioxidant Effect

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Phyllanthus emblica L. (amla) managed in Ayurveda as potent rasayan in treating hepatic disorders. *Phyllanthus emblica* Linn (*Emblica officinalis* Gaertn) widely reputed as Amla or Indian Gooseberry a well-known tree used in production of herbal pharmacological medicines. A highly nutritious plant reported with dietary source of vitamin C, Minerals and amino acids. This plant is of superior value in Medicine, Ayurveda. Amla fruits are widely employed in treatment of diarrhea, jaundice and inflammation. The plant has proven its efficiency in treating antidiabetic, hypolipidemic, antibacterial, antioxidant, spasmolytic, antiulcerogenic, hepatoprotective, gastroprotective and chemoprotective property. All the parts of plants are rich in medicinal value. The plant consists of various phytoconstituents like alkaloids, phenols, tannins, minerals, vitamins, amino acids, fixed oils, multi vitamins and inorganic compounds. Organic chemicals like Ellagic

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acid, Gallic acid, Emblicanin A & B, Phyllembein, Quercetin and Ascorbic acid are decided to be efficient for health. The various other Ayurvedic potentials of *P. emblica* are yet to be proven scientifically in order to explore its broad spectrum of therapeutic effects. In the current review, the conventional Amla use for household treatment in indigenous people and its activities will be of tremendous potential and importance. Therefore, an effort has been made to increase knowledge of the medical importance and use of Amla as a rich natural source of novel bioactive components.

Keywords: Amla; conventional medicines; coronary; antioxidant; treatment applications.

1. INTRODUCTION

"The Indian gooseberry, *Phyllanthus emblica* Linn. (syn. *Emblica officinalis*), widely reputed as Aamla or Amla in Hindi and amalika in Sanskrit, a deciduous tree belonging to Family Euphorbiaceae" [1-4]. "An edible fruit that is sour, bitter, astringent and quite fibrous" [5,6]. "All parts of the plant have medicinal properties" [7]. "Conventional Amla, a rich natural source of vitamin C , Embilicanin A, Emblicanin B, Phyllaemblicin B, Punigluconin and also consists of Ellagic acid, Chebulinic acid, Chebulagic acid, Gallic acid, Quercetin, Apigenin, Leutolin, Corilagin . etc.", [8-11]. "The fruits are widely used either alone or in combination with other traditional herbs in preparation of medicines" [12,13]. A massive research studies have been performed on the plant in exploring its medicinal properties [14].

Fig. 1. Figure showing the fruits of *Emblica officinalis* [15]

1.1 Systematic Position of *Phyllanthus Emblica*: [16,17]

Cultivated (gramya) and wild (vanya) varieties of Amla are found in India. The wild amla is small smooth and juicy.

Taxonomic hierarchy of *Phyllanthus emblica*:

Kingdom: Plantae -plants
Sub-kingdom: Tracheobionta -vascular plants
Super Division: Spermatophyta- seed plant
Division: Magnoliophyta-Flowering plant
Class: Magnoliopsida-Dicotyledons.
Sub-class: Rosidae. Order: Malpighiales
Family: Phyllanthacae
Genus: Phyllanthus L. (Leaf-flower)
Species: *Phyllanthus emblica* L. (Emblic)

The common names of Amla are mentioned below in the Table 1.

2. CHEMICAL CONSTITUENTS OF *Phyllanthus emblica*: [18,19]

The chemical constituents of *Phyllanthus emblica* are listed below in Table 2.

3. NUTRITIONAL VALUE OF AAMLA OR AMLA [20]

- Raw Amla provides 600 milligram Vitamin C per 100 gram.
- Pressed juice provides 920 milligram / 100ml.
- Dehydrated Amla provides 2500 to 3500 milligram Vitamin C per 100 gram.
- Dried and powdered Amla provides 1800 to 2600 milligram Vitamin C per 100 gm.

4. REPORTED ACTIVITIES OF *Phyllanthus emblica*

a: Analgesic activity: Amla is one among the most frequently exploited herb in indigenous medicine. Analgesic activity of amla is screened by eddy's hot plate and acetic acid induced writhing's method. Pentazocin (10 mg/kg, i.p.) is considered as standard with respect to test groups receiv fruit powder at dose of 600mg/kg, oral. In the hot plate latency method the amla powder exhibit effective analgesic effect at 9.59±1.99sec (heat latency) at 150min while the standard drug exhibit 13.41±1.81sec (heat latency)at 150 min. *Emblica officinalis* was unveiled with analgesic activity compared with the control group in hot plate latency with

abdominal writhing method. Amla exhibited 33.6% of reduction in pain caused by edema while the standard shows 60% of inhibition of pain at 3.00±0.89writhes. "*Emblica* produced a statistically significant reduction in abdominal writhing. Since the plant extract extensively reduced the number of writhes in abdominal writhing model, but do not increase hot plate latency, the commercially available crude extract of *Emblica officinalis* exhibit analgesic activity involving peripheral mechanisms" [21,22].

b: Anti-inflammatory: Anti-inflammatory activity is screened employing leaves and fruits of *Phyllanthus emblica*. Extraction is done with ten different solvents namely n-hexane, diethyl ether, methanol, tetrahydrofuran, acetic acid, dichloromethane,1,4-dioxane, toluene, chloroform &water. Screening is done using dextran and carrageenan induced paw edema model. Invitro polymorphonuclear leukocyte inhibition was also evaluated. The inhibitory activity on receptor mediated migration & degranulation of human polymorphonuclear leucocyte was assessed by normal phase thin layer chromatography (TLC) by using the polar compounds containing the extract of emblica. "The extract of diethyl ether at 50mg/ml inhibit the ionophore A23187-induced leukotriene B4release from human polymorphonuclear leucocyte by 40%, thromboxane B2 production in platelets during blood clotting by 40% & adrenaline-induced platelet aggregation by 36%. *Emblica* have inhibitory activity on polymorphonuclear leucocyte and platelets. The plant has proven its efficiency in analgesic and anti-inflammatory activity" [23-26].

c: Antioxidant Effect: Methanolic extract of leaves of *P.emblica* is screened for antioxidant activity. The presence of ascorbic acid, tannins and polyphenolics made the researcher to focus light on antioxidant activity. *Invivo* and *invitro* screening of antioxidant activity was evaluated . The *invitro* antioxidant activity was assessed by scavenging of DPPH (1-Diphenyl-2-picryl-hydrazyl), nitric oxide and anti-lipid peroxidation assays. *Invivo* screening is performed by treating Sprague Dawley rats with 1ml/kg CCL_4 (with olive oil or DMSO). Test groups are treated with plant extracts at doses 200and 400mg/kg and standard group with silymarin (100 mg/kg). "The inhibitory constant (IC_{50}) value obtained for ascorbic acid was 28.91 ± 1.35µg/mL while plant extract had an IC_{50} value of 39.73 ± 2.12 µg/Ml. The extract has proven its efficiency in treating antioxidant activity. Reduced levels of antioxidant enzyme activities viz., superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GSH-Px) and reduced glutathione (GSH) whereas enhanced levels of total extractable proteins, lipid peroxides (TBARS), nitrite and H_2O_2 were induced by CCl_4 administration in lungs of rat. Co-administration of *Phyllanthus emblica* extract to rats exhibited a dose dependent decline in the oxidative injuries induced in these parameters"[27-30].

d: Antidiabetic – hypoglycaemic action: Type 2 Diabetes, a major health problem ruling the world, results due to peripheral insulin resistance and impaired insulin secretion. Increased oxidative stress due to chronic hyperglycemia is a widely accepted factor in the progression of diabetes and its complications. Antidiabetic activity was screened using aqueous extract of seeds of emblica. Seeds are boiled to separate seeds that were shade dried, grinded and extracted using water by Soxhlet apparatus. The extract was made solvent free and the yield is subjected for phytochemical screening. *Invivo* screening was done using male albino wistar rats. Diabetes is induced by intraperitoneal injection of streptozocin (50 mg/kg). After treating, the animals with hyperglycemia are selected for study and divided into groups. "Dose-dependent improvements in fasting blood sugar, improved glucose tolerance and restoration of pancreatic tissue architecture, which may be due to inhibition of enzymatic pathways in intestinal carbohydrate digestion and glucose storage" [31-35].

e: Immunomodulatory:

Immuno stimulant: Immune system strengthens human body by eliminating toxic or allergic substances from body. Immunomodulatory activity was screened *invivo* utilizing immunomodulatory rats. Animals are divided into groups and treated with cyclophosphamide for immunosuppression followed by treating with standard and test doses at 250 and 500mg/kg. The dosing of drugs is continuous for a span of 45 days followed by frequent analyzing CD4, CD8, CD16 and CD19 cells. The extracts receiving test groups showed better CD cell count proving the efficiency of plant as immunomodulator. Researchers predict that the activity is majorly due to presence of glycosides, polysaccharides, alkaloids, saponins, flavonoids, sterols [36-40].

Table 1. Table Indicating the traditional names of Amla.

Languages	Traditional names
English	Gooseberry, Embolic Myrobalan
Hindi	Amla
Latin	*Emblica officinalis*, Gaerte
Sanskrit	Amalaki, Dhatri Pacifies Tridoshas
Tamil	Nelli
Kannada	Nellaka
Telugu	Usirikaya
Malayalam	Nellimaram
Marathi	Amla
Bangla	Aamalki
Tibetan	Skyu-ru-ra
Portuguese	Mirabolano emblica
Malaysian	Popok Melaka
Nepalese	Amba
Chinese	An Mole
Italian	Mirabolano emblica
German	Amla

Table 2. Table showing the chemical constituents in *Phyllanthus emblica*.

Sr. No.	Type	Chemical Constituents
1	Hydrolysable Tannins	Emblicanin A and B, Punigluconin, Pedunculagin, Chebulinic acid (Ellagitannin), Chebulagic acid (*Benzopyran tannin*), Corilagin (Ellagitannin), Geraniin (Dehydroellagitannin), Ellagotannin
2	Alkaloids	Phyllantine, Phyllembein, Phyllantidine
3	Phenolic compounds	Gallic acid, Methyl gallate, Ellagic acid, Trigallayl glucose
4	Amino acids	Glutamic acid, Proline, Aspartic acid, Alanine, Cystine, Lysine
5	Carbohydrates	Pectin
6	Vitamins	Ascorbic acid
7	Flavonoids	Quercetin, Kaempferol
8	Organic acids	Citric acid

f: Anticancer Effect: "Cholangiocarcinoma (CCA) is the most common biliary epithelial malignancy screened employing bark extract of *Phyllanthus emblica* (PE) using methanol as solvent. Screening is performed using MTT assay employing KKU-452 cell lines. Cell proliferation, apoptosis and migration were evaluated. Reactive oxygen species (ROS) was determined by DCFH-DA fluorogenic dye staining. Induction of cell growth is observed at 52.2 µg/ml. The extract at 50 µg/ml induced oxidative stress via ROS production at 31% when compared with non-treated cells. Phenolic acids and flavonoids are the important constituents present in this plant are responsible for anticancer activity". [41-43].

g: Dermato-protective: From ancient time, herbs have been used in medicines and cosmetics due to their potential in treating skin ailments and improve skin appearance. Clinical trials and laboratory outcomes have identified the favourable action of natural ingredients for skin. Antioxidants, flavonoids and phenolic compounds present in herbs play critical roles to counteract free radicals, the main cause of various unfavourable skin changes"[44].

h: Antitussive Effect: "The antitussive activity of *E. officinalis* was tested in conscious cats by mechanical stimulation of the laryngopharyngeal and tracheobronchial mucous regions of airways. The ethanol extract of the fruits of *E. officinalis* seems has beneficial capacity to inhibit mechanically provoked cough, but only at higher doses (200 mg/kg body weight) suggesting the presence of antitussive activity of *E. officinalis* in conscious cats, showed a dose-dependent but higher than the antitussive activity of the commonly used non-narcotic antitussive drug, dropropizine. It is supposed that the antitussive activity of the dry extract of *E. officinalis* is due to its antiphlogistic, anti spasmolytic and antioxidant

efficacy effects but also due to its effect on mucus secretion in the airways" [45,46].

i: Metabolic syndrome: The plant employed in ayurveda and numerous medical diseases is exposed for fructose induced metabolic syndrome using rats. Ethyl acetate is used as solvent for extraction. Animals divided into groups are treated with high fructose diet for two weeks along with standard and test drugs. "Serum glucose, TAG, total cholesterol and blood pressure levels of the high-fructose diet-fed rats were increased compared with standard and test groups. The extract of amla ameliorated the high fructose-induced metabolic syndrome, including hypertriacyl glycerolaemia and hyper cholesterolaemia. Amla extract inhibited the increase of cyclo-oxygenase-2 with the regulation of NF-kappaB and bcl-2 proteins in the liver, while the elevated expression level of sbax was significantly decreased by 8.5 and 10.2 % at the doses of 10 and 20 mg/kg body weight respectively" [47,48].

j: Anti-bacterial: Fresh *Phyllanthus emblica L* fruits are screened for anti-bacterial activity. The fruits are extracted with distilled water and screened for anti-bacterial activity. Screening is done for Salmonella typhi, Escherichia coli, Staphylococcus aureus, Vibrio cholerae, Salmonella paratyphi A, Salmonella Para typhi B, Shigella spp., and Bacillus cereus. The primary antibacterial activity of aqueous *Phyllanthus emblica* fruit extract (APE) was screened by agar well diffusion method using Mueller-Hinton (MH) agar. Zones of inhibition of growth of bacteria is observed by digging bores where test drug is placed at concentrations of (25%, 50%, 75% and 100%, v/v) compared with standard drug amikacin (30µg/ml). Zones of inhibition of growth was observed in a dose dependent manner. The theoretical support for activity was found due to presence of flavonoids, triterpenoids, glycosides, tannins, anthraquinones in anti-bacterial [49-52].

k: Hepatoprotective: Ayurveda espousals the use of Phyllanthus for hepatoprotective activity. Hepatoprotective activity is screened using hydroalcoholic extract of bark of *Phyllanthus emblica* at ratio of 7:3 using Soxhlet apparatus. Evaporation is performed using rotary evaporator. Total phenolic, flavonoids and tannins concentration were analyzed from extracts. Animals are treated with silymarin at dose 25mg/kg per oral to induce hepatotoxicity followed by treating with extracts for 30 days. After 30 days the animals are sacrificed and are estimated for enzymes namely alkaline transferase, aminotransferase, alkaline phosphatase and total phosphorus and also by liver histopathology. Test groups recieving dose 500mg showed good hepatoprotective action [53-55].

l: Anti-ulcer activity: "The anti-ulcerogenic activity of fresh fruit juice of *Emblica officinalis* and its methanol extract were evaluated in absolute ethanol-, indomethacin- and histamine-induced experimental ulcers in rats. Gastric ulcers induced by oral administration of absolute ethanol (5 ml/kg) to fasted rats were reduced dose-dependently by oral pretreatment of animals with either *E. officinalis* fruit juice or its methanol extract (25–100 mg/kg). Ethanol administration caused severe gastric damage with an ulcer index of 4.6 ± 0.5, a 44% reduction in glutathione (GSH) content of gastric mucosa, an increase in stomach weight due to inflammation (1.24 ±0.12 g/100 g body weight), intraluminal bleeding (100%) and increased mortality rate (44%). *E. officinalis* fresh fruit juice administration (50 mg/kg) 30 min before alcohol challenge, reduced the ulcer index to 1.8 ± 0.7, limited the depletion of GSH to 15.2%, reduced the stomach weight to 0.75 ± 0.12 g/100 g body weight and afforded 100% protection against mortality and intraluminal bleeding. Administration of standard drugs indomethacin (25 mg/kg) and histamine (10 mg/kg) increased the ulcer index to 2.2 ± 0.7 and1.8 ± 0.7 respectively and a 28.5% depletion in mucosal GSH, respectively, as compared to normal rats. *E. officinalis* administration showed a dose-dependent protective effect against gastric damage induced by indomethacin and histamine. The protection afforded by *E. officinalis* fruits was found to be better than that of ranitidine (50 mg/kg). The results of this study suggested the novel cytoprotective activity of *E. officinalis* fruits on gastric mucosal cells [56-59].

m: Antimicrobial Activity: "Approximately 50 to 20% of deaths are caused by infectious diseases in tropical areas and America respectively. Chemical constituent obtained from medicinal plants are being in used to cure antimicrobial infection since over hundred years" (Mahady, Huang, Doyle, & Locklear, 2008). "The organic solvent (like CHCl3, CH3OH) extract of amla (*E. officinalis*) shows efficient inhibition of growth against few gram +ive and gram negative bacteria. On other hand Vijayalakshmi *etal* discussed anti-microbial nature of aqueous *E. officinalis* fruit

pulp extract along side gram positive bacteria and gram-negative bacteria. However, in future the *E. officinalis* drugs will serve as low-cost and safe medicines due to its antimicrobial activities" [60-63].

n: Antiproliferative Effect: The antiproliferative activity was screened using aqueous and alcoholic extract of *P.emblica* and *H.cordata*. "Screening is done using MTT assay using HeLa, HT29, HCT116, MCF7 and Jurkat cells and flow cytometric analysis and cell cycle arrest. Dose dependent decrease in cell growth is observed. Ethanolic extract was more effective at inducing apoptosis than water extract. Cell cycle arrest was found to be another mechanism behind growth inhibition in Jurkat and HCT116 cells. HPLC analysis demonstrated that the powder mix extracts contained seven identified phenolic acids namely gallic, p-hydroxybenzoic, vanillic, syringic, p-coumaric, ferulic and sinapinic acids, where p-coumaric acid was detected in the highest concentration followed by ferulic acid" [64-66)].

o: Antidiarrheal Effect: The antidiarrheal potential of the methanol extract of the fruit of *Emblica officinalis* was evaluated using several experimental models of diarrhea in albino wistar rats. The screening models employed was castor oil-, magnesium sulphate-, Prostaglandin E2 (PGE2)-induced enteropooling methods in rats. In castor oil induced method methanolic extract of amla at 150mg/kg reduced the number of wet feces excreted to 1.4 ± 0.73, while the standard drug, loperamide at 3mg/kg exhibited anti-diarrhoeal activity (0.00) and $p < 0.01$ compared with control. "During magnesium sulfate diarrhoea induced method amla at 150mg/kg reduced the no.of wet feces to 0.60 ± 0.40 & the loperamide at 3kg/mg exhibit anti-diarrheal activity & the $p < 0.01$ compared with control examined by Dunnett's t-test. The extract (MEO) at doses of 50, 100, and 150 mg/kg significantly inhibited PGE2-induced enteropooling in rats PGE2 induces a significant increase in the fluid volume of the rat intestine when compared with vehicle control group; which receiveing ethenol in normal saline. Due to the presence of phenolic compounds and tannins of amla fruit exhibit anti-diarrheal activity" [67,68].

p: Anti-urolithiatic activity: "A study on the effect of *P. niruri* extract on calcium oxalate (CaOx) crystallization in vitro showed

Table 3. Table showing the list of activities with author, year of publication with reference

S. No	Name of activity	Author	Published Year	References No.
1	Analgesic activity	Goel, B et al..	2014	[21,22]
2	Anti-inflammatory activity	Rao, T. P., et al..	2013	[23-26]
3	Antioxidant activity	Chaphalkar, R et al..	2017	[27-30]
4	Antidiabetic-hypoglycaemic activity	Srinivasan, P., et al..	2018	[31-35]
5	Immunomodulatory activity	Kumar, S., et al..	2011	[36-40]
6	Anticancer activity	Zhao, T., et al..,	2015	[41,42,43]
7	Dermato-protective activity	Kunchana, K., et al..,	2021	[44]
8	Antitussive activity	Nosal'ova, G., et al ..	2003	[45,46]
9	Metabolic syndrome activity	Kim, H. Y ., et al..	2010	[47,48]
10	Anti-bacterial activity	Dharajiya, D., et al..	2015	[49-52]
11	Hepatoprotective activity	Srirama, R., et al..	2012	[53-55]
12	Anti-ulcer activity	Rajeshkumar, N. V., et al.	2001	[56-59]
13	Anti-microbial activity	Jamali, M., et al..	2016	[60-63]
14	Anti-proliferative activity	Kumnerdkhonkaen, P., et al..	2018	[64-66]
15	Anti-diarrheal activity	Perianayagam, J.B., et al..	2005	[67,68]
16	Anti-urolithiatic activity	Lee, N.Y., et al..	2016	[69-71]

that *P. niruri* restricted CaOx crystal growth and aggregation, showing its potential to disrupt the early stages of stone formation. *P. niruri* also changed the shape of calculus in rats into a smoother and possibly more fragile with easy removal and dissolution of calculi. A clinical study showed that *P. niruri* lowers urinary calcium in hypercalciuric patient's subset among 69 calcium stone-forming patients. Post extracorporeal shock with lithotripsy patients who underwent therapy with Uriston, a *P. niruri* extract had higher stone decreasing rates" [69-71].

The reported activities on amla are listed in the Table 3 above.

5. CONCLUSION

Medicinal plants have been used since prehistoric period for the cure of various diseases. Even to date nearly about 80% of the world's populations still depend upon traditional remedies. *Emblica* with its multi-faceted properties is occupying prominent position in herbal Medicinal systems. It is for sure that herbal medicine may become a new era of medical system in the next few decades for the management of human diseases. However, advancement of modern drug development sometimes tends to make people adopt faster Healing procedures ignoring the rich ayurvedic heritage of our country. In such situations, it is Necessary to generate ethnobotanical awareness among people along with sensible use of These exhaustive resources for healthy life. It is also the need of hour to develop and Characterize new natural drugs from plants and other natural sources with the aid of better Screening methods.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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