A REVIEW ON PHYTOCHEMICAL, PHARMACOLOGICAL AND POTENTIAL THERAPEUTIC USES OF PHYLLANTHUS EMBLICA

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ABSTRACT

Amla has a hallowed position in Ayurveda- an Indian indigenous system of medicine. According to belief in Indian mythology, Amla is the first tree to be created in the universe; which belongs to the family of Euphorbiaceae and is also known as Phyllanthus emblica or Indian gooseberry. Amla is native to India and also grows in tropical and subtropical regions of Pakistan, Uzbekistan, Sri Lanka, South East Asia, China and Malaysia.¹ The fruits of Amla are widely used in the Ayurvedic preparation and are believed to increase defence against diseases. It has a beneficial role in degenerative diseases like cancer, diabetes, liver treatment, ulcer, anaemia, heart trouble¹ and also is an important constituent in hepatoprotective formulas available.²

KEYWORDS: Medicinal plant, Phyllanthus emblica, pharmacology, phytochemistry.

INTRODUCTION

SCIENTIFIC CLASSIFICATION

Synonym: Phyllanthus emblica Linn

Kingdom: Plantae
Division: Angiospermae
Class: Dicotyledonae
Order: Geraniales
Family: Euphorbiaceae
Genus: Emblica
Species: officinalis Geartn.
VERNACULAR NAMES

**English:** Emblic myrobalan, Indian Goose berry, **Sanskrit:** Aamalaki, **Hindi:** Amla, **Kannada:** Nelli Kayi, **Marathi:** Amla, **Gujarati:** Ambla, **Malayalam:** Nelli Kayi, **Tamil:** Nelli, **Telugu:** Usirikaya, **Kashmir:** Aonla.

**Botanical description**

A small to medium sized deciduous tree, 8-18 meters height with thin light grey bark exfoliating in small thin irregular flakes, leaves are simple, subsessile, closely set along the branchlets, light green having the appearance of pinnate leaves; flowers are greenish yellow, in axillary fascicles, unisexual, males numerous on short slender pedicels, females few, subsessile, ovary 3-celled; fruits globose, fleshy, pale yellow with six obscure vertical furrows enclosing six trigonous seeds in 2-seeded 3 crustaceous cocci.[3]

**Geographical distribution**

Amla is found throughout India, the sea-coast districts and on hill slopes up to 200 meters, and is also cultivated in plains.[4] It is a potential crop which grows in the marginal soils and various kinds degraded lands such as salt-affected soils, saline’s and dry and semi-dry regions. It is common all over tropical and sub-tropical India and also found in Burma[5], it is abundant in deciduous forests of Madhya Pradesh also grows in tropical and subtropical parts of Ceylon, Malay Peninsula and China.[6]

**PHYTOCHEMISTRY OF PHYLLANTHUS EMBLICA**

**Amla Fruit:** The average composition of Amla fruits are: moisture 81.2%, protein 0.5%, fat 0.1%, carbohydrates 14.1%, mineral matter 0.7%, fiber 3.4%, Ca 0.05%, K 0.02%, Fe 1.2 mg/100g, nicotinic acid 0.2 mg/g, phyllemblin, phyllemblic acid, gallic acid, emblicol,
quercetin, hydroxymethyl furfural, ellagic acid, pectin[7-8], putranjivan A,[9] two new hydrolysable tannins called emblicannin A and B, punigluconin and pendunculagin.[10]

**Seeds**

A fixed oil, phosphatides and a small quantity of essential oil are present in seed. The fixed oil yield (16%) has the following physical and chemical properties: acid value 12.7, saponification value 185, acetyl value 2.03, iodine value 139.5, unsaponifiable matter 3.81%, sterol 2.70%, saturated fatty acids 7%, linolenic acid (8.78%), linoleic acid (44.0%), oleic acid (28.40%), stearic acid (2.15 %), palmitic acid (2.99%) and myristic acid (0.95%). Arora et al. (2011)14 also reported that the seed oil is rich in unsaturated fatty acids like linoleic acid (18:2n-6) and oleic acid.[11]

**Leaves & Bark**

Gallic acid, ellagic acid, chebulic acid, chebulagic acid, chebulinic acid, a gallotannins called amlic acid, alkaloids, phyllatidine and phyllantine are reported to be present in Amla tree leaves.[13-14] Leucodephinidin, tannin and proanthoyanidin have been reported in the bark of Amla tree.[13]

**Table: 1 The classes of chemical constituents reported in Amla plant[12]**

<table>
<thead>
<tr>
<th>Class</th>
<th>Compound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkaloid</td>
<td>Phyllantine, phyllantidine, zeatin, zeatin nucleotide, zeatin rioside</td>
</tr>
<tr>
<td>Benzoid</td>
<td>chebulic acid, chebulinic acid, chebulagic acid, gallic acid ellagic acid, amlaic acid, 3-6-di-O-galloyl-glucose, ethyl gallate b-glucogallin, 1,6-di-O-galloyl-b-D-glucose, putranjivan A, digallic acid, phylemblic acid, emlicol music (= galacteric acid)</td>
</tr>
<tr>
<td>Diterpene</td>
<td>gibberellin A-1, gibberellin A-3, gibberellin A-4, gibberellin A-9</td>
</tr>
<tr>
<td>Triterpene</td>
<td>lupeo</td>
</tr>
<tr>
<td>Flavonoid</td>
<td>Leucodelphinidin, kaempherol, kaempherol-3-glucoside, rutin Quercetin, kaempherol-3-O- β -D-glucoside, quercetin -3-O- β -D glucoside</td>
</tr>
<tr>
<td>Furanolactone</td>
<td>Ascorbic acid</td>
</tr>
<tr>
<td>Sterol</td>
<td>β-sitosterol</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>glucose</td>
</tr>
</tbody>
</table>
TRADITIONAL USES

The fruits are sour, astringent, bitter, acrid, sweet, cooling, anodyne, ophthalmic, carminative, digestive, stomachic, laxative, alterant, aphrodisiac, rejuvenative, diuretic, antipyretic and tonic. They are useful in vitiated conditions of tridosha, diabetes, cough, asthma, bronchitis, cephalalgia, ophthalmopathy, dyspepsia, colic, flatulence, hyperacidity, peptic ulcer, erysipelas, skin diseases, leprosy, haematogenesis, inflammations, anemia, emaciation, hepatopathy, jaundice, strangury, diarrhoea, dysentery, hemorrhages, leucorrhoea, menorrhagia, cardiac disorders, intermittent fevers and greyness of hair. \[15-20\]
PHARMACOLOGICAL ACTIVITIES OF PHYLLANTHUS EMBLICA

Antitumor Activity

Aqueous extract of emblica officinalis was found to be cytotoxic to L 929 cells in culture in a dose dependent manner. Concentration needed for 50% inhibition was found to be 16.5 g/ml. Emblica officinalis and chyawanprash (a non-toxic herbal preparation containing 50% E. extracts were found to reduce ascites and solid tumoues in mice induced by DLA cells. Animals treated with 1.25 g/kg b.wt. of emblica officinalis extract increased life span of tumour bearing animals (20%) while animals treated with 2.5 g/kg b.wt of Chyavanaprash produced 60.9% increased in the life span. Both emblica officinalis and chyavanaprash significantly reduced the solid tumours. Tumour volume of control animals on 30th day was 4.6 ml whereas animals treated with 1.25 g/kg b.wt of emblica officinalis extract and 2.5 g/kg b.wt chyavanaprash showed tumour volume of 1.75 and 0.75 ml, respectively emblica officinalis extract was found to inhibit cell cycle regulating enzymes cdc 25 phosphates in a dose dependent manner. Concentration needed or 50% inhibition of cdc 25 phosphatase was found to be 5 g/ml and that needed for inhibition of cdc2 Chinese was found to be>100g/ml. The results suggest that antitumor activity of emblica officinalis extract may partially be due to its interaction with cell cycle regulation.[21-24]

Hepatoprotective Activity

Hepatoprotective activity of emblica officinalis (EO) and chyavanaprash (CHY) extracts was studied using Carbon tetrachloride induced liver injury model in rats. EO and CHY extracts were found to inhibit the hepatotoxicity produced by acute and chronic administration as seen from the decreased levels of serum and liver lipid peroxides (LPO), glutamate-pyruvate transaminase (GPT) and alkaline phosphatase (ALP). Chronic CCI (4) administration was also found to produce liver fibrosis as seen from the increased levels of collagen hydroxyl proline and pathological analysis. EO and CHY extracts were found to reduce the elevated levels significantly, indicating that the extract could inhibit the induction of fibrosis in rats.[21-24]

Antioxidant Activity

Pre-treatment with the butanol extract of the water fraction of Phyllanthus emblica fruits at the dose of 100 mg/kg body-weight, orally administered to rats for 10 consecutive days, was found to enhance secretion of gastric mucus and hexosamine (P<0.001) in the Indomethacin induced ulceration of rats. The morphological observations also supported a protective effect
of the stomach wall from lesion. The Indomethacin treatment of the prem edicated animals with the drug hardly affected either the malondialdehyde (MDA) or superoxide dismutase (SOD) level in gastric tissue while the ulcerative agent itself significantly enhanced both the levels. An antioxidant property appears to be predominantly responsible for this cytoprotective action of the drug. The antioxidant activity of tannoid active principles of E. officinalis consisting of emblicanin A (37%) emblicanin B (33%), punigluconin (12%) and pedunculagin (14%), was investigated on the basis of their effects on rat brain frontal cortical and striatal concentrations of the oxidative free radical scavenging enzymes, superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX) and lipid peroxidation, in terms of thiobarbituric acidreactive products. The results were compared with effects induced by depresn1, a selective monoamine oxidase (MAO) B inhibitor with well documented antioxidant activity. The active tannoids of E. officinalis (EOT), Administered in the doses of 5 and 10 mg/kg, i.p and deprenyl (2 mg/kg, i.p), induced an increase in both frontal cortical and striatal SOD, CAT and GPX activity, with concomitant decrease in lipid peroxidation in these areas when administered once daily for 7 days. Acute single administration of EOT and deprenyl had insignificant effects. The results also indicate that the antioxidant activity of E. officinalis may reside in the tannoids of the fruits of the plant, which have vitamin Clike properties rather than vitamin C itself.[21-24]

Cancer
Triphala has been reported to exibit chemopreventive potential. The presence of Triphala in diet had significantly lowered the benzo(a)pyrene [B(a)P] induced forestomach papillomagenesis in mice. It was more effective in reducing tumor incidences compared to its individual constituents. Triphala also significantly increased the antioxidant status of animals which might have contributed to the chemoprevention.[25] The breast cancer is one of the most common cancers in women. Lipid-metabolizing enzymes, lipids and lipoproteins have been associated with the risk of breast cancer. Kalpaamruthaa (KA) is a modified Siddha preparation containing EO, Semecarpus anacardium (SA and honey. The elevated levels of free cholesterol, total cholesterol, triglycerides, phospholipids and free fatty acids and decreased levels of ester cholesterol in plasma, kidney and liver found in cancer suffering animals were reverted back to near normal levels on treatment with KA and SA.[26] Chemoprevention with food phytochemicals is presently considered as one of the most important strategies to control cancer. EO is valued for its unique tannins and flavanoids, which exhibit very powerful antioxidant properties. The inhibition of tumor incidences by
fruit extract of this plant has been evaluated on two-stage process of skin carcinogenesis in Swiss albino mice. Chemopreventive potential of EO fruit extract on 7,12-dimethylbenz(a)anthracene (DMBA) induced skin tumorigenesis in Swiss albino mice have been found.\[^{27}\] The cytotoxic effects of aqueous extract of Triphala were investigated on a transplantable mouse thymic lymphoma (barcl-95) and human breast cancer cell line (MCF-7). The differential response of normal cells and tumor cells to Triphala *in vitro* and the substantial regression of transplanted tumor in mice fed with Triphala indicate to its potential use as an anticancer drug for clinical treatment.\[^{28}\] The suppression of the growth of cancer cells due to the gallic acid-a major polyphenol as observed in "Triphala" have been reported.\[^{29}\] Ethanolic extract of EO was experimentally evaluated for protection against genotoxicity induced by DMBA. EO fruit administered orally at different concentrations (100, 250, 500 mg/kg b.wt) for seven consecutive days in Swiss albino mice prior to a single intraperitoneal injection of DMBA decreased the frequency of bone marrow micronuclei. The protection provided by EO may be due to its antioxidant capacity and through its modulatory effect on hepatic activation and detoxifying enzymes.\[^{30}\] Phenolic compounds derived from plant exhibit a number of beneficial effects and can potentially inhibit several stages of carcinogenesis. Efficacy of EO polyphenol fraction (EOP) on the induction of apoptosis in mouse and human carcinoma cell lineses and its modulatory effect on N-nitrosodiethylamine (NDEA) induced liver tumors in rats was also investigated. EOP treatment could induce apoptosis in Dalton's Lymphoma Ascites (DLA) and CeHa cell lines. EOP also inhibited DNA topoisomerase I in *Saccharomyces cervisiae*, mutant cell cultures and the activity of cdc25 tyrosine phosphatase.\[^{31}\] *In vitro* antiproliferative activity of extracts from medicinal plants toward human tumor cell lines, including human erythromyeloid K562, T-lymphoid Jurkat, B-lymphoid Raji, erythroleukemic HEL cell lines were compared. Extracts from EO were the most active in inhibiting *in vitro* cell proliferation have been found.\[^{32}\] Cyclophosphamide is one of the most famous alkylating anticancer drugs in spite of its toxic side effects including hematotoxicity, immunotoxicity and mutagenicity. EO or its medicinal preparations may prove to be beneficial as a component of combination therapy in cancer patients under cyclophosphamide treatment.\[^{33}\] Phenolic compounds and the major components from the fruit juice of EO and from the branches, leaves and roots showed stronger inhibition against B16F10 cell growth than against HeLa and MK-1 cell growth. Norsesquiterpenoid glycosides from the roots showed significant antiproliferative activities.\[^{34}\]
Diabetes
Oral administration of the extracts (100 mg/kg body weight) reduced the blood sugar level in normal and in alloxan (120 mg/kg) diabetic rats significantly within 4 hours. EO and an enriched fraction of its tannoids are effective in delaying development of diabetic cataract in rats. Aldose reductase (AR) has its involvement in the development of secondary complications of diabetes including cataract. EO is proved as an important inhibitor of AR. Exploring the therapeutic value of natural ingredients that people can incorporate into everyday life may be an effective approach in the management of diabetic complications.

Cardioprotective Activity
The effects of chronic oral administration of fresh fruit homogenate of Amla on myocardial antioxidant system and oxidative stress induced by ischemic-reperfusion injury (IRI) were investigated on heart in rats. Chronic EO administration produces myocardial adaptation by augmenting endogenous antioxidants and protects rat hearts from oxidative stress associated with IRI.

Anti-ulcer Activities
A herbo mineral formulation of the Ayurveda medicine named Pepticare, composed of EO, Glycyrrhiza glabra and Tinospora cordifolia was tested for its anti-ulcer and anti-oxidant activity in rats. Reports were made that Pepticare exhibit anti-ulcer activity, which can be attributed to its anti-oxidant property. Methanolic extract of EO (EOE) was studied against ulcer. EOE had significant ulcer protective and healing effects and this might be due to its effects both on offensive and defensive mucosal factors.

Immunomodulation
Immunomodulatory effect of aqueous extracts of Amla was examined by Suja et al. (2009) on Swiss Albino mice. Administration of extracted Amla powder increased the haemagglutination antibody titre, sheep red blood cells (sRBCs) in dose dependent manner and also induced the delayed type of hypersensitivity reaction, macrophage migration index, and respiratory burst activity of the peritoneal macrophages, total leukocyte count, percentage lymphocyte distribution, serum globulin and relative lymphoid organ weight.

Oxidative stress
Ischemia-reperfusion (IRI)-induced oxidative stress reduced the activities of cardiac superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) and increased
lipid peroxidation in rat. Administration of Amla juice (50 -100 mg/kg body wt.) or vitamin E (200 mg/kg body wt) reduced the IRI-induced effects.\(^{[41]}\) Amla fruit was also found to be effective against mercury induced oxidative stress in rat erythrocytes.\(^{[66]}\) Mercury chloride oxidative stress decreased the glutathione (GSH), SOD and catalase activity, while increasing the lipid peroxidation (LPO). Amla extract 100 mg/kg was found to be effective in ameliorating oxidative stress significantly, while 50 mg/kg of Amla fruit extract could only reverse the values of LPO and catalase.\(^{[42]}\)

**In alcohol induced damage**

Chronic alcohol consumption may lead to tissue and organ damage, coronary heart diseases, alcohol liver disease and several other diseases.\(^{[43-44]}\) Reddy et al. (2007) administered 33% (v/v) alcohol (10 g/kg body weight) and aqueous extract of Amla powder (250 mg/kg body weight/day) once a day for 60 days. Aqueous Amla extract supplementation increased the GSH content and also the increased the activities of SOD, CAT and GPx.\(^{[45]}\)

**Lipid damage**

Membrane phospholipases, alteration of the membrane lipid packing and penetration of water molecule may induce formation by products of lipid oxidation.\(^{[46-47]}\) The induced alterations in permeability of membranes, transport systems, and loss of membrane-bound enzymes can eventually lead to cell lysis and death under certain conditions.\(^{[48]}\) The assessment of the efficiency of Amla to prevent lipid peroxidation was measured by thiobarbituric acid-reactive substrates, lipid hydroperoxide, conjugated diene and 4-hydroxynonenal.\(^{[49]}\) Amla extracts have capability to afford excellent protection against iron-mediated lipid peroxidation that might also be useful in reducing photo-induced iron toxicity. The efficiency of Amla extracts to protect against lipid damage was correlated with phenolics.\(^{[49]}\) Anila and Vijaya Lakshmi in 2003 reported that administration of Amla significantly reduced the lipid peroxide content in cholesterol fed rat.\(^{[50]}\)

**Memory enhancing ability**

Amla powder showed a dose-dependent improvement in memory scores of young and aged mice.\(^{[75]}\) Supplementation of Amla reversed the amnesia induced by scopolamine (0.4 mg/kg, i.p.) and diazepam (1 mg/kg, i.p.); brain cholinesterase activity and total cholesterol levels were also reduced on administration of Amla powder for 15 days.\(^{[75]}\) Their studies revealed that the Amla may be a useful remedy for the management of Alzheimer's disease on account
of its multifarious beneficial effects such as memory improving property, cholesterol lowering property and anticholinesterase activity.\textsuperscript{[51]}

**CULTURAL AND RELIGIOUS SIGNIFICANCE**

Amla has been regarded as the sacred tree in India. The tree was worshipped as Mother earth and is believed to nurture Human kind because the fruits are very nourishing. The leaves, fruits and Houses are used in worship in India. Kartik Mahatma and Vrat Kaumudi order the worship of this tree. The leaves are offered to the lord of shri Satyanarayana Vrata, Samba on Shri Shani Pradosha Vrata and Shiva and Gowri on Nitya Somvara Vrata. In Himachal Pradesh, this tree is worshipped in the month Kartik as propitious and chaste.\textsuperscript{[52]}

**CONCLUSION**

The significance of *Phyllanthus emblica* and its extracts as source of medicines dates back to centuries and hence it is mentioned in age old art of medicine the “Ayurveda”. It is remarkably evident that its juice effectively reduces many diseases including the digestive disorders, respiratory disorders, kidney related problems, cardiovascular disorders, Cancer. Proper conservation and sustainable use of such plant resources may enhance the longevity of human life as well as contribute considerably against the drug resistant microorganisms. In the developing countries, increased cost of medication and their side effects are of great concern to general public hence opening new channels of pharmacological investigations focusing on natural medication and diverting human trends toward natural cure. It is strongly believed that detailed information as presented in this review on the phytochemical and various biological functions of the extracts might provide detailed evidence for the use of this plant in different medicines.

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