PHYTOCONSTITUENTS AND THERAPEUTIC POTENTIAL OF PHYLLANTHUS EMBLICA: A REVIEW.

Potawale S. E.^{1*}, Vetal Y. D.¹, Mehta U.K.¹, Md.Waseem Md.Sadiq¹, Luniya K.P.¹ Mantri R.A.¹, Deshmukh R.S.²

- 1. A.I.S.S.M.S College of Pharmacy, Kennedy Road, Pune-411001
- 2. Sinhgad College of Pharmacy, Vadgaon, Pune-411041.

Summary

Medicinal plants are the nature's gift to human being to make disease free healthy life. It plays a vital role to preserve our health. India is one of the most medicoculturally diverse countries in the world where the medicinal plant sector is part of a time-honored tradition that is respected even today. Medicinal plants are believed to be much safer. In our country more than two thousand medicinal plants are recognized. *Phyllanthus emblica* is a deciduous tree of the Euphorbiaceae family. It has been used in many local traditional systems, such as Chinese herbal medicine, Tibetan medicine and Ayurvedic medicine. It has been used to cure anaemia, liver diseases, dyspepsia, haemorrhage and diarrhoea. The fermented liquor prepared from fruits is used in jaundice. *Phyllanthus emblica* contains innumerable constituents in varying amounts falling in broad classes of alkaloids, benzenoid derivatives, diterpenes and triterpenes, furanolactones, flavonoids and sterols. This review presents phytochemistry, pharmacologic activities of *Phyllanthus emblica* and insights on its products Triphala and Anwala Churna.

Keywords: Phyllanthus emblica, amla, pharmacology, phytochemistry, review

*Address for correspondence: Mr. S.E. Potawale Department of Pharmacognosy, A.I.S.S.M.'S College of Pharmacy, Kennedy Road, Pune-411001 Phone: 09881363782, 09270050808 E-mail: sachin potawale@yahoo.co.in

Introduction

Plants have been one of the important sources of medicines since the beginning of human civilization. There is a growing demand for plant based medicines, health products, pharmaceuticals, food supplements, cosmetics, etc. According to WHO survey 80% of the populations living in the developing countries rely almost exclusively on traditional medicine for their primary health care needs (1). The term herb refers to a plant used for medicinal purpose. Medicinal herbs and plant extracts play a major role in modern pharmacy (2). The use of traditional medicines, mainly derived from plant sources, has been a major part in the management of many chronic ailments, particularly in countries like India (3-6). Since the use of herbal medicines has increased, the issues regarding safety, quality and efficacy in industrialized and developing countries are cropped up (7).

Phyllanthus emblica fruit is one of the top selling botanicals having diverse applications in healthcare, food and cosmetic industry (8). An official drug of Ayurvedic Pharmacopoeia (9) and Indian Herbal Pharmacopoeia (10), it forms a main ingredient of various multi-component formulations (8). The whole plant, especially its fruit, is widely used to treat diseases associated with atherosclerosis (11). The active principles or extracts of *Phyllanthus emblica* have been shown to possess several pharmacologic actions, e.g., antitumor, and cytotoxic activities (12-14). Phyllanthus emblica commonly known as amla is extensively used in many preparations of Ayurveda and also against many chronic ailments including diabetes (15-18). It has been used to prepare polyherbal formulations e.g. triphala. Triphala has been reported to possess antioxidant rich herbal formulation and it improves the mental faculties and also assists in the weight loss (19-22). Phyllanthus emblica is used both as a medicine and as a tonic to build up lost vitality and vigor. According to the two main classic texts on Ayurveda. Charaka Samhita and Sushruta Samhita, Amalaki is regarded as "the best among rejuvenative herbs." "Useful in relieving cough and skin diseases" and "the best among the sour fruits." All parts of the plant are used for medicinal purposes (23). The fruit pulp is used in several indigenous medical preparations against variety of conditions like headache, dizziness, liver injury, atherosclerosis and diabetes (24-27). Amla is highly nutritious and could be an important dietary source of vitamin C, minerals and amino acids (23).

Vernacular Names (28):

Sanskrit: *amalaka* Hindi: amla Bengali: *amlaki* Nepali: *amala* Malayalam: *nellikka* Assamese: *amlakhi* Telugu: *usirikai* Kannada and Tamil: *nellikkaai* Other languages: *aonla, aola, ammalaki, dharty, aamvala, aawallaa, emblic, emblic myrobalan*, Malacca tree, *nillika*, and *nellikya*.

Taxonomy (28):

Kingdom: Plantae Division: Flowering plant Class: Magnoliopsida Order: Malpighiales Family: Phyllanthaceae Tribe: Phyllantheae Subtribe: Flueggeinae Genus: Phyllanthus Species: P. emblica

Botanical Description (28):

The tree is small to medium sized, reaching 8-18m in height, with crooked trunk and spreading branches. The branchlets are glabrous or finely pubescent, 10-20 cm long, usually deciduous; the leaves simple, subsessile and closely set along branchlets, light green, resembling pinnate leaves (29). The flowers are greenish-yellow. The fruit is nearly spherical, light greenish yellow, quite smooth and hard on appearance (figure 1), with 6 vertical stripes or furrows. Ripening in autumn, the berries are harvested by hand after climbing to upper branches bearing the fruits (30). The taste of Indian gooseberry is sour, bitter and astringent, and is quite fibrous.

Figure 1 (103):



Geographical Source:

Phyllanthus emblica is a shrub or tree growing in the tropical and subtropical parts of Southeast Asia, particularly in southern China, India, Indonesia, and the Malay Peninsula (12, 31). Its natural habitat, like other members of its family, extends from Burma in the east to Afghanistan in the west and Sri Lanka in the south. The tree is found growing in the plains and sub-mountain on tracts all over the Indian subcontinent from 200 to 1300m. altitude. The tree is especially widespread in Uttar Pradesh (32).

Phytochemistry:

The fruit pulp, which constitutes 90.97 per cent of the whole fruit, contains 70.5 per cent moisture. The total soluble solids constitute 23.8 per cent of the juice. The acidity of Amla is 3.28 per cent on pulp basis. The pulp contains 5.09 percent total sugars and 5.08 per cent reducing sugars. The ascorbic acid content is 1,094.53 mg per 100 ml of juice. The tannins and pectin content of the pulp is 2.73 per cent and 0.59 per cent respectively. The fruit pulp contains 0.75 percent protein. The mineral content of the edible portion, as represented by its ash, is 2.922 per cent. The percentage content of the mineral elements, viz. phosphorus, potassium, calcium, magnesium, and iron is 0.027, 0.368, 0.059, 0.248 and 0.004 respectively (33). *Phyllanthus emblica* contains innumerable constituents in varying amounts falling in broad classes of alkaloids, benzenoid derivatives, diterpenes and triterpenes, furanolactones, flavonoids and sterols (34,35). The previous chemical

investigations of Phyllanthus emblica led to the isolation of several novel sesquiterpenoids from the roots (36, 37), new organic acid gallates and polyphenols from the fruit juice (38, 39), and new ellagitannins and flavonoids from the branches and leaves (39, 40). Among them, phyllaemblic acid (1) and its glycosides phyllaemblicins A-C (2-4) were the major sesquiterpenoids from the roots, and organic acid gallates, L-malic acid 2-O-gallate (5), and mucic acid 2-O-gallate (6) together with hydrolysable tannins, 1-O-galloyl- β -D-glucose (7), corilagin (8), and chebulagic acid (9) were found to be the major phenolic constituents of fruit juice. Elaeocarpusin (10) and putranjivain A (11) were the other two main ellagitannins obtained from the fruit juice. Moreover, seven other tannins and flavonoids, geraniin (12), phyllanemblinins C and E (13 and 14), prodelphinidin B_1 (15), prodelphinidin B₂ (16), (-)-epigallocatechin 3-O-gallate (17), and (S)-eriodictyol 7-[6-O-(E)-p-coumaroyl]- β -D-glucoside (18) were the main phenolic compounds isolated from the branches and leaves of the plant. Continuous studies on the 60% aqueous acetone extract of the roots of *Phyllanthus emblica* led to the isolation of a major component, proanthocyanidin polymer phyllemtannin (19) (12). The major constituents also contain vitamin C (20), gallic acid (21) and ellagic acid (22) (41) (Table 1). Although many studies have so far been carried out on the chemical components of *Phyllanthus emblica* (42-47), its detailed active principles are generally not well known.







Phyllanemblinin E (14) R= neochebuloyl

241





Epigallocatechin 3-O-gallate (17)



(S)-eriodictyol 7-[6-O-(E)-p-coumaroyl]-β-D-glucoside (18)



QН HO. :0 н· H он с́н₂он









Ellagic acid (22)

243

Traditional Uses:

Phyllanthus emblica has been used in many local traditional medicinal systems, such as Chinese herbal medicine, Egyptian medicine (31), Tibetan medicine and Ayurvedic medicine. The fruit is edible and the fruit juice is produced as a beverage in Yunnan Province, People's Republic of China (12). The fruits are widely consumed raw, cooked or pickled (3). The fruit of *Phyllanthus emblica* is effective in treating diseases associated with atherosclerosis in traditional Chinese medicine (11). Phyllanthus emblica has been well studied for immunomodulatory (48) and antiulcer (49) activities. It possesses anti-inflammatory, antipyretic, anticancer (12), antidiabetic (50), hypocholesterolemic (18), anticarcinogenic (51), antioxidant (52-55) activity and it is free radical scavenger (56) and hepatoprotective (57). It protects the skin from UV radiation (58) and also reduces the ulcers of the stomach (59). It has been used to cure anaemia, liver diseases, dyspepsia, haemorrhage and diarrhoea. The fermented liquor prepared from fruits is used in jaundice (60). It was found to be antimutagenic and reduced the clastogenicity induced by various metals (61). The fruit of Phyllanthus emblica forms a major constituent in many potent Avurveda preparations (62) which are widely used for their preventive, curative, health restorative properties. A Polyherbal preparation like Brahma Rasayana contains Phyllanthus emblica which have excellent radioprotective activity in animal models as well as human volunteers (63, 64).

Pharmacology:

Antiatherogenic Activity (11):

Phyllanthus emblica has been found to possess antiatherogenic activity. The two compounds previously extracted from *Phyllanthus emblica* i.e. corilagin and its analogue Dgg16 (1, 6-di-*O*-galloyl-beta-*d*-glucose) show strong antioxidation (38); corilagin has strong effects against platelet aggregation (65) and inflammation (66). Vitamin E, a well known bioreducer, was used as a positive control in the study. Corilagin and Dgg16 inhibited lipid oxidation, prevented endothelial injury, and prevented endothelia from being adhered to by monocytes in a dose dependant manner. The potency of corilagin, Dgg16, and vitamin E in preventing proliferation and adhesion are in proportion to their antioxidant activity to a certain extent. Corilagin and Dgg16 easily binding to lipid or lipoid, are the main soluble components in the fruit of *Phyllanthus emblica* and have many reductive phenol hydroxide groups (38). As has been reported, corilagin can inhibit platelet

aggregation (65) and local inflammation (66), which may also participate in its antiatherogenic effects.

Antiproliferative Activity (12):

The antiproliferative activity of eighteen main compounds previously isolated from *Phyllanthus emblica* together with a main constituent against MK-1 (human gastric adenocarcinoma), HeLa (human uterine carcinoma) and B16F10 (murine melanoma) cells using an MTT method has been estimated. The antiproliferative activity of the main constituents was determined by a 3-(4, 5-di-methylthiazol-2yl)-2, 5-diphenyl tetrazolium bromide (MTT) assay, using three tumor cell lines, MK-1, HeLa and B16F10 cells. Their 50% growth inhibition (GI₅₀ µg/ml) values were recorded. The antiproliferative activity of main constituents from different parts of *Phyllanthus emblica* was determined against MK-1, HeLa and B16F10 cells. L-Malic acid 2-*O*-gallate, mucic acid 2-*O*- gallate, 1-*O*-galloyl- β -D-glucose, corilagin and chebulagic acid in the fruit juice exhibited certain levels of cytotoxicity against the tumor cells. The antiproliferative activity of these compounds against B16F10 cells, some of which were comparable with those of the positive controls, was stronger than against that HeLa and MK-1 cells. These major components are possibly responsible for the folk anticancer uses of this plant.

Radioprotective Activity (56):

The fruit pulp of *Phyllanthus emblica* has been found to reduce the bioeffects of radiation. Since radiation causes enormous damage to normal cells several strategies are designed in order to minimize the lethal consequences of radiation exposure to normal cells. Use of radioprotectors is one among such strategy in which radioprotective agents like sulfhydryl compounds like cysteine, WR2721, antioxidants like vitamin C and E, cytoprotective agents like MESNA and several biological modifiers like γ -interferon have been tried (67). The myelosuppression produced as a result of whole body irradiation is significantly lowered by continuous administration of Phyllanthus emblica extract. Whole body irradiation increased the levels of tissue lipid peroxidation. Treatment of Emblica was found to be effective in reducing the lipid peroxidation. Phyllanthus emblica extract has been shown to have significant antioxidant activity, which reduces the oxidative changes induced by radiation. Phyllanthus emblica extract was also found to inhibit mutagenesis by direct binding to certain mutagens as well as by inhibiting carcinogen activation. It produces a protective layer in stomach thus reduces the mucosal damage of gastrointestinal linings during irradiation.

Antifibrotic Activity (34):

A hydroalcoholic (50%) extract of *Emblica officinalis* (fruit) (EO-50) reduced the severity of hepatic fibrosis induced by carbon tetrachloride and thioacetamide. Liver protective action of *Phyllanthus emblica* (*Emblica officinalis*) has been documented previously. Excess oxygen derived free radicals (ODFR) play a major mediatory role in inducing synthesis of fibrillar extracellular matrix (68). EO-50 acts as scavenger of ODFR at the initiation phase (whether the superoxides are generated by enzymic or non-enzymic reaction) and also at the terminal stage suppressing lipid peroxidation. The antifibrotic activity of EO-50 could be attributed to its mechanistic intervention with several cellular events to provide beneficial effects against this multifactorial process of fibrogenesis, most importantly by (a) attenuating the oxidative stress (b) stabilizing the membrane against fibrotic challenge (c) preventing from the CYP2E1 mediated bioactivation.

Gastroprotective Activity (69):

Phyllanthus emblica has been found to possess antisecretory, antiulcer, and cytoprotective activities. An ethanol extract of Amla was examined for these activities. Oral administration of Amla extract at doses 250 mg/kg and 500 mg/kg significantly inhibited the development of gastric lesions in all test models used. It also caused significant decrease of the pyloric-ligation induced basal gastric secretion, titratable acidity and gastric mucosal injury. Besides, Amla extract offered protection against ethanol-induced depletion of stomach wall mucus and reduction in nonprotein sulfhydryl concentration.

Antitussive Activity (70):

The antitussive activity of *Phyllanthus emblica* has been previously reported. Conscious cats were tested for antitussive activity by mechanical stimulation of the laryngopharyngeal and tracheobronchial mucous areas of airways. At a dose of 50 mg/kg body wt. perorally, the cough suppressive effect of *Phyllanthus emblica* is not unambiguous. A higher dose (200 mg/kg body wt.) of this substance perorally was more effective, especially in decreasing the number of cough efforts and frequency of cough. The cough suppressive activity of *Phyllanthus emblica* was found to be dose-dependent. The antitussive activity of the dry extract of *Phyllanthus emblica* was supposed to be not only due to antiphlogistic, antispasmolytic and antioxidant efficacy effects, but also due to its effect on mucus secretion in the airways.

Antiulcerogenic Activity (71):

The ulcer protective potential of methanolic extract of *Phyllanthus emblica* was assessed in different acute gastric ulcer models in rats induced by aspirin, ethanol, cold restraint stress and pyloric ligation and healing effect in chronic gastric ulcers induced by acetic acid in rats. The methanolic extract of *Phyllanthus emblica* 10-50mg/kg administered orally, twice daily for 5 days showed dose-dependent ulcer protective effects in all the acute ulcer models and significant ulcer healing effect in dose of 20mg/kg after 5 and 10 days treatment. Thus, the methanolic extract of *Phyllanthus emblica* was found to possess significant ulcer protective and healing effects.

Antipyretic Activity (72):

The ethanol and aqueous extracts of *Phyllanthus emblica* has been studied for its antipyretic activity in several experimental models. A single oral dose of ethanol and aqueous extracts of *Phyllanthus emblica* (500 mg/kg, i.p.) showed significant reduction in brewer's yeast induced hyperthermia in rats. Preliminary phytochemical screening of the extracts showed the presence of alkaloids, tannins, phenolic compounds, carbohydrates and amino acids, which may be responsible for antipyretic activity of *Phyllanthus emblica*.

Analgesic Activity (72):

Phyllanthus emblica was studied for its analgesic activity using its ethanol and aqueous extracts in several experimental models. The extracts elicited pronounced inhibitory effect on acetic acid-induced writhing response in mice in the analgesic test. Both the extracts did not show any significant analgesic activity in the tail-immersion test. Tannins, phenolic compounds, amino acids, alkaloids and carbohydrates were supposed to be responsible for the analgesic activity.

Superoxide-Scavenging Activity (73):

Phyllanthus emblica have been found to possess superoxide-scavenging activity. This activity has been evaluated using the enzymatic method with cytochrome c (cyt c) (74) and non-enzymatic method with nitro blue tetrazolium (NBT) (75). *Phyllanthus emblica* showed the superoxide-scavenging activity by both assay methods. The 50% O_2^- -scavenging concentration from *Phyllanthus emblica* methanol extract was found to be 13.17µg/ml.

Newsletter

Prolyl Endopeptidase Inhibitory Activity (73):

Phyllanthus emblica has been identified as one of the strongest Prolyl Endopeptidase (PEP) inhibitory plant sample. PEP plays an important role in regulating the biological activity of peptides. A Z-Gly-Pro-pNA substrate was used to evaluate the PEP inhibitory activity. It showed 78.80% PEP inhibitory activity. The PEP inhibitory concentration from *Phyllanthus emblica* methanol extract was found to be 26.10µg/ml.

Diabetic Cataract (3, 15):

Phyllanthus emblica and an enriched fraction of its tannoids have been found to be effective in delaying development of diabetic cataract in rats. Prolonged exposure to uncontrolled chronic hyperglycemia in diabetes can lead to various complications in the eye including cataract and retinopathy (76, 77). The onset of cataract due to hyperglycemia was observed in diabetic animals after four weeks of STZ injection. The whole Phyllanthus emblica was found to be effective than its tannoid fractions in delaying the onset of cataract. At the end of eight weeks, the severity of cataracts was significantly lower in rats receiving AIN-93 diet containing 0.2% tannoids mixture and rats receiving 2.0% emblica powder than in rats receiving AIN-93 diet. This indicates that Phyllanthus emblica and its constituent tannoids delayed the maturation of diabetic cataract due to slow progression. Tannoids of Phyllanthus emblica have been found to inhibit Aldose reductase (AR) which has been a drug target because of its involvement in the development of secondary complications of diabetes including cataract. Aqueous extracts of *Phyllanthus emblica* inhibited rat lens AR, with an IC₅₀ (50% inhibition concentration) value of 0.72 mg/ml. The extract also inhibited human recombinant AR to the same extent as that of rat lens AR with an IC₅₀ value of 0.88 mg/ml.

Polyherbal Formulations:

Triphala:

Triphala is a traditional Ayurvedic herbal formulation, consisting equal parts of three medicinal plants namely *Terminalia chebula*, *Terminalia belerica* and *Phyllanthus emblica* (19). Fruits of Triphala are claimed to have various biological activities such as antiviral (78), antibacterial, antiallergic (79), antimutagenic (80), exerts a marked heart-protective and cardio-tonic effect, improves digestion (81), and improves liver function and hepatoprotective (82). It is prescribed for various symptoms of infections, obesity, anaemia, fatigue, poor digestion, assimilation and

infectious diseases like tuberculosis, pneumonia and AIDS (83). Triphala formulation has been found to be associated with hypolipidemic effect on the experimentally induced hypercholesterolemic rats. Triphala supplementation may exert antioxidant effect and can be regarded as a protective drug against stress.

Effect of Anwala Churna on memory deficit rats (23):

Ayurvedic preparation Anwala churna consisting of *Phyllanthus emblica* has been found to possess beneficial effects such as memory improvement and reversal of memory deficits. Amnesia was induced in rats by intraperitoneal injection of scopolamine or diazepam, in addition to aging-induced amnesia. Phyllanthus emblica reversed memory deficits in aged rats when administered for 15 days. Ascorbic acid and tannoids present in Amla have been reported to have antioxidant activity in rats (55, 85). An increase in antioxidant activity prevents (86) or ameliorates (87) the impairment of memory capacity in rats. The antiinflammatory effect of *Phyllanthus emblica* would act against the inflammatory component of the memory deficits. Furthermore, flavonoids from Phyllanthus emblica were conformed to decrease cholesterol and triglycerides in the liver, heart, kidney, and aorta of rats, which may be responsible for the pronounced memory enhancing effect seen in aged rats (88). The combination of antiinflammatory, antioxidant, hypolipidemic, and neuroprotective role could contribute to the memory enhancing effect of Anwala churna. Thus, Anwala churna can be a useful remedy for the management of Alzheimer's disease.

Toxicity Studies:

Phyllanthus emblica was found to be non-toxic to human and experimental animals (56). The *Phyllanthus emblica* fruit or its extract has not been reported to have any side effects even after prolonged use (89, 90). In toxicity studies in rats, no toxicity was observed in single- or chronic-dose administration. Additionally, no detrimental effect was noted on liver or renal function (91, 92). No chromosomal aberrations were found following 7- and 14-day treatment regimens in rats with crude fruit extract (93). In another experiment, no toxicity or mutagenicity were observed in rats even at the highest doses administered (94). The results with large doses in animals reveal that atropinization completely blocked the hypotension in dogs and spasmogenic effect on rabbit ileum (95). No major toxicities related to *Phyllanthus emblica* have been reported (91).

Dosage:

Powder – 3-6g (41, 96, 97) Dry extract 4:1 – 350-500mg Juice fresh fruit – 10-20ml Juice powder 20:1 – 250mg Skin care formulations – 0.5% to 0.75% Hair care products – 0.1% to 0.5% (89) Decoction – [5g boiled in 80ml water till 20ml left] twice daily after meals (41, 96, 97) Amla capsules – Pediatric (5-10 Years) dose is one capsule morning and evening with honey or milk. Adult dose is 1-2 capsules morning and evening after meals (98).

A LD $_{50}$ in rats has been suggested at 1 g/kg body weight, but 2.5 g/kg has been used in cancer studies in animals (92, 99).

Contraindications (91):

Contraindications have not been identified.

Pregnancy and Lactation: Information regarding safety and efficacy in pregnancy and lactation is lacking.

Analytical Methods / Phytochemical Analysis:

Warude Dnyaneshwar *et al.* developed DNA based marker for identification of *Phyllanthus emblica*. Sequence Characterized Amplified Region (SCAR) primers D1 and D2 amplified the expected 343 bp DNA fragment in all tested samples confirming the presence of *Phyllanthus emblica*. The results substantiate the applicability of the designed primers as a qualitative diagnostic tool for identification of *Phyllanthus emblica* (8).

The determination of tannins can be done by method published by World Health Organization (WHO) wherein plant extract is used for determination and the determined quantity is procured as % tannins (89). Tannins can also be determined by a method wherein drug extract is diluted with water. A quantity of this mixture is further diluted with distilled water and indigosulphonic acid is added to this and titrated with 0.1N potassium permanganate solution to a golden yellow colour as the end point. The amount of tannins eventually obtained is expressed as percent total tannins. This method may respond to some polyphenols other than tannins. Hence, the result may display errors (89). Analysis of tannins can also be done by

High Performance Capillary Electrophoresis [HPCE] (100). The assay of ascorbic acid is done by HPLC. The chromatographic equipment consists of a solvent delivery system (Perkin-Elmer isocratic LC pump 250) and a 20µl sample injector. Mobile phase used is 2% KH₂PO₄ [pH 2.3]. IP-1996 method have been used for estimation of ascorbic acid wherein extract dissolved in mixture of distilled water and 1M sulphuric acid is titrated with 0.05M iodine using starch solution as indicator (89). TLC method for ascorbic acid is available wherein solvent system used is ethanol and 10% acetic acid and stationary phase used is Silica gel G or Silica gel F – 254. TLC method for gallic acid is also available in which the solvent system used is toluene, ethyl acetate, glacial acetic acid and formic acid in the proportion of 20:45:20:5 respectively (89).

Discussion

Alternative systems of medicine viz. Ayurveda, Siddha, and Chinese Medicine have become more popular in recent years (101,102). As the global scenario is now changing towards the use of nontoxic plant products having traditional medicinal use, development of modern drugs from *Phyllanthus emblica* should be emphasized for the control of various diseases. In the present review we have made an attempt to congregate the botanical, phytochemical, ethnopharmacological, pharmacological and toxicological information on *Phyllanthus emblica*, a medicinal herb used in the Indian system of medicine.

Acknowledgement

Authors are thankful to Principal A.I.S.S.M.S. College of Pharmacy, Pune for providing valuable support.

References

- 1. Goyal BR, Goyal RK, Mehta AA, Pharmacognosy Reviews 2007; 1(1):143-150.
- 2. Sathiyanarayanan L. Arulmozshi S. Pharmacognosy Reviews 2007; 1(1):157-162.
- 3. Suryanarayana P. Kumar AP, Saraswat M. Petrash MJ, Reddy BG, Molecular Vision 2004; 10:148-154.
- 4. Swanston-Flatt SK, Flatt PR, Day C. Bailey CJ, Proc Nutr Soc 1991;50:641-51.
- 5. Grover JK, Yadav S. Vats V. J Ethnopharmacol 2002; 81:81-100.

- 6. Oubre AY, Carlson TJ, King SR, Reaven GM, Diabetologia 1997; 40:614-617.
- 7. Lavhale MS, Mishra SH, Pharmacognosy Reviews 2007; 1(1):105-113.
- 8. Warude D. Chavan P. Joshi K. Patwardhan B. Biol Pharm Bull 2006; 29(11):2313-2316.
- 9. Government of India, "The Ayurvedic Pharmacopoeia of India," Controller of Publications, Delhi 2001.
- 10. "Indian Herbal Pharmacopoeia," Indian Drug Manufacturer's Association, Mumbai 2002.
- 11. Duan W. Yu Y. Zhang L. Pharmaceu Soc Jap 2005; 125(7):587-591.
- 12. Zhang Y-J, Nagao T. Tanaka T. Yang C-R, Okabe H. Kouno I. Biol Pharm Bull 2004; 27(2):251-255.
- 13. Ihantola-Vormisto AJ, Summanen H. Kankaaranta H. Vuorela ZM, Asmawi C. Moilanen E. Planta Med 1997; 63:518-524.
- 14. Mohamed SM, Mackeen MM, Lajis NH, Rahma AA, Nat Prod Sci 1999;5:172-176.
- 15. Suryanarayana P. Saraswat M. Petrash MJ, Reddy BG, Molecular Vision 2007; 13:1291-1297.
- 16. Sabu MC, Kuttan R. J Ethnopharmacol 2002; 81:155-160.
- 17. Scartezzini P. Speroni E. J Ethnopharmacol 2000; 71:23-43.
- 18. Thakur CP, Experientia 1985; 41:423-424.
- 19. Saravanan S. Srikumar R. Manikandan S. Jeva Parthasarathy N. Sheela Devi R. Pharmaceu Soc Jap 2007; 127(2):385-388.
- 20. Srikumar R. Jeya Parthasarathy N. Manikandan S. Sathya Narayanan G. Sheela Devi R. Mol Cell Biochem 2006; 283:67-74.
- 21. Antarkar DS, Vaidya AB, Doshi JC, Athavale AV, Vinchoo KS, Natekar MR, Tathed PS, Ramesh V., Kale N., Indian J Med Res 1980;72:588-593.
- 22. Hashimoto M. Nakajima Y. Jpn. Kokai. Tokkyo. Koho. JP 1997; 9:227-398.
- 23. Vasudevan M. Parle M. Pharmaceu Soc Jap 2007; 127(10):1701-1707.
- 24. Perry LM, Medicinal Plants of East and South East Asia: Attributed Properties and Uses, MIT Press, Cambridge 1980:149-150.
- 25. De S. Ravishankar B. Bhavsar GC, Indian Drugs 1993; 30:355-363.
- 26. Thakur CP, Thakur B. Singh B. Singh S. Sinha PK, Sinha SK, Indian J Cardiol 1988;21:167-175.
- 27. Sabu MC, Kuttan R. J Ethnopharmacol 2002;81:155-160.
- 28. Available at http://en.wikipedia.org/wiki/Indian_gooseberry_
- 29. Available at http://www.toddcaldecott.com/amalaki.html
- 30. Available at http://www.itmonline.org/arts/amla.htm
- 31. Xia Q. Xiao P-G, Wang L-W, Kong J. Zhongguo Zhongyao Zazhi 1997; 22:515-518.

- 32. Available at http://www.haryana-online.com/Flora/amla.htm
- 33. Available at http://www.planetayurveda.com/amlasaar.htm
- 34. Tasduq SA, Mondhe DM, Gupta DK, Baleshwar M. Johri RK, Biol Pharm Bull 2005; 28(7):1304-1306.
- 35. Sumannen JO, http://ethesis.helsinki.fi/english.html
- 36. Zhang Y-J, Tanaka T. Iwamoto Y. Yang C-R, Kouno I. J Nat Prod 2000;63:1507-1510.
- 37. Zhang Y-J, Tanaka T. Iwamoto Y. Yang C-R, Kouno I. J Nat Prod 2001;64:870-873.
- Zhang Y-J, Tanaka T. Yang C-R, Kouno I. Chem Pharm Bull 2001; 49:537-540.
- 39. Zhang Y-J, Abe T. Tanaka T. Yang C-R, Kouno I. J Nat Prod 2001;64:1527-1532.
- 40. Zhang Y-J, Abe T. Tanaka T. Yang C-R, Kouno I. Chem Pharm Bull 2002;50:841-843.
- Indian Herbal Pharmacopoeia, A joint publication of Regional Research Lab (CSIR) and Indian Drug Manufacturers Association (Mumbai) 1999; 2:50-57.
- 42. Basa SC, Shrinivasulu C. Indian J Nat Prod 1987; 3:13-14.
- 43. El-Mekkawy S. Meselhym R. Kusumoto IT, Kadota S. Hattori M. Namba T. Chem Pharm Bull 1995; 43:641-648.
- 44. Hui BW, Sung ML, Aust J Chem 1968; 21:2137-2140.
- 45. Subramanian SS, Nagarajan S. Sulochana N. Phytochemistry 1971; 10:2548-2549.
- 46. Theresa YM, Rajandurai S. Sastry KNS, Nayudamma Y. Leather Science 1967; 14:16-17.
- 47. Theresa YM, Sastry KNS, Nayudamma Y. Leather Science 1965; 12:327-328.
- 48. Ganju L. Karan D. Chanda S. Srivastava KK, Sawhney RC, Selvamurthy W. Biomed Pharmacother 2003; 57:296-300.
- 49. Al-Rehaily AJ, Al-Howiriny TA, Al-Sohaibani MO, Rafatullah S. Phytomedicine 2002;9:515-522.
- 50. Sabu MC, Kuttan R. J Ethnophramacol 2002; 81:155-160.
- 51. Khan MT, Lampronti I. Martello D. Bianchi N. Jabbar S. Choudhuri MS, Datta BK, Gambari R. Int J Oncol 2002; 21:187-192.
- 52. Sabu MC, Kuttan R. J Ethnopharmacol 2002; 81:155-160.
- 53. Khopde SM, Pryadarshini KI, Mohan H. Gawandi VB, Satav JG, Yakhmi JV, Bhanavaliker MM, Biyani MK, Mittal JP, Curr Sci 2001;81:185-190.
- 54. Bhattacharya A. Chatterjee A. Ghosal S. Bhattacharya SK, Indian J Exp Biol 1999;37:676-680.

- 55. Bhattacharya A. Ghosal S. Bhattacharya SK, J Exp Biol 2000; 38:877-880.
- 56. Hari Kumar KB, Sabu MC, Lima PS, Kuttan R. J Radiat R 2004; 45(4):549-555.
- 57. Jeena KJ, Kuttan R. J Ethnopharmacol 2000; 72:135-140.
- 58. Chaudhuri RK, Skin Pharmacol Appl Skin Physiol 2002; 15:374-380.
- 59. Rajesh Kumar NV, Therese M. Kuttan R. Pharm Biol 2001; 39:375-380.
- 60. Kiritikar KR, Basu BD, Indian Medicinal Plants, International Book Distributors, Dehradun, India 1987; 1.
- 61. Dhir H. Agarwal K. Sharma A. Talukder G. Cancer Lett 1991; 59:9-12.
- 62. Satyavati GV, Raina MK, Sharma M. Medicinal plants of India. New Delhi: Indian Council of Medical Research 1976.
- 63. Praveenkumar V. Kuttan R. Kuttan G. Ind J Exp Biol 1996; 34:845-850.
- 64. Joseph CD, Praveenkumar, Kuttan G. Kuttan R. J Exp Clin Cancer Res 1999; 18:325-329.
- 65. Shen ZQ, Dong ZJ, Peng H. Liu JK, Planta Med 2003; 69:1109-1112.
- 66. Luo H. Chen L. Li Z. Ding Z. Xu X. Anal Chem 2003; 75:3994-3998.
- 67. Nair CKK, Parida DK, Nomura T. J Radiat Res 2001; 42:21-37.
- 68. Caro AA, Cederbaum AI, Annu Rev Pharmacol Toxicol 2004; 44:27-42.
- 69. Al-Rehaily AJ, Al-Howiriny TS, Al-Sohaibani MO, Rafatullah S. Phytomedicine 2002; 9(6):515-522.
- 70. Nosalova G. Mokry J. Tareq Hassan KM, Phytomedicine 2003; 10(6, 7):583-589.
- 71. Sairam K. Rao V. Dora Babu M. Vijay Kumar K. Agrawal VK, Goel RK, J Ethnopharmacol 2002; 82(1):1-9.
- 72. Perianayagam JB, Sharma SK, Joseph A. Christina AJM, J Ethnopharmacol 2004; 95(1):83-85.
- 73. Khanom F. Kayahara H. Tadasa K. Biosci Biotechnol Biochem 2000; 64(4):837-840.
- 74. McCord JM, Fridovich IJ, J Biol Chem 1969; 244:6049-6055.
- 75. Zhang HY, Lu CS, Acta Biochem Biophys Sinica 1990; 22:593-594.
- 76. Brownlee M. Nature 2001; 414:813-820.
- 77. Baynes JW, Thorpe SR, Diabetes 1999; 48:1-9.
- 78. Hozumi T. Oyama H. Jpn Kokai Tokkyo Koho JP 0987185 1997.
- 79. Takagi N. Sanashiro T. Jpn Kokai Tokkyo Koho JP 1000070 1996.
- 80. Rani G. Bala S. Grover IS, J Plant Sci Res 1994; 10:1-4.
- 81. Chawla YK, Indian J Med Res 1982; 76:95-98.
- 82. Gulati R. Agarwal S. Agarwal SS, Indian J Exp Biol 1995; 33:261-268.
- 83. El-Mekkawey M. Merelhy M. Chem Pharm Bull 1995; 43:641-648.
- Bhattacharya A. Ghosal S. Bhattacharya SK, Indian J Exp Biol 2000; 38:877-880.

- 85. Scartezzini P. Antognoni F. Raggi MA, Poli F. Sabbioni C. J Ethnopharmacol 2006; 104:113-118.
- 86. Hashimoto M. Hossain S. Shimada T. Sugioka K. Yamasaki H. Fujii Y. Yutaka Ishibashi Y. Oka J. Shido O. J Neurochem 2002; 81:1084-1091.
- 87. Hashimoto M. Tanabe Y. Fujii Y. Kikuta T. Shibata H. Shido O. J Nutr 2005; 135:549-555.
- 88. Anila L. Vijayalakshmi NR, J Ethnopharmacol 2002; 79:81-87.
- Br. Rajpal V. Standardization of botanicals, Eastern publishers 2005; 2:240-257.
- 90. Mathur R. Sharma A. Dixit VP, Verma M. J Ethnopharmacol 1996; 50:61-68.
- 91. Available at http://www.drugs.com/npp/emblica.html
- 92. Rege NN, Thatte UM, Dahanukar SA, Phytother Res 1999; 13:275-291.
- 93. Jose JK, Kuttan G., Kuttan R. J Ethnopharmacol 2001; 75:65-69.
- 94. Sharma N. Trikha P. Athar M. Raisuddin S. Drug Chem Toxicol 2000; 23:477-484.
- 95. Biswas S., Talukder G., Sharma A. Phytotherapy research 1999; 13(6):513-516.
- 96. Banu N. ,Patel V. Chansouria JPN, Malhotra OP, Udupa KN, J Res Edu Indian Med 1982;1:29.
- 97. The Ayurvedic Pharmacopoeia of India: Ministry of Health and Family Welfare, Dept. of Health, Govt. of India, Part 1, 1st edi 1989;1:5.
- 98. Available at http://www.ayurvedatoday.org/amla.htm
- 99. Biswas S., Talukder G., Sharma A. Phytother Res 1999; 13:513-516.

100. Ding G. Lu Y. Ji C. Liu Y. Acta Pharmaceutica Sinica 2001; 36(4):292-295.

101. Eisenberg DM, Kessler RC, Foster C. Norlock FE, et al. NEJM 1993; 328:246-252.

102. Khan MY, Panchal S. Vyas N. Butani A. Kumar V. Pharmacognosy Reviews 2007; 1(1):114-118.

103.Available at

http://www.nationaalherbarium.nl/thaieuph/ThPspecies/ThPhyllanthus.htm