

## Phytochemistry, pharmacological activities and traditional uses of *Phyllanthus emblica* (Amla) along with its mechanism of action in anticancer activities: A review

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### Abstract

There are lots of information from *in vitro* and *in vivo* studies that the fruit extract of the *Phyllanthus emblica* tree, commonly known as Indian Gooseberry, has powerful anticancer properties. The bioactivity present in this extract is considered to be principally mediated by polyphenols, especially tannins and flavonoids. But it is not yet cleared that how polyphenols from *Phyllanthus emblica* can enter both cancer-preventative and antitumor properties. The antioxidant function of *Phyllanthus emblica* is responsible for some of the anticancer activity, but other mechanism of actions are also equally important. Herein, this paper provide a brief overview of the proof supporting anticancer activity of *Phyllanthus emblica* (Indian Gooseberry) extract.

**Keywords:** anticancer, antioxidant, *Emblca officinalis*, gallic acid, Indian gooseberry, *Phyllanthus emblica*

### Introduction

In developed countries, lung carcinoma is the chief cause of cancer death in men, while the most frequent cause of death in women is breast carcinoma. Studies suggests that to reduce the risk of breast cancer related mortality, antioxidant supplements might be helpful and also consuming food and beverages rich in polyphenols (eg: catechins, flavones and anthocyanins) is associated with a lower incidence of cancers [1].

*Phyllanthus emblica* (family- phyllanthaceae) also known as *Emblca officinalis* is commonly known as 'Amla' in Hindi, 'Amalki' in Sanskrit and 'Indian Gooseberry' in English. It is a medium sized deciduous tree with 7.5 – 18 meters height and can reach up to 30 meters. Which is found in tropical south eastern Asia, especially in central and southern India, Pakistan, Bangladesh, Malaysia, Sri Lanka, Mascarene Islands and Southern China. In India, amla trees are found in the forest of tropical area ascending up to 4500 ft on hills [2]. Indian Gooseberry or Amla is rich in iron, carbohydrates, fiber and is proved as the richest source of vitamin C. The fruit or amla is also used in a combination form known as Triphala, meaning a mixture of three fruits which is a Thai traditional herbal formulation composed of *Emblca officinalis*, *Terminalia belerica* and *Terminalia chebula* [3].

The raw fruit of *Phyllanthus emblica* is used for a broad variety of human disease or disorders including cancer. *Phyllanthus emblica* possesses several pharmacological actions such as antioxidant, anti-mutagenic, anti-inflammatory, antibacterial, analgesic, antitumor, antipyretic, chemopreventive and hepatoprotective activities. Extracts of *Phyllanthus emblica* reduces solid tumors in mice and other studies demonstrated that *Phyllanthus emblica* extracts are cytotoxic and inhibits the *in vitro* generation of many tumor cell lines such as human gastric adenocarcinoma (MK-1) and murine melanoma (B16F10) [13]. Phenolic compounds isolated from the fruit extract of *Phyllanthus emblica* are responsible for chemotherapy demonstrated that pyrogallol, which is active compound present in both crude and n-butanol fractions,

inhibits proliferation of human lung cancer cells by apoptosis mechanism. However, the mechanism by which *Phyllanthus emblica* makes cytotoxicity in cancer cell needs further illustration. In this article, the anticancer activity of *Phyllanthus emblica* has been discussed by various types of mechanism [5].

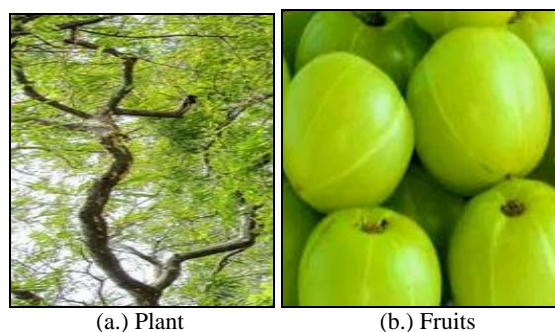


Fig 1: Picture of *Phyllanthus emblica*.

### Plant Anatomy/ Classification of plant

- **Kingdom:** Plantae
- **Division:** Flowering plant
- **Class:** Magnoliopsida
- **Order:** Malpighiales
- **Family:** Phyllanthaceae
- **Tribe:** Phyllanthae
- **Subtribe:** Fluegginae [6].

### Vernacular Names

- **English:** Emblic myrobalan, Indian Gooseberry
- **Hindi:** Amla
- **Sanskrit:** Aamalaki
- **Marathi:** Amla
- **Malayalam:** NelliKayi
- **Telugu:** Usirikaya
- **Kannada:** NelliKayi
- **Gujarati:** Ambla
- **Tamil:** Nelli
- **Kashmir:** Aonla [7].

### Morphology

Amla tree is a small to medium sized deciduous tree which is having a height of about 7.5 – 18 meters, with thin light grey bark exfoliating in small thin irregular flakes, exposing the fresh surface of different color underneath the older light grey bark. The average circumference of the main stem is 70 cm. The main trunk is divided into 2 to 7 scaffolds very near to the base in most of the cases. Leaves are 10 – 13 mm long and 3 mm wide, closely set in pinnate fashion which makes the branches feathery. Leaves is developed after setting of the fruits. They have unisexual flower flowers, 4 to 5 mm in length, color is pale green, borne in leaf axils in cluster of 6 to 10. Fleshy fruits, almost depressed to globose shape, 2.1 – 2.4 cm in diameter, 5.3-5.7 gm in weight, 4.5 – 5.0 mL in volume. Fruit's stone is 6 ribbed, splitting into three segments<sup>16</sup> each containing two seeds usually; seeds are 4 – 5 mm long and 2 – 3 mm wider, weight of each seed is 572 – 590 mg<sup>18</sup>.

### Chemical Composition of *Phyllanthus emblica*

Amla is most broadly studied plants. The chemical constituents of *Phyllanthusemblica* contains alkaloids, amino acids, vitamins, organic acids, hydrolysable tannins, phenolic compounds, carbohydrates, flavonoids. The mentioned constituents can be further elaborated as, it contains alkaloids such as Phyllantine, Phyllembin, and Phyllantidine. The amino acids present are Glutamic acid, Proline, Aspartic acid, Alanine, Cystein, Lysine. The vitamins present is Ascorbic acid. The organic acid present is Citric acid. The hydrolysable tannins present are Emblicanin A and B, Pedunculagin, Ellagitannin, Geraniin (Dehydroellagitannin), Corilagin (Ellagitannin), Chebulagic acid (Benzopyran tannin), Chebulinic acid (Ellagitannin), Punigluconin. The phenolic compounds present are Gallic acid, Ellagic acid, Methyl gallate, and Trigallayl glucose. The carbohydrate present is Pectin. The flavonoids present is Quercetin and Kaempferol<sup>19</sup>.

### Nutritive value

Amla also known as Indian Gooseberry is known for its nutritional activity. It contains high amount of polyphenols, minerals and is considered as one of the richest and tremendous source of vitamin C (200-900 mg per 100 gm). Main nutritional important components are reported in the table 1<sup>9, 10</sup>.

**Table 1:** Nutritive value of fruit of *Phyllanthus emblica* (Amla) in percentage

Chemical components	Percentage
Protein	0.5%
Mineral matter	0.7%
Carbohydrate	14.1%
Phosphorus	0.02%
Vitamin C	600mg/100g
Fruits: moisture	81.2%
Fat	0.1%
Fibre	3.4%
Calcium	0.05%
Iron	1.2mg/100g
Nicotinic acid	0.2mg/100g

### Distribution of *Phyllanthus emblica*

*Phyllanthus emblica* is widely distributed in most tropical and subtropical countries including Southern India,

Pakistan, Bhutan, China, Indonesia, Malay Peninsula, Nepal, Bangladesh, Sri-lanka, Myanmar, Malaya and Mascarene Islands. It is abundant in the deciduous forests of Madhya Pradesh. Originally, *Phyllanthus emblicawas* cultivated in Madascar<sup>4, 11</sup>.

### Propagation of *Phyllanthus emblica*

*Phyllanthus emblica* is generally propagated by seed propagation method. However, in commercial purpose the grafting methods have also been used. Propagation studies revealed that, season of grafting had profound influence on graft success. The maximum success achieved is 87.50% was recorded in November grafting followed by 66.69% in case of December<sup>12</sup>.

### Phytochemistry

Amla is one of the widely studied plant and the research proves that it contains phenolic compounds, alkaloids and tannins. Amla is also a rich source of vitamin C (478.56 mg/100 ml) which is more than those in lemon or tangerines and oranges<sup>13</sup>.

Amla contains many bioactive compounds such as apigenin, ellagic acid, quercetin, corilagin, methyl gallate, gallic acid, chebulinic acid, chebulagic acid, isostrictiniin, luteolin and so on. Emblicanin A, Emblicanin B, phyllaemblicin B, pedunculagin and punigluconin are the tannins which are present in *Phyllanthus emblica*<sup>14</sup>.

Glutamic acid (29.6%), proline (14.6%), aspartic acid (8.1%), alanine (5.4%), and lysine (5.3%) are the values of total amino acid. The portion of fruits which are pulpy, dried and freed from nuts contains: tannins and gum, crude cellulose, moisture, gallic acid, albumin, mineral matter are 13.75%, 17.08%, 3.83%, 1.32%, 13.08% and 4.12% respectively. *Phyllanthus emblica* fruit ash contains zinc, 4ppm; copper, 3ppm; and chromium, 2.5ppm.(24) Metals like lead and nickle were not found in leaves of *Phyllanthus emblica*. Copper level was found higher in the leaves of *Phyllanthus emblica* as compared to zinc, manganese and chromium<sup>15</sup>.

**Seeds:** A fixed oil, small amount of essential oil and phosphatides. The fixed oil (saponification value 185; acetyl value 2.03; sterol 2.70%; acid value 12.7; iodine value 139.5; unsaponifiable matter 3.81%; saturated fatty acid 7%. Contains linolenic acid (8.78%), linoleic (44%), steric (2.15%), miristic acid (0.95%), oleic (28.40%) and palmitic (2.99%)<sup>13</sup>.

**Roots:** Contain ellagic acid and lupeol<sup>13</sup>.

**Leaves:** It contains chebulic acid, chebulinic acid, chebulagic acid, alkaloids, phyllantidine, gallic acid, ellagic acid, amlic acid and phyllantine<sup>13</sup>.

**Barks:** It contains proanthocyanidine, leukodelphinidin and tannin<sup>13</sup>.



Fig 2: Picture of *Phyllanthus emblica*

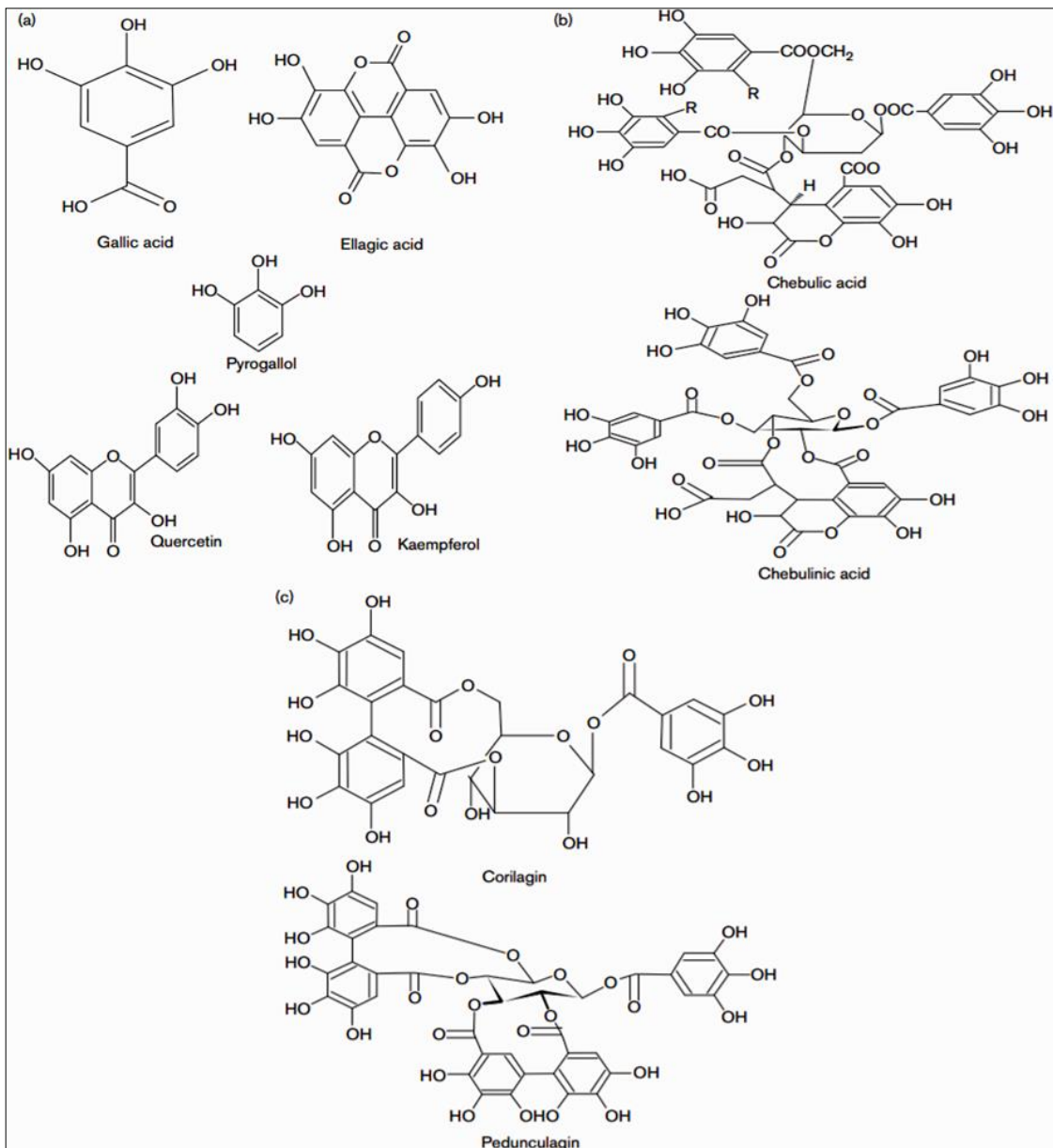


Fig 3: Some important phytochemicals of *Phyllanthus emblica*

## Cancer Prevention

Everyday we come in contact with the agents in our environment and through our diet they can probably deal with the integrity of our genome. Plenty of xenobiotics and the reactive oxygen species are generated during cell respiration are harmful. Thus, by reducing our contact or exposure to harmful xenobiotics and growing our capacity to “soak up” reactive oxygen species express a potential means to decrease the possibility of cancer. Using the classic measure of carcinogenicity, the Ames test, it was surely determined that *Phyllanthus emblica* prevents metagenesis *in vitro*. Confirming this concept *in vivo* is not as truthful. Measuring cancer prevention in humans is a true consuming and complex struggle and effort, involving many confusing factors. Thankfully, chemopreventive properties of substance can be tested by using the rodent model of various cancers [16].

Taken preventively, *Phyllanthus emblica* extract reduced the toxic effect of heavy metals and the carcinogen benzopyrene in murine models. In a murine model of skin cancer, continuous administration of *Phyllanthus emblica* extract at 100mg/kg reduced tumor rate by ~60%. Similarly two independent studies showed that the polyphenols of *Phyllanthus emblica* administered at 60-250mg/kg inhibited N-nitrosodiethylamine induced hepatocellular carcinoma by ~80-100%. However, such exciting results were not reported when *Phyllanthusemblica* extract was examined for chemoprevention of liver tumors induced by beginning with diethylnitrosamine and after that promotion with 2-acetylaminofluorene [9]. This difference specify that *Phyllanthus emblica* has the capacity to prevent the onset of some, but not all cancers, according to the initiators. This become fairly clear when one believes that carcinogenic compound have different modes of action; thus a single extract could not be hoped to be universally chemopreventive. Hopefully, future studies will raise on these studies to investigate the ability of *Phyllanthus emblica* to prevent tumor initiated by a wider variety of carcinogens at various tissue sites [16].

## Cancer Therapy

*Phyllanthus emblica* extracts have been proved to have potent tumor inhibitory properties against a number of cancer types both *in vitro* and *in vivo*. Preclinical proofs using a different panel of cancer cell lines shows aqueous extract from *Phyllanthus emblica* berries caused apoptosis at concentrations ranging from 50-100 micrograms/MI [4].

## Anticancer Activity of *Phyllanthus emblica*

*Phyllanthus emblica* prohibit the growth and spread of cancers, along with breast, liver cancer, uterus, malignant ascites, pancreas and stomach. It decreases the side effects of chemotherapy and radiotherapy. *Phyllanthus emblica* decreases the cytotoxic effect in mice dosed with carcinogens. *Phyllanthus emblica* has been reported to possess many medical action, along with immune-stimulator and antitumour activities. Amla (Indian Gooseberry) fruit contains 18 compounds that stops the growth of tumour cells including gastric and uterine cancer cells. It increases natural killer (NK) cell activity in various tumour. Its extracts decreases the ascites and solid tumour influenced by Dalton's lymphoma ascites cells in mice. Emblicanins A and B (tannins) present in amla have been proved to possess strong antioxidant and anticancer properties [19].

*Phyllanthus emblica* shows its activity by inhibiting the activator protein-1 and targets transcription of viral oncogens responsible for increasing cervical cancer thus demonstrating its potential efficacy for therapy of human papillomavirus- induced cervical cancer [21].

Chemoprevention with food phytochemicals is now a days considered as one of the most important gameplay to control cancer [20].

## In-vitro Study

The cytotoxic effect of *Phyllanthus emblica* (PE) extract was measured by using Sulforhodamine B colorimetric assay system currently accepted in the *in vitro* anticancer drug screening of the National Cancer Institute (NCI) in the United States of America (USA). The assay was performed in a 96-well format using the human cell lines. Normal lung fibroblasts, MRC5 were covered in the assay to assess whether the PE extract is cytotoxic to cancer cells [4].

In short, the cells were inoculated into 96-well microliter plates in 100  $\mu$ L RPMI-1640 media at density of plating at 7500 cells/well. Each cell line was plated on duplicate plates and incubated in a humidified chamber at 37°C, 5% CO<sub>2</sub>. After 24h, one plate of each cell line was fixed in situ with 10% (w/v) cold TCA, to represent the cell number at the time of PE addition at day 0. Aliquots of 100  $\mu$ L of the PE extract were added to the appropriate wells on the parallel plate to get a final concentration of 6.25, 12.5, 25, 50, 100, 200 and 400  $\mu$ g/mL. Then, the plates were incubated for more 48h at 37°C, 5% CO<sub>2</sub>. At the end of each exposure time (day 2), the culture medium was separated. The cells were gently fixed with 10% (w/v) cold TCA and stained with 0.4% (w/v) Sulforhodamine B in 1% acetic acid solution. The absorbance were measured at a wavelength of 492 nm. Biotrak™ II Visible Plate Reader. The optical density (OD) value was obtained after subtracting the blank background control [4].

Dose-response curve (DRC) had been plotted as percent cell growth vs the extract concentration on a log scale. Three dose response parameter were calculated as GI so which is the concentration which result in 50% growth inhibition in control cells during the treatment, TGI which is the concentration which results in total growth inhibition (the same number of cells as placed), and LC so which is the concentration which results in a 50% loss of cells at the end of the treatment as compare with the cells at the beginning [4].

## In-vivo Study

The anticancer activity of the *Phyllanthus emblica* fruit extract was evaluated by a 7, 12-dimethylbenz[a]anthracene (TPA) - induced skin tumourigenesis in mice. The experimental protocol was inspected and approved by The Animal Ethics Committee of Faculty of Medicine, Thammasat University, Pathum Thani, Thailand (NO. 0001/2006) [4].

All group of mice had been treated with topical application of 390 nmol DMBA in 0.1 mL acetone or the solvent alone on their shaven backs. One week after initiation, 4 nmol of TPA in acetone (0.1 mL) was topically applied twice weekly to the skin for 20 weeks. For the treated groups, animals were topically treated with the PE fruit extract (1, 2 or 4 mg in 0.1 mL acetone) 1 hour prior to each TPA application before the termination of the experiment. Once a week, the papillomas present were counted and measured

using a caliper (Vernier caliper). The results were declared as the average number of tumours per mouse (multiplicity) and percentage of tumour bearing mice (incidence) [4].

### Mechanism of Action

#### Amla and some of its constituents cause apoptosis and cytotoxicity of cancer cells

Apoptosis, a process by which the cell is resulted to death by not beginning an inflammatory response, is vital in regulating tissue homeostasis [22]. A large group of research has proved that the process of cancer cell transformation, progression, and metastasis include conversion of the normal apoptotic pathway and that the number of cell death is very less in these cells [22]. Therefore, the selection of apoptosis is reasonably the most potent defence against cancer as it completely knockout the mutated and severely damaged cell. Accordingly, constituents that can eliminate mutated, pre-cancer and cancer cells by sparing the normal cell are supposed to be an effective anticancer agent and to offer the therapeutic advantage in the elimination of cancer cells [22].

The ability of the extractssss of *Phyllanthus emblica* and some of its phytochemicals constituents to induce apoptosis in cancer cell should give the understanding of its anticancer potential. Studies have shown that gallic acid, pyrogallol, quercetin and ellagic acid also possess cytotoxic and apoptogenic effects on the cancer and transformed cells, but not in normal cells. Altogether, all these observations clearly suggests that the presence of all these constituents in amla resulted in the elimination of the mutated and cancer cell and resulted in the expected effect of anticancer [23].

#### Traditional Use of *Phyllanthus emblica*

Amla possess a number of medicinal properties and it is a necessary constituent of many Ayurvedic formulations [24]. Various polyherbal formulations, such as Amlakadi Tailya, Amlakadi Ghrita, Aamalaki Rasayanam, Avipatikara Churnam, Dasamularishta, Dhatriyarista, Panchatikaguggulu Ghritam, Triphala Guggulu, Alakyadichurna, Asokarista, Chyavananaprasa Leham, Dhatrilauha, Panchatikaguggulu, Triphala Lepam, and Triphala Ghritam are commonly used to treat various illness [24, 25].

It is also used in Unani Tibetan, Siddha, Sri lankan, and Chinese system of medicine [24, 25]. In Ayurveda, amla is examined to be a potent rasayana (rejuvenator) and to be useful in stopping the degenerative and senescence process, to promote benefits of eye, longevity, stimulate hair growth, enhance digestion, enliven the body, to treat constipation, enhance the intellect, reduce fever, strengthen the heart, reduce cough alleviate asthma, and purify the blood [26].

#### Other Use of *Phyllanthus emblica*

##### Action on Diabetes

Amla fruit powder increases the high blood pressure control. Triphala comprises of three herbs which is amla, harada and bihara. The research says that the blood sugar level is increased by the action of an enzyme alanine transaminase which is present in liver. This enzyme can be controlled by taking one teaspoonful of this mixture (equal quantities of amla, jamun and bitter ground powder) once or twice per

day. Chromium is a mineral which is present in amla is responsible for the anti-diabetic effect [27].

### Impedes Constipation

The infrequent and irregular evacuation of the bowels is known as constipation. This problem can be cured by taking one teaspoon of amla powder with milk or water every morning. On the other hand, four tea spoon of fresh amla juice and three teaspoon of honey mixed with water can also cure the constipation. If constipation is caused by parasites, take 20 gm of fresh amla juice everyday, this can destroy the parasitic worms [28].

#### 1. Gout

Gout is the inflammation of the big toe caused by defects in uric acid metabolism which result in acid deposit and its salts in blood and joints. This problem can be cured by taking amla juice with old ghee makes softening of joints and helps in curing gout and also removing the spots caused by measles, chicken pox, and small pox [7].

#### 2. Respiratory disorder

Research has been proved that amla can retrieve the normal respiration while the system gets affected. The paste which is made up of 10 gm leaves of *Phyllanthusemblica*, 5 fruits of Terminalia chebula, 9 seeds of Piper nigrum, 1 garlic are crushed over and mixed with 25 ml of ghee made from cow's milk and a clove. The fresh juice of amla which is mixed with the honey can get back best from cough, asthma, and also from other respiratory disorder [7].

#### 3. Migraine

Migraine is a severe vascular headache in female rather than in male. Migraine can be cured by applying the paste made by dried amla powder with kumkum, neelkamal, and rose water [7].

#### 4. Eye tonic

Triphala powder (made by mixing Hirda, behde and amla powder) with honey makes the eye vision bright and keeps shining and also its god for our digestive system [29].

#### 5. Jaundice

Fresh amla fruits are kept for soaking with 4 munnakkas, both are grind with amla juice after one hour. This can give relief in jaundice [7].

#### 6. Piles

Drinking of fresh amla juice with half teaspoon of ghee and one teaspoon of honey and 100 gm of milk after lunch can cure chronic piles problem [7].

#### 7. Urinary problem

The paste made by 20 gm of pulp of dried amla in 160 gm of water till 40 gm is left in it. This is again mixed with 20 gm of Gur. Regular use of this portion may cure the urinary problem [7].

#### 8. Antioxidant effect

Earlier many researches have been studied about the antioxidant and free radical scavenging activity of *Phyllanthus emblica* and the main reason is the constituents of the *Phyllanthus emblica* which is ascorbic acid, tannins and polyphenols. Researchers have been proved that the phytochemicals from the *Phyllanthus emblica* are good

metal ion chelator as it prevent the oxidative cascades [25, 30, 31, 32].

### 9. Anti-inflammatory effect

Aller-7, a polyherbal formulation containing *Phyllanthus emblica* possess a powerful anti-inflammatory activity against 48/80-induced paw edema in both Balb/c mice and Swiss Albino mice and also against carrageenan-induced paw edema in Wistar albino rats [33].

### 10. Hepatoprotective effect

*Phyllanthus emblica* and its flavonoid quercetin has been found to be hepatoprotective against acetaminophen-induced liver damage in Albino rats and mice. The research has also reported that *Phyllanthus emblica* has strong hepatoprotective effect against carbon tetrachloride-induced hepatic damage [34, 35].

### 11. Cardioprotective effect

The earlier research supports the claim that the anti-oxidants of *Phyllanthusemblica* may acts as a cardioprotective agents [36].

### 12. Antitussive effect

The ethanolic extract of the fruit of *Phyllanthus emblica* seems to have a good ability to inhibit mechanically-provoked cough, but only at a higher dose of about 200 mg/kg of body weight. It acts on the mucus secretion in the airways [37].

### 13. Antimicrobial effect

Aqueous infusion extract of *Phyllanthus emblica* presented potent antimicrobial activity against *Enterobacter cloacae* followed by *Escherichia coli* and *Klebsiella pneumoniae*. Aqueous decoction of *Phyllanthus emblica* exhibited strong antibacterial activity against *E. coli*, *K. ozaenae*, *K. pneumoniae*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *S. typhi*, *S. paratyphi*, and *S. paratyphi B* [38].

### 14. Analgesic and Antipyretic effect

*Phyllanthus emblica* leaves decoction is used to treat fever and the fresh fruit is refrigerant. The seeds are given internally as a cooling remedy in bilious affections and nausea, and also in fever. A modified indigenous Siddha formulation Kalpaamruthaa, which contains *Semecarpus anacardium* nut milk extract, dried powder of *Phyllanthus emblica* fruit and honey is reported to have good antipyretic activity. In some another studies, the ethanol and aqueous extract of *Phyllanthus emblica* fruit at a single dose of 500 mg/kg caused lowering in the rectal temperature of hyperthermic rat [39].

### Conclusion

According to the preclinical studies which is carried out in the last two decades have clearly said that amla possess anticancer chemopreventive, radioprotective and chemomodulatory effect. The studies on the effects of amla on some cancer cell lines and animals proves its effectiveness, infinite possibility for investigation still remains. Applicable animals and cell culture studies are needed to understand the basic mechanism of action, especially with the phytochemicals. A quality control set for the authenticity of the plant and the presence of the active constituents, phytochemicals, especially ellagic acid,

quercetin, corilagin, luteolin, emblicanin A and emblicanin B, gallic acid, chebulinic acid, kaempferol, chebulagic acid, apigenin in the required levels. Experiments should also be done to understand that which of the phytochemicals are useful along with their mechanism of action.

Many studies and researches indicates that the amla and some of its phytochemical constituents (ellagic acid, gallic acid, quercetin, pentagalloyl glucose and kaempferol) are cytotoxic to cancer cells, where as the normal non-cancer cells are unaffected. It is also possible that these constituents exerts their effects on cancer cells that have an abnormal cell cycle progression. It has also been observed that these molecules induce apoptosis and cytotoxicity by balancing the proteins involved in cell progression, and the observations of some research support the hypothesis. However, detailed research and studies is needed on this parameters.

Although due to its low cost and safety in consumption, amla remains a plant with tremendous potential and infinite possibilities for further research. Amla has the potential to become a harmless (nontoxic) anticancer, chemopreventive agent, and as a support to radiotherapy and chemotherapy. The conclusion of such studies may be useful for the clinical application of amla in human in treatment of different cancers and may come with the new therapeutic approach.

### References

1. Divisi D, Di Tommaso S, Salvemini S, Garramone M, Crisci R. Diet and cancer. *Acta Biomed*,2006;77(2):118-123.
2. Rai N, Tiwari L, Sharma RK, Verma AK. Pharmacobotanical Profile on *Emblica officinalis* Gaertn. -A Pharmacopoeial Herbal Drug. *SMT Journals*,2012;1(1):29-41.
3. Phetkate P, Kummalue T, U-pratya Y, Kietinun S. Significant increase in Cytotoxic T Lymphocytes and Natural Killer cells by Triphala: A clinical phase I study. *Evidence-Based Complementary and Alternative Medicine*, 2012, 1-6.
4. Ngamkitidechakul C, Jaijoy K, Hansakul P, Soonthornchareonnon N, Sireeratawong S. Antitumor effects of *Phyllanthus emblica* L.: induction of cell apoptosis and Inhibition of *in vivo* tumour promotion and *in vitro* invasion of human cancer cells. *Phytotherapy Research*,2010;24(9):1405-1413.
5. Tanimura S, Kadomoto R, Tanaka T, Zhang YJ, Kouno I, Kohno M. Suppression of tumour cell invasiveness by hydrolyzable tannins (plant polyphenols) via the inhibition of matrix metalloproteinase-2/-9 activity. *BiochemBiophys Res Commun*,2005;330(4):1306-1313.
6. Sumalatha D. Antioxidant and Antitumour activity of *Phyllanthus emblica* in colon cell lines. *International Journal of Current Microbiology and Applied Sciences*,2013;2(5):189-195.
7. Kaushik Vilas Kulkarni, Shrishail M Ghurghure. Indian Gooseberry (*Emblica officinalis*): Complete pharmacognosy review. *International Journal of Chemistry Studies*,2018;2(2):05-11.
8. Scartezzini P, Speroni E. Review on some plants of Indian traditional medicine with antioxidant activity. *J Ethanpharmacol*,2000;71(1-2):23-43.
9. Bharthakur NN, Arnold NP. Chemical analysis of the emblica (*Phyllanthus emblica* L.) and its potential as a

- food sources. *Scientia Horticulture*,1991;47(1-2):99-105.
10. Gopalan, Rama Sastri BV, Balasubramanian SC. Nutritive value of Indian foods. National Institute of Nutrition: Hyderabad, India, 1991.
  11. Zhang YJ, Tanaka T, Iwamoto Y, Yang CR, Kouno I. Phyllaemblic acid, a novel highly oxygenated norbisabolane from the root of *Phyllanthus emblica*. *Tetrahedron Lett*,2000;41:1781-1784.
  12. Morton J. The Emblic (*Phyllanthus emblica* L.). *Economic Botany*,1960;14:119-128.
  13. Khan KH. Roles of *Emblica officinalis* in medicine – A review. *Bot Res Int*,2009;2:218-228.
  14. Kumar A, Singh A, Dora J. Essential perspective for *Emblica officinalis* *Int. J Pharma. Chem. Sci*,2012;1(1):11-18.
  15. Kumar VN, Vibha, Ashwani K. A Comparative study of heavy metals in *Emblica officinalis*, *Phyllanthus emblica* and *Azadirachta indica*. *Int. Res. J. Biological Sci*,2013;2(8):16-19.
  16. Tiejun Zhao, Qiang Sun, Maud Marques, Michael Witcher. Anticancer Properties of *Phyllanthus emblica* (Indian Gooseberry). *Oxidative Medicine and Cellular Longevity*, 2015, 1-7.
  17. Nandi P, Talukder G, Sharma A. Dietary chemoprevention of clastogenic effect of 3, 4-benzo(a)pyrene by *Emblica officinalis* Gaertn. fruit extract. *British Journal of Cancer*,1997;76(10):1279-83.
  18. Sultana S, Ahmed S, Jahangir T. *Emblica officinalis* and hepatocarcinogenesis: a chemopreventive study in Wistar rats. *Journal of Ethnopharmacology*,2008;118(1):1-6.
  19. Pandey Govind. Some important anticancer herbs: A review. *Int. Res J Pharm*,2011;2(7):45-52.
  20. Madhuri S, Pandey Govind, Verma Karuna S. Antioxidant, immunomodulatory and anticancer activities of *Emblica officinalis*: an overview. *International Research Journal of Pharmacy*,2011;2(8):38-42.
  21. Mahata S, Pandey A, Shukla S, Tyagi A, Husain SA, Das BC *et al.* Anticancer Activity of *Phyllanthus emblica* Linn. (Indian Gooseberry): Inhibition of Transcription Factor AP-1 and HPV Gene Expression in Cervical Cancer Cells. *Nutrition and Cancer*,2013;65(1):88-97.
  22. Ghobrial IM, Witzig TE, Adjei AA. Targeting apoptosis pathways in cancer therapy. *CA Cancer J Clin*,2005;55:178-194.
  23. Losso JN, Bansode RR, Trappey A II, Bawadi HA, Truax R. *In vitro* antiproliferative activities of ellagic acid. *J Nutr Biochem*,2004;15:672-678.
  24. Warriar PK, Nambair VPK, Ramankutty C. *Indian Medicinal Plants*. Hyderabad, India: Orient Longman Ltd,1996;5:225-228.
  25. Kulkarni RD. Principles of pharmacology in ayurveda. Mumbai, India: Ram Sangam Graphics, 1997.
  26. Pandey G. *Dravyaguna Vijnana (Materia Medica-Vegetable Drugs) Part IV* Varanasi, India: Krishnadas Academy,2002;2:102.
  27. Devalaraja S, Jain S, Yadav H. Exotic fruits as therapeutic complements for diabetes, obesity and metabolic syndrome. *Food Research International*,2011;44:1856-1865.
  28. Thakur RS, Puri HS, Husain, Akhtar. Major Medicinal Plants of India. Central Institute of Medicinal and Aromatic Plants. Lucknow, 1989.
  29. Biswas NR, Gupta SK, Das GK, Kumar N, Mongre PK, Haldar D *et al.* Evaluation of Ophthacare eye drops- a herbal formulation in the management of various ophthalmic disorders. *Phytotherapy Research*,2001;5(7):618-20,22.
  30. Saito K, Kohno M, Yoshizaki F, Niwano Y. Extensive screening for edible herbal extracts with potent scavenging activity against superoxide anions. *Plant Foods Hum Nutr*,2008;63:65-70.
  31. Kumaran A, Karunakaran RJ. Nitric oxide radical scavenging activity components from *Phyllanthus emblica* L. *Plant Foods Hum Nutr*,2006;61:1-5.
  32. Scartezzini P, Antognoni F, Raggi MA, Poli F, Sabbioni C. Vitamin C content and antioxidant activity of the fruit and of the Ayurvedic preparation of *Emblica officinalis* Gaertn. *J Ethnopharmacol*,2006;104:113-118.
  33. Bandyopadhyay SK, Pakrashi SC, Pakrashi A. The role of antioxidant activity of *Phyllanthus emblica* fruit on prevention from indomethacin induced gastric ulcer. *J Ethnopharmacol*,2000;70:171-176.
  34. Gulati RK, Agarwal S, Agarwal SS. Hepatoprotective studies on *Phyllanthus emblica* Linn. and quercetin. *Ind J Exp Biol*,1995;33:261-268.
  35. Lee CY, Peng WH, Cheng HY, Chen FN, Lai MT, Chiu TH. Hepatoprotective effect of *Phyllanthus* in Taiwan on acute liver damage induced by carbon tetrachloride. *Am J Chin Med*,2006;34:471-482.
  36. Bhattacharya SK, Bhattacharya A, Sairam K, Ghosal S. Effect of bioactive tannin principles of *Emblica officinalis* on ischemia-reperfusion-induced oxidative stress in rat heart. *Phytomedicine*,2002;9:171-174.
  37. Nosal'ova G, Mokry J, Hassan KM. Antitussive activity of the fruit extract of *Emblica officinalis* Gaertn. (Euphorbiaceae). *Phytomedicine*,2003;10:583-589.
  38. Rahman S, Akbor MM, Howlader A, Jabbar A. Antimicrobial and cytotoxic activity of the alkaloids of Amalki (*Emblica officinalis*). *Pak J Biol Sci*,2009;12:1152-1155.
  39. Sairam K, Rao Ch V, Babu MD, Kumar KV, Agarwal VK, RK KG. Antiulcerogenic effect of methanolic extract of *Emblica officinalis*: an experimental study. *J Ethnopharmacol*,2002;82:1-9.