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Emblica officinalis medicinal plants: A new approach in traditional herbal medicine

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***Abstract*---**The herbal medicine is in the great demand in the developed as well as developing countries for primary health care because of their large biological activities, higher safety margin and lesser cost. one of the common traditional herbal drugs is *Emblica officinalis*, commonly known as Amla, is a member of a small genus Emblica (Euphorbiaceae). The earlier study has demonstrated potent anti-microbial, adaptogenic, hepatoprotective, anti-tumour and anti-ulcerogenic activities in the fruits of *Emblica officinalis*. Leaf extracts have been shown to possess anti-inflammatory activity. vitamin C, tannins and flavonoids present in amla have very powerful antioxidant activity. Due to rich in vitamin C amla is successfully use in the treatment of human scurvy. The extracts from various parts of *E. officinalis*, especially fruit, contain numerous phytoconstituents viz. higher amount of polyphenols like gallic acid, ellagic acid, different tannins, minerals, vitamins, amino acids, fixed oils, and flavonoids like rutin and quercetin. The extract or plant is identified to be efficacious against diversified ailments like inflammation, cancer, osteoporosis, neurological disorders, hypertension together with lifestyle diseases, parasitic and other infectious disorders. These actions are attributed to either regulation of various molecular pathway involved in several pathophysiology's or antioxidant property which prevents the damage of cellular compartments from oxidative stress. However, serious efforts are required in systemic research to identify, isolate and evaluate the chemical constituents for nutritional and therapeutic potentials.

***Keywords*---**Amla, *Emblica officinalis,* Medicinal uses, Pharmacology, Phytochemistry.

Introduction

Emblica officinalis (EO) enjoys a hallowed position in Ayurveda- an Indian indigenous system of medicine. According to believe in ancient Indian mythology, it is the first tree to be created in the universe. It belongs to family *Euphorbiaceae*. It is also named as Amla, *Phyllanthus Emblica or* Indian gooseberry. Other vernacular names of EO are Dhatriphala, Amla, Amaliki, Amalakan, Sriphalam, Vayastha [1]. It grows in tropical and subtropical regions including Pakistan, Uzbekistan, Srilanka, South East Asia, China and Malaysia. The fruits of EO are widely used in the Aryuveda and are believed to increase defence against diseases. It has its beneficial role in cancer, diabetes, liver treatment, heart trouble, ulcer, anemia and various other diseases. Similarly, it has application as antioxidant, immunomodulatory, antipyretic, analgesic, cytoprotective, antitussive and gastroprotective. Additionally, it is useful in memory enhancing, ophthalmic disorders and lowering cholesterol level. It is also helpful in neutralizing snake venom and as an antimicrobial [2].

General Description Of Amla Plant

Amla tree medium in height grows up to 8 meters with slightly curved trunk. Branchlets are finely pubescent 10-20 cm long. Amla Leaves are finely and closely set along the branchlets. Amla Leaves have pinnate resemblance, very tiny, simple and attached by the base to branchlets. Color of Amla flowers are yellowish. Amla tree contains hard, smooth and spherical fruit yellowish green in color with six vertical stripes. Taste of Amla is sour, bitter and astringent and edible fruit is a great source of fiber [3].

E. officinalis Geart. genus *Phyllanthus* (Euphorbiaceae) is widely distributed in most tropical and subtropical countries. It grows in tropical and subtropical parts of China, India, Indonesia and on the Malay Peninsula and indigenous to tropical India and Southeast Asia [4]. It can be easily found growing in semi–arid regions and plains of northern India. Uttar Pradesh, Tamil Nadu, Rajasthan and Madhya Pradesh are preferable subtropical area for cultivation of amla. The fruits are available from October till May during which time they are also collected and preserved in large numbers to be made available during the rest of the year [5]. Various application of amla are shown in figure 1.

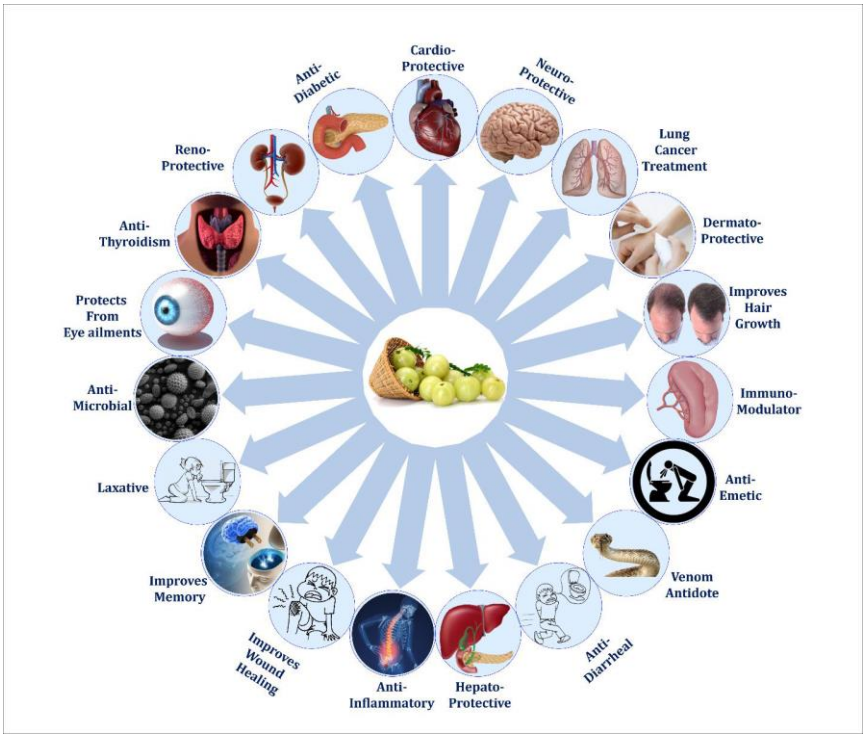

Figure 1. Different application of amla

Phytochemical constituents

E. officinalis, well known for its nutrient qualities, contains a variety of chemical constituents including tannins, mucic acid, amino acids, alkaloids, flavone glycosides, phenolic glycosides, flavonol glycosides, phenolic acids, sesquiterpenoids, nor sesquiterpenoids and carbohydrates [6]. Fruit juice of *E. officinalis* contains the highest amount of vitamin C (478.56 mg/100 ml) as compared to other fruits, such as apple, lime, pome-granate, Perlette grape, and Pusa Navrang grape [7]. However, previous report falsely claimed that instead of vitamin C, *E. officinalis* contains two low molecular weight hydrolysable tannins, namely emblicanin A and emblicanin B with punigluconin and pedunculagin. The presence of vitamin C in fruits of *E. officinalis* is debatable as there are many controversial data available. Recently in 2014, Bansal et al. has quantified various phytoconstituents, viz. gallic acid, chlorogenic acid, ellagic acid and quercetin from the fruit juice of *E. officinalis* and found to have 37.95, 17.43, 71.20 and 2.01 mg/100 ml of fruit juice, respectively [8]. Gallic acid; 1-*O*-galloyl-β-d-glucose (known as Glucogallin); 3,6-di-*O* galloyl-d-glucose; 1,6-di- *O*-galloyl-β-d-glucose; chebulinic acid; quercetin; chebulagic acid; corilagin; 3-ethylgallic acid (3-ethoxy-4,5-dihydroxy-benzoic acid); isostrictiniin; kaempferol-3-*O*-α-L-(6'-methyl)-rhamnopyranoside; kaempferol-3-*O*-α-L-(6'-ethyl)-rhamnopyranoside and various phenolic compounds like L-malic acid 2-*O*-gallate; mucic acid 2-*O*-gallate; mucic acid 1,4-lactone 2-*O*gallate; mucic acid 1,4-lactone 5-*O*-gallate; mucic acid 1,4-lactone 3-*O*-gallate and mucic acid 1,4-lactone 3,5-di-*O*-gallate have been isolated from fruit juice of *E. officinalis* [9]. Three nor sesquiterpenoids, namely phyllaemblicin-A, B and C; phyllaemblic acid (methyl ester of highly oxygenated

norbisabolane) along with bisabolene-type sesquiterpenoids like phyllaemblic acid B, phyllaemblic acid C and phyllaemblicin D with phenolic glycosides, 2-carboxylmethylphenol 1- *O*-β-d-glucopyranoside and 2,6-dimethoxy-4-(2-hydroxyethyl) phenol 1-*O*-β-d-glucopyranoside were isolated from the root of *E. officinalis* [10]. Gallic acid; 1-*O*-galloyl-β-d-glucose (known as Glucogallin); 3,6-di-*O*-galloyl-d-glucose; 1,6-di- *O*-galloyl-β-d-glucose; chebulinic acid; quercetin; chebulagic acid; corilagin; 3-ethylgallic acid (3-ethoxy-4,5-dihydroxy-benzoic acid); isostrictiniin; kaempferol-3-*O*-α-L-(6'-methyl)- rhamnopyranoside; kaempferol-3-*O*-α-L-(6'-ethyl)-rhamnopyranoside and various phenolic compounds like L-malic acid 2-*O*-gallate; mucic acid 2-*O*-gallate; mucic acid 1,4-lactone 2-*O*gallate; mucic acid 1,4-lactone 5-*O*-gallate; mucic acid 1,4-lactone 3-*O*-gallate and mucic acid 1,4- lactone 3,5-di-*O*-gallate have been isolated from fruit juice of *E. officinalis* [11]. Three nor sesquiterpenoids, namely phyllaemblicin-A, B and C; phyllaemblic acid (methyl ester of highly oxygenated norbisabolane) along with bisabolene-type sesquiterpenoids like phyllaemblic acid B, phyllaemblic acid C and phyllaemblicin D with phenolic glycosides, 2-carboxylmethylphenol 1-*O*-β-d-glucopyranoside and 2,6-dimethoxy-4-(2-hydroxyethyl) phenol 1-*O*-β-d-glucopyranoside were isolated from the root of *E. officinalis* [12,13].

Pharmacological and Biological Activities

Antioxidant activity

In this study the antioxidant activity of free and bound phenolics of amla (*Emblica officinalis*) and turmeric (Curcuma longa) was investigated. The *Emblica officinalis* free (EOFP) and bound phenolics (EOBP) showed between four- to 10-fold higher levels of antioxidant activity as evaluated by both free radical scavenging and reducing power assays compared to that of Curcuma longa free (CLFP) and bound phenolics (CLBP). Higher level of antioxidant activity in E. officinalis has been attributed to the phenolic content (12.9%, w/w, correlation coefficient R ¼ 0:74) in them. results clearly suggest the presence of potent antioxidants such as gallic acid in E. officinalis and protocatechuic acid and ferulic acid in C. longa, in addition to the known ascorbic acid and curcumin in E. officinalis and C. longa, respectively [14].

Potential Therapeutic Application

Every part of *Emblica officinalis* is useful owing to its medicinal and pharmaceutical properties. The plant has been reported to have antioxidant, anti-inflammatory, anticancer, adaptogenic, antidiabetic, nootropic, antimicrobial and immunomodulatory potential [15]. Besides having beneficial actions in various disorders, *E. officinalis* also prevents hyperlipidemia, osteoporosis 8 and several other ailments [16]. The studies showed that Amla preparations contained high levels of the free-radical scavenger, superoxide dimutase (SOD), in the experimental subjects Amla is believed to increase *ojas*, and is considered to be one of the strongest rejuvenate herbs in Ayurvedic medicine. It is the primary ingredient used in one of the renowned Ayurvedic herbal formulae, called *Chayavanprasha* which has great respect as a tonic. The preparation is named after Chayavan who was sitting in the forest when the Emperor's daughter

who was playing while blindfolded in the forest fell over him. Not knowing he was a stranger, she ran her fingers through his hair and decorated him with a garland of flowers, which must have been quite an accomplishment while wearing a blindfold! Needless to say, her father found out and insisted that the wise old sage marry his daughter (as a woman was only allowed to be touched by one woman in her lifetime). The old sage created *chayavanprasha* and lived on it for 2 months, during which time he regained youthfulness and sexual vitality. Reddy et al. and Andican et al. investigated the ameliorative effect of E. officinalis fruit extract against alcohol-induced oxidative stress and established the favourable role of polyphenols such as flavonoids, tannins and other compounds such as ascorbic acid in mitigating oxidative stress. These polyphenols are mainly present in E. officinalis fruit extract, responsible for protection against alcohol-encouraged oxidative stress owing to scavenging effect on NOx which behaves as an antioxidant and pro-oxidant simultaneously [17]. Similar antioxidant properties of E. officinalis were perceived by Shivananjapaa and Joshi in cellular oxidative stress using a hepatocyte cell line (HepG2). Aqueous extract of fruits of *E. officinalis* significantly improved the antioxidant capacity by increasing the levels of GSH and antioxidant system enzymes like superoxide dismutase, catalase, GSH peroxidase, GSH reductase and GSH S-transferase. Additionally, levels of lipid peroxidase and SOD were found to be diminished [18]. Similar studies were accomplished by different research groups, using in vivo and in vitro tools and antioxidant 10 role of polyphenolic compounds; including flavonoids and tannoids was confirmed [19]. Although, whole fruit of E. officinalis is well known for having antioxidant property, the pulp and seed have their own different phyto-pharmacological roles. Nambiar et al. found that pulp of *E. officinalis* showed superior antioxidant potential than seeds with IC50 values for DPPH radical scavenging activity being 6 µg/ml and 13 µg/ml, respectively [20]. Zhang et al. revealed, based on their cellular models, that phyto-chemicals including some new compounds isolated from E. officinalis resemble to sesquiterpenoids and diphenyl ether, and were responsible for providing cytoprotective activities against H_2O_2 induced $PC1_2$ cell damage. This activity is attributed to antioxidant potential as all the compounds were found to show significant DPPH scavenging activity with IC50 values in range of 3.25-4.18 µM [21].

Anti-diabetic and related metabolic functions

Diet plays a major role in the management of diabetes and related metabolic complications. Various traditional herbs have been reported to have varying degrees of hypoglycaemic and antihyperglycemic activity. These activities seem to be mediated through increased insulin secretion via stimulation of pancreatic β-cells, interfering with dietary glucose absorption or through insulin sensitizing action [22]. Various non-clinical and clinical studies have established antihyperglycemic activity of *E. officinalis* [23].

A clinical study involving treatment with *E. officinalis* for 21 days showed that *E. officinalis* not only significantly reduced fasting and 2 hours post-prandial blood glucose level in diabetic human volunteers but also produced reduction in total cholesterol and triglyceride (TG) levels in subjects receiving 1, 2 or 3 g *E. officinalis* powder per day. Moreover, healthy and diabetic human volunteers receiving 2 or 3 g *E. officinalis* per day, showed significant improvement in high

density 11 lipoprotein-cholesterol (HDL) and reduction in low density lipoprotein-cholesterol (LDL) levels [24]. To confirm protective action of *E. officinalis* on diabetic complications, a three-month clinical study was conducted by Chen et al. on uremic patients suffering from diabetes. It was observed that oxidative stress increased due to activation of neutrophils during regular hemodialysis therapy. Numerous plasma biomarkers were screened after giving an equal mixture of (-)-epigallocatechin gallate (EGCG) and extract of *E. officinalis.* Results showed significant improvement in antioxidant defence system with decreased diabetic and atherogenic indices in patients treated with extract of *E. officinalis*. Moreover, hepatic function, renal function and inflammatory responses remained unchanged suggesting that administration of *E. officinalis* does not lead to adverse drug reactions [25].

Cyto-protective and Immunomodulatory property

In this study the fruits extracts of *Emblica officinalis* (Amla) have been reported to have strong anti-oxidant properties. There is a paucity of studies on the immunomodulatory properties of fruit extracts of Amla in immuno-compromised states, with the emphasis on lymphocytes. Therefore, the aim of the study was to determine the anti-oxidant and immunomodulatory properties of Amla using chromium (VI) as an immunosuppressive agent. Chromium (Cr) treatment results in enhanced cytotoxicity, free radical production, lipid peroxidation and decreased glutathione peroxidase (GPx) activity and diminished glutathione (GSH) levels [26].

Anti-hyperlipidemic and related metabolic syndrome

Ischemic heart diseases, obesity, metabolic syndrome related type-2 diabetes, hypertension and stroke are major health woes in western as well as developing countries. Numerous plants and their derivative obtained thereof possess hypolipidemic potential owing to the presence of flavonoids and other phyto-constituents [27]. Kim et al. established *in vivo* and *in vitro* anti-hyperlipidemic activity of extract of *E. officinalis* using cholesterol-fed rats and Cu+2 induced LDL-oxidation respectively, and presented substantial reduction in total as well as free cholesterol level in a dose-dependent manner. Oxidized-LDL (Ox-LDL) is regarded as a key marker for the early development of atherosclerosis, where the administration of *E. officinalis* showed drop in the level of Ox-LDL level in cholestesterol-fed subjects and prevented the advancement to atherosclerosis due to potential antioxidant property [28]. Similarly, another report showed hypolipidemic activity as a result of inhibition of hepatic 3-hydroxy 3-methylglutaryl coenzyme A (HMG-CoA) reductase and elevated Lecithin-cholesterol acyltransferase (LCAT). This action is attributed to flavonoids, which inhibit the synthesis and degradation of lipids [29]. A clinical trial conducted on class-I obese subjects, having body-mass index between 25-35, found that administration of *E. officinalis* extract, in a dose of 500 mg twice15 a-day for 12 weeks, significantly reduced total cholesterol, LDL-cholesterol and high-sensitive Creative protein (hr-CRP) levels. Inspite of having anti-atherogenic potential, *E. officinalis* decreased ADP and collagen prompted platelet aggregation and eventually reduced diabeto cardiac malaise [30].

Anti-aging tonic

In this study use of *Emblica officinalis* in daily diet for prevention and treatment is described. Cultural beliefs, experiences and availability of various herbs in India has made herbal preparations a part of Indian daily food supplements. The use of functional foods and nutraceuticals can be traced back to ancient Indian system of medicine Ayurveda, a 5000-year-old medical science. The classic texts of Ayurveda are full of references of the effects of food in various health conditions. Ayurveda clearly defines the use of food products for improving quality of life and general rejuvenation. Long before there were vitamins, minerals and antioxidant supplements, there was Chyawanprash (Cha-van-prash). One of the most respected anti-aging tonics used in Ayurveda [31].

Atherosclerosis treatment

According to this study *Emblica officinalis* found to be effective for the reversal dyslipidaemia and intema media thickening and the plaque formation in the aorta in hyper cholesterolaemic rabbit in this study the cholesterol powder (100mg/kg body weight) was administered orally to the white healthy rabbit for four months to induce hypercholesterolaemia and there after amla extract was given into two dose 10 and 20 mg/kg body weight. For four months [32].

Cardio-protective

Numerous preclinical studies with laboratory animals showed that *E. officinalis* has cardioprotective and anticoagulant efficacy and hence could be an effective therapy in delaying and/or preventing various cardio related ailments. This protective action of *E. officinalis* is attributed to the presence of tannoids, specifically emblicanin-A and –B, gallic acid, ellagic acid and corilagin [33]. Oxidized low density lipoprotein-cholesterol is a major factor in the development of atherosclerosis, rather than LDL-cholesterol. In virtue of oxidative stress, antioxidants are considered as effective treatment therapy for atherogenesis. Duan et al. evaluated *in vitro* antiatherogenic potential of *E. officinalis* on human umbilical vein endothelial cells (HUVECs) and rat vascular smooth muscle cells and results showed that the two compounds; corilagin (β-1-*O*galloyl-3,6-(*R*)-hexahydroxydiphenoyl-d-glucose) and its analogue (1,6-di-*O*-galloyl-β-dglucose) from *E. officinalis* were effective by reduction in oxidative stress and inhibiting ox-LDLcholesterol induced vascular smooth muscle proliferation [34].

Anticancer and anti-proliferative

From the age of mythology, plants have been used for the treatment of various ailments including neoplasia. Nowadays, plant-originated natural products constitute a considerable proportion of commercial anticancer drugs [35]. Experimental evidence from different non-clinical and clinical studies has shown potential anticancer activity of plant derived polyphenols. Polyphenols act on multiple pathways including inhibition of oxidative stress, generation of pro-inflammatory molecules, DNA damage and increasing the rate of apoptosis. However, reported effects of polyphenols and flavonoids are controversial due to lack of correlation between *in vitro* effects and *in vivo* evidence. Amalgamation of

chemotherapy and food phytochemicals is considered as one of the efficacious approaches to control cancer. The extract contained 20.55 mg gallic acid equivalent/gm of dry weight of extract. Total reducing power was estimated to be 75.8 mg ascorbic acid equivalent per gram of dry weight of extract. Antioxidant activity was checked by 2,2'-azino-bis (3- ethylbenzthiazoline-6-sulphonic acid (ABTS), 1,1-diphenyl-2-picrylhydrazyl (DPPH) and ferric reducing antioxidant power (FRAP). Trolox Equivalent Antioxidant Capacity (TEAC) was 175.76 mg/gm of dry weight of extract when checked by ABTS assay. Thus, total phenolics, flavanoids, reducing power and the antioxidant properties of amla is very well retained in the ethanolic extract and makes it suitable for a therapeutic use against *H. pylori* infection and gastric ulcer [36].

Antitussive activity

According to the study the antitussive activity of *Emblica officinalis* Gaertn. (*E. officinalis, Fam. Euphorbiaceae*) was tested in conscious cats by mechanical stimulation of the laryngopharyngeal and tracheobronchial mucous areas of airways. The results showed that at a dose of 50 mg/kg body wt. perorally, the cough suppressive effect of *E. officinalis* 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 (NE), frequency of cough (NE/min–1) and the intensity of cough attacks in inspirium (IA+) and expirium (IA–) was more pronounced. These results showed that the cough suppressive activity of *E. officinalis* is dose-dependent. We could also demonstrate that the antitussive activity of *E. officinalis* is less effective than shown by the classical narcotic antitussive drug codeine, but more effective than the non-narcotic antitussive agent dropropizine. It is supposed that the antitussive activity of the dry extract of *Emblica officinalis* is due not only to antiphlogistic, antispasmolytic and antioxidant efficacy effects, but also to its effect on mucus secretion in the airways [37].

Anti-venom

As per this study concern the methanolic root extracts of *Vitex negundo* Linn. and *Emblica officinalis* Gaertn. were explored for the first time for antisnake venom activity. The plant (*V. negundo* and *E. officinalis*) extracts significantly antagonized the *Vipera russellii* and *Naja kaouthia* venom induced lethal activity both in in vitro and in vivo studies. *V. russellii* venom-induced haemorrhage, coagulant, defibrinogenating and inflammatory activity was significantly neutralized by both plant extracts. No precipitating bands were observed between the plant extract and snake venom. The above observations confirmed that the plant extracts possess potent snake venom neutralizing capacity and need further investigation [38].

Anti-mutagenic

Many researchers mapped out different secondary metabolites, for instance, phenolates, glycosides, flavonoids and terpenoids etc. that have anti-mutagenic property. Jose et al. found that aqueous extract of *E. officinalis* was found to inhibit 20-methylcholanthrene-induced sarcoma and to inhibit activation and

mutagenicity of 2-acetamidofluorene. Direct mutagenicity of *N*methyl-*N*-nitro-*N*-nitroso guanidine and 4-nitro-*O*-phenylenediamine (NDP) was also found to be inhibited. The anti-mutagenic activity was credited to its potency to inhibit phase-I enzymes and free radical scavenging properties [39]. Haque et al. has established the protective role of *E. officinalis* against cyclophosphamide-induced mutagenicity in mice.

Different extracts of *Triphala*, an ayurvedic proprietary formulation having *E. officinalis* in significant amounts, were investigated for anti-mutagenic potential by using Ames histidine reversal assay having TA98 and TA100 tester strains of *salmonella typhimurium* against direct acting mutagens, NDP and sodium azide, and indirect acting pro-mutagen, 2-aminofluorene, in the presence of phenobarbitone-induced rat hepatic S9 liver homogenate fraction. Results revealed that treatment with *E. officinalis* can inhibit mutagenicity induced by direct and indirect mutagens. In 2015, Tenzin and its colleagues found that treatment with *Yukyunk* Karne, a traditional Tibetan medicine which contains *E. officinalis* as one of the active ingredients, showed significant anti-metastatic activity in ovarian cancer cell line SKOV6. Recently, Thakur and Rao have evaluated *in vitro* Geno protective activity of *E. officinalis* extract in a dose of 20 µg against fluoride (17, 34 and 51 µM) on human blood lymphocytes. Cells treated with extract of *E. officinalis* showed significant reduction in genotoxic indices through reduction in sister chromatid exchanges (SCEs), and regulation of cell cycle proliferation. The Geno protective efficacy of *E. officinalis wa*s accredited to its strong antioxidant and free radical scavenging potential with EC50 value of 55.44 and 17 µg/ml respectively [40].

Conclusion

Research in traditional plants has added an additional focus due to unsolicited adverse effects of the other medicinal systems which may lead to serious complications. All over the world, plant derived drugs are extensively utilized as a nutraceutical for primary health care. Many of our current drugs like atropine, scopolamine, quinine, morphine and many more are acquired either directly or indirectly from medicinal plants. Clinical study on plant-derived novel chemical entities i.e. vincristine, etoposides and camptothecins have revealed potential anticancer efficacy leading to their worldwide usage. In the current review, efforts were made to summarize all the therapeutic aspects of *Emblica officinalis* based on published reports. It realize that many diseases occur due to the imbalance between the prooxidants and antioxidants homeostasis phenomena in the body and amla balance these because of its antioxidant activity *Emblica officinalis* also reduce the side effect of chemotherapy and radiotherapy with all these potential amla may prove a miracle drug in the field of pharmaceutical sciences. so serious attempts should be taken for proper identification of chemical constituents present in the amla. So that its therapeutic properties should come in focus which are still unknown.

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