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RESEARCH ARTICLE

A review of the antidiabetic, antihyperlipidemic, and related metabolic disorder documented activities of Emblic fruits (*Phyllanthus emblica* L.)

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ABSTRACT

Diabetes is a risky metabolic chronic sickness that threatens the lives and health of individuals, families, and communities everywhere. Management of diabetes and related metabolic syndrome (MS) relies heavily on diet. There are reports of folk plants showing varying levels of antihyperglycemic activity. *Phyllanthus emblica* Linn (syn. *Emblica officinalis*) (often referred to Emblic, Indian gooseberry, or amla) is a perennial tree in the Euphorbiaceae family. Due to the high concentration of phenolic compounds, Emblic fruit may be considered a plant source of natural antioxidants. Numerous studies have demonstrated Emblic fruit's benefits on humans and animals that are antihyperglycemic, anti-inflammatory, antihyperlipidemic, antibacterial, analgesic and antipyretic, adaptogenic, hepatoprotective, anticancer, antiulcerogenic, and antioxidant. This review provided an overview of the published scientific studies (experimental and clinical) that documented the potential antidiabetic and antihyperlipidemic benefits associated with consuming Emblic fruits. In addition, the possible activity regarding related metabolic syndrome and diabetes complications was assessed.

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INTRODUCTION

Over 8,000 plant species have been used medicinally worldwide, *Phyllanthus emblica* Linn (syn. *Emblica officinalis*) (often referred to asEmblic, amla, or Indian gooseberry) is a perennial tree in the Euphorbiaceae family. Emblic fruits are edible and are mainly distributed in India, Pakistan, China, Iran, and Southeast Asia.[2,3] Dry Emblic fruit is an important source of carbohydrates, containing over 70 g per 100 g. In addition to protein, minerals, and fat (ranging from 2.0-4.5, 2.1-3.1, and 0.2-0.6 g/100 g dry weight, respectively). Fiber is also an important component (7.2-16.5 g /100g).[4-6] Emblic fruits is rich source of vitamin C than any other fruits as lime, pomergranate, and apple, ranging from (193-720 mg/100g) therefore, 2-3 pieces of fresh amlafruits (100g) covered the vitamin C daily recommended requirements.[7,8] In addition, Emblic contains relevant other nutrients including calcium and iron (25 mg and 1 mg/ 100g, respectively), also thiamin and tocopherols vitamin (30 and 0.17 mg/100g, respectively).[6]

Emblic reported having abundant phytoconstituents that are dispersed throughout the plant (fruits, leaves, and roots). The primary class of secondary metabolites is polyphenols, many of which are phenolic acids, flavonoids, tannins, other phenolics, and analogs. Concerning the phenolic acids, the fresh fruit was found to contain the following hydroxybenzoic acids: 4-hydroxybenzoic acid, coumaric acid, gallic acid (GA), protocatechuic acid, syringic acid, and vanillic acid [9-13], Besides Emblic fruits were found to have hydroxycinnamic acids (caffeic acid and chlorogenic acid). [9,11,13] The only hydroxybenzoic acid found in leaves and branches is GA.[13] Flavonoids are a different class of chemicals found in the Emblic plant. Fruits, leaves, branches, and shoots contain flavonols (kaempferol, quercetin, and their derivatives).[11,14,15] The fresh fruits contained apigenin, luteolin, and myricetin in terms of flavones.[10,11] Only leaves and branches were found to have flavanones and flavan-3-ols. Eriodictyol, naringenin, and their derivatives were the flavanones that were detected. Epicagallocatechin, epigallocatechin 3-O-gallate, and gallocatechin were the flavan-3-ols that were discovered[3]

Another significant class of phenolic chemicals in Emblic fruits, leaves, and branches are tannins, including ellagitannins, ellagic acid and its derivatives, hydrolyzable tannins, and tannic acid.[14,16-18]

Emblic fruit could be viewed as a plant source of natural antioxidants and therapeutic components because of the high concentration of phenolic compounds in the fruit. In several studies, Emblic fruit has shown antihyperglycemic, anti-inflammatory, antihyperlipidemic, antimicrobial, analgesic and antipyretic, adaptogenic, hepatoprotective, antitumor, antiulcerogenic, and antioxidant effects in humans and animals.[19,20]

Diabetes is a dangerous metabolic chronic disease that poses significant risks to the lives and health of individuals, families, and communities everywhere. It is one of the top 10 factors estimated to have caused 4 million adult deaths in the world in 2017.[21]. By 2030, there will likely be 643 million diabetics globally, up from an estimated 537 million in 2021.[20] The International Diabetes Federation (IDF) estimates that 18.3% of adults in Saudi Arabia currently have adult diabetes. The IDF ranked Saudi Arabia as having the 7th increased number of newly-diagnosed cases of type 1 diabetes each year.[22] In the rate of diabetes Saudi Arabia ranks the 2nd highest in the Middle East and the 7th golobaly.[23] Approximately 13% of Saudis have type 2 diabetes (Type2D), contrasted with a worldwide prevalence of 2.8% to 4.4%. One in ten of the country's remaining residents is at risk of getting the disease (prediabetes) [24] The management of diabetes and its associated metabolic problems heavily relies on diet. There have been reports of folklore plants having variable levels of antihyper- glycemic action. These actions appear to be achieved by augmented insulin production by pancreatic -cells, preventing dietary glucose absorption, or by insulin-sensitizing effect. Emblic fruits have been shown to have antihyperglycemic effects in numerous clinical and non-clinical trials [1]

This review aimed to provide an overview of the published scientific studies (experimental and clinical) that documented the potential antidiabetic and antihyperlipidemic benefits associated with the consumption of Emblic fruits. In addition, the possible activity regarding related metabolic syndrome and diabetes complications will be assessed.

Experimental studies documented Emblic fruits' activity against diabetes and its complications

Since starch is hydrolyzed into glucose by the digestive enzymes α-amylase and mucosal α-glucosidase, blocking these enzymes is regarded as a critical therapy option for hyperglycemia. A newly published study attempted to quantify the phytochemicals, total phenolic and flavonoid contents (TPC and TFC, respectively), antioxidant capacity, and enzyme inhibitory activity of Emblic fruit extract in relation to mucosal α-glucosidase and α-amylase. Higher TPC and TFC concentration were found in the ethyl acetate extract. The Embelic ethyl acetate extract showed a strong antioxidant effect (IC_{50} 11.98 ± 0.36 g/ml). As a result, Emblic's secondary metabolites can be used as potent digestive enzymeantagonists.[25]

The therapeutic plants might operate as organic substitutes for synthetic antidiabetic drugs like dipeptidyl peptidase-4 (DPP-4) inhibitors, frequently recommended in clinics. The purpose of the Mohanty et al. investigation was to confirm Emblic's antidiabetic benefits in the streptozotocin (STZ) diabetes model and to clarify the mechanism of DPP-4 suppression. DPP-4 can be inhibited by Emblic, which also has antidiabetic effects in an animal form of diabetes mellitus. Using an in silico analysis compared to vildagliptin, a synthetic DPP-4 antagonist, the binding locations and affinities of the active ingredients in Emblic (pyrogallol, beta-glucogallin, and GA) responsible for inhibiting the DPP-4 enzyme were discovered. Emblic's DPP-4 inhibiting effect causes them to have an antidiabetic impact. In docking studies, beta-glucogallin was reported to have a stronger inhibitory activity on DPP-4 than vildagliptin.[26]

Another recently published study Variya et al. [27] examined the antidiabetic efficacy of Emblic fruit juice and its active component, GA, in 3T3-L1 preadipocytes (an *in vitro* model) and numerous animal models, including db/db mice and rats given fructose (*in vivo* models). Their findings showed that administration of Emblic fruit juice and GA increased insulin sensitivity, improved glucose tolerance, decreased overweight, controlled hypertension, reduced TC levels, and stimulated adipogenesis in 3T3-L1 adipocytes. Through the activation of C/EBPs, the intervention boosted PPAR-γ expression while also accelerating Glut4 translocation in 3T3-L1 adipocytes. Additionally, GA administration enhanced insulin sensitivity *via* activating the Akt signaling route instead of the AMPK signaling pathway, whereas Emblic fruit juice displayed simultaneous Akt and AMPK stimulation.

Majeed et al.28 examined the antidiabetic and antioxidant properties of a standardized Emblic fruit extract containing hydrolyzable tannins and 100 g/kg β-glucogallin. With the use of yeast and starch α-glucosidase, the effect of Emblic fruit extract on inhibiting pancreatic and salivary α-amylase enzymes was investigated. The substrate used was 4-nitrophenyl α-D-glu- copyranoside. Additionally, the radical scavenging action of Emblic fruit extract was tested against 2,2-diphenyl-1-picryl- hydrazyl radical. With IC50 values of 135.70 g/ml and 106.70 g/ml, respectively, Emblic fruit extract significantly lowered the functions of α-amylase in the pancreas and saliva in a dose-dependent pattern. Additionally, it demonstrated suppression of the enzyme action of α-glucosidase (IC50 562.9 g/ml) and DPP-4 (IC50 3770 g/ml). The effects elicited could be linked to the fruit extract's phytoconstituents. The fruit extract is a powerful antioxidant that exhibits free radical scavenging ability (IC50 2.37 g/ml) and protects against cellular reactive oxygen species (ROS) (IC50 1.77 g/ml).

The results of Singh et al.[29] study revealed a preventive effect of Emblic on arsenic-induced type2D in mice. In mice, long-term consumption of arsenic (3 mg/kg/day for 30 days) modified glucose homeostasis and dramatically decreased hepatic glucose regulatory enzymes. Besides balancing blood glucose and hepatic carbohydrate regulatory enzymes

(glucokinase 68%, glucose-6 phosphate dehydrogenase 37%, and malic enzyme 45%), co-consumption of arsenic and Emblic (500 mg/kg/day for 30 days) also significantly reduced blood ion levels (lactate 20%, Na+ 4.6%, Cl- 6.7%, and anion gap 5.2%), pancreas inflammatory marker (interleukin-1beta (IL-1ß) 31% and TNF-α 24%). Emblic consumption significantly increased serum insulin (57%) and c-peptide (31%) in arsenic-treated mice.

Insulin production from pancreatic beta-cells is hampered by glucolipotocixity's induction of IL-1ß secretion. An excellent source of ellagic acid (Ell) is Emblic. Under glucolipotoxic circumstances, the effects of Ell and Ell-rich emblic extract on inflammation were studied *in vitro*. Rat NIT-1 cells were cultured in circumstances that were glucolipotoxic (33.3 mM glucose, 250 mM palmitic acid, or 33.3 mM glucose + 250 mM palmitic acid) with Ell or Ell-rich Emblic extracts that were standardized to their Ell concentration. ELISA study of insulin and IL-1ß production revealed the presence of inflammation. Better than pure Ell, Emblic extract rich in Ell increased insulin release dose-dependently and negatively regulated IL-1ß.[30]

In another study, 24 healthy Swiss Albino rats were used to compare the hypoglycemic effects of 500 mg/kg ethanolic extract of Emblic fruit to the antidiabetic glibenclamide in alloxan-produced hyperglycemia. Serum glucose concentrations in the study's normal control rats were 5.18 ± 0.14 mmol/L on average, while serum glucose levels in the alloxan-treated group were 12.35 ± 0.42 mmol/L. At the same time, the serum glucose levels in the ethanolic extract-treated and glibenclamide-treated rats were 7.7 ± 0.18 mmol/L and 6.4 ± 0.30 mmol/L, respectively. The 500 mg doses of the ethanolic extract of Emblic fruits' ability to reduce glucose levels are approximately as effective as glibenclamide.[31]

Pramod et al.[32] study examined the antidiabetic and antitoxic properties of Emblic fruit extract on mice that had been made diabetic by injecting STZ (100 mg/kg). Control (n=6), STZ (n=12) divided to diabetic and diabetic trated with Emblic, and Emblic group (n=6, aqueous fruit extract, four weeks) were the three groups of the study. The group of diabetic treated with Emblic fruits had a considerable drop in serum glucose, indicating antidiabetic activity. Emblic significantly reduced urea, uric acid, and creatinine levels, suggesting that it has a nephroprotective effect.

According to Musman et al. study, phenolic extract from Emblic flesh can lower blood glucose levels in diabetic-induced rats. Glucose-induced rats received Emblic phenol extract for 14 days. In diabetic rats, the phenolic extract at 100 and 200 mg/kg doses decreased blood glucose levels. The post hoc Dunnet test revealed that giving the extract to the rats at a concentration of 100 mg/kg caused a remarkable drop in blood sugar levels and produced greater cell repair than giving them the extract at a 200 mg/kg dose. According to the data, the phenolic extract of Emblic flesh can be used to treat type2D without harming other tissues [33].

In a different study, hyperglycemic rats injected with alloxan were used to test the aqueous extract of the Emblic fruit for its ability to reduce blood sugar levels. Two dosages of the aqueous extract (250 and 500 mg/kg each) were given orally daily for four weeks. Estimates of the fasting blood glucose levels were collected every week. In non-diabetic rats, an aqueous extract of the Emblic fruit had no blood glucose-reducing effect. But diabetic rats treated with an aqueous extract of the Emblic fruit compared to diabetes control, there was a significant decline in blood glucose levels ($p<0.001$). Similar outcomes were observed when compared to glibenclamide at a dose of 5 mg/kg. In diabetic rats, an aqueous extract of 500 mg/kg results in the most significant reduction in glucose levels [34].

A study established the efficacy of Emblic fruit extract in lowering blood glucose concentration in balb/c mice given alloxan as an inducer. Compared to the treatment group, Emblic fruit extract at a dose of 40 mg/20 g BW was similar to the positive control of glibenclamide at a dose of 3 mg/20 g BW. According to the results of this study, the optimal dose of Emblic fruit extract for lowering blood sugar was 40 mg/20 mg BW, which resulted in a 56.93% reduction in the blood glucose level and an effective dose (ED_{50}) of 34.00 mg/20 g BW[35]

Emblic extract was the subject of an *in vivo* experiment to investigate its antioxidant and antidiabetic properties and an HPLC assay to ascertain their active components. Emblic fruit aqueous extract contains tannins, saponins, quinones, phenols, carbohydrates, and glycosides. TPC concentrations in the aqueous extract of Emblic fruits were determined to be 315.6 mgGAE/g. The extract's *in vivo* antioxidant, and antidiabetic properties were tested on 42 diabetic rats over 21 days. Data indicated that the aqueous extract of Emblic fruits had potent antioxidant and antidiabetic properties. The percentages of inhibition displayed by the aqueous extract of Emblic fruits in the 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay were reported to be 97.8%.[36]

A study examined Emblic *in vitro* and *in vivo* antidiabetic effects and its active ingredient, Ell. For four weeks, a methanolic extract of Emblic (250 and 500 mg/kg) was administered to newborn STZ-induced type 2D rats. A concentration- and time-dependent reduction in fasting blood sugar was observed after dosing with Emblic extract. It dose-dependently elevated serum insulin. Treatment with Emblic also resulted in a rise in the insulin-to-glucose proportion. Pancreatic immunostaining revealed that whereas Emblic 500 increased beta-cells' frequency, Emblic 250 increased beta-cells' size. Emblic markedly enhanced plasma total antioxidants, hepatic reduced glutathione (GSH), and thiobarbituric acid reactive substance (TBARS). Ell increased isolated islet insulin production in response to glucose and reduced diabetic rats' glucose intolerance.[37]

In STZ (35mg/kg)-induced diabetic rats, Pathak et al.[38] observed that commercial products extract of Emblic has considerable antidiabetic action. From the fourth week on, Emblic's smaller dose (200 mg/kg/day) and large dose (400 mg/kg/day) significantly reduced blood sugar levels ($p<0.01$) (duration of study 6 weeks) relative to the diabetic rats.

Nishamalaki (NISH) is a 1:1 (w/w) combination of the dried fruits of Emblic and the powdered rhizome of Curcuma longa (turmeric). NISH has similar antidiabetic potency to glyburide in rats and provides superior antioxidant defense. NISH powder (0.9 g/kg) was given to one group of STZ-induced diabetic rats, and glyburide (4 mg/kg) was given to another group for 30 days. Compared to glyburide, NISH therapy significantly reduced plasma glucose and HbA1c in diabetic animals ($p<0.001$). Both medicines similarly decreased erythrocyte membrane LPO ($p<0.001$). Erythrocyte GSH and glutathione peroxidase (GSH-Px) activity improved more in NISH-treated rats than in glyburide-treated rats ($p<0.001$).[39]

In a high fructose diet (HFD)-induced rat model of insulin resistance, Prativadibhayankaram et al. examined the potential antidiabetic activities of fruit extracts from the Emblic. The animals received a HFD for 40 days, with fruit extract added for the final 20 days. Normalization of fasting blood sugar levels was achieved by Emblic consumption.[40]

Experimental studies documented Emblic fruits' activity against hyperlipidemia

In comparison to gliclazide, Arbaeen and Abdelaziz [41] examined the hypo-glycemic and hypo-lipidemic capabilities of an aqueous extract of Emblic pulp in STZ (40 mg/kg)-induced type 2 diabetes (Type2D) in male Wister rats (150–180g). The rats were divided into 5 groups (n=8) following the establishment of Type2D: non-diabetic, Type2D, Type2D + gliclazide (10 mg/kg), Type2D + Emblic pulp extract low dose (200 mg/kg), and Type2D + Emblic pulp extract high dose (400 mg/kg). Therapy of Type2D rats with both dosages of Emblic fruit extract significantly ($p<0.001$) decreased the raised concentrations of blood glucose, HbA1c, serum insulin, total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL), and HOMA-IR. The two doses led to a notable decrease in malondialdehyde (MDA) levels and GSH. In contrast to the gliclazide-treated group, both Emblic fruit extract doses significantly reduced ($p<0.05$) serum levels of insulin, TC, TG, LDL, and MDA. However, there was a significant increase ($p<0.01$) in serum GSH concentration.

The results of Variya et al. [42] research revealed that GA, the promising principle constituent of Emblic, might be a prospective medication for controlling hyperlipidemia. Rats were given elevated fat food, Tyloxapol, and Poloxamer-407 to induce dyslipidemia. GA and Emblic fruit juice treatment reduced hepatic and aortic fat infiltration and plasma TC. In terms of mechanism, Emblic lowered the function of liver lipogenic enzymes (glucose-6-phosphate dehydrogenase, fatty acid synthase, and malic enzyme) and upregulation of peroxisome proliferator-activated receptors gamma (PPARγ) and lipid oxidation (LPO) through carnitine palmitoyl transferase. Emblic also boosted TC absorption by increasing the expression of LDL receptors on hepatocytes and reduced LDL receptor destruction by reducing the expression of proprotein convertase subtilisin/Kexin type 9. The concurrent restoration of glucose homeostasis by Emblic extract was demonstrated by enhanced adipose tissue expression of the proteins Glut4 and PPARγ.

People with obesity and insulin resistance have higher levels of methylglyoxal in their bodies. Methylglyoxal promotes oxidative stress, glycation, and inflammatory responses that are directly related to insulin resistance. One study examined how Emblic fruit water extract and its concentrated component, Ell, affected 3T3-L1 cellular responses to methylglyox- al-induced inflammation, insulin resistance, and adipogenesis. Methylglyoxal induced CCAAT/enhancer-binding protein alpha (C/EBPα) and PPARγ, which may promote adipogenesis in adipocytes. Furthermore, methylglyoxal enhanced the production of the proinflammatory cytokine IL-6 by activating NF-kB and MAPK. It also enhanced monocyte chemoattractant protein 1 expression and caused macrophage infiltration. Methylglyoxal dramatically decreased glucose absorption, suggesting a possible connection between methylglyoxal production and insulin resistance in obese people. By blocking the JNK and NF-kB p65 pathways, Emblic extract and Ell successfully reduced IL-6 protein expression. Emblic extract and Ell significantly enhanced glucose uptake and decreased insulin resistance. Emblic extract also suppressed MG-induced fat deposition proteins such as PPARγ and C/EBPα and lowered protein-tyrosine phosphatase 1B to improve insulin sensitivity.[43]

The characteristics of diabetes have been linked to long-term intake of arsenic via drinking water as well as environmental exposures. Administration with Emblic has been shown to guard against arsenic-induced elevated oxidative stress, inflammatory processes, hyperlipidemia, and liver toxicity in mice. The findings of Singh et al. [44] study support the idea that Emblic, a herbal extract, may reduce the detrimental effects of arsenic on lipid profiles. Co-administration of Emblic (500 mg/kg) and arsenic (3 mg/kg) for one month resulted in significantly improved serum TC (0.83-fold), TG (0.92-fold), LDL (0.72-fold), and phospholipid (1.29-fold) levels, as well as higher levels of high-density lipoprotein (HDL) (1.4-fold).

A study investigated the antihyperglycemic activity of formula made from Emblic's spray-dried powder of fruit juice on a rat model of type1D produced by STZ (45 mg/kg i.v.). The spray of Emblic was consumed orally (100 mg/kg) for a period of 4 weeks. The Emblic spray formula significantly improved glucose and lipid dysfunction (significant drop in serum glucose, AUC glucose, TG, TC, LDL, and very low-density lipoprotein (VLDL)). It effectively alleviated oxidative stress (reduced MDA level and enhanced antioxidant enzyme activity). Increased peripheral glucose absorption, decreased insulin resistance, or the formula's antioxidant effects could all contribute to Emblic's antidiabetic outcomes.[45]

According to Elobeid and Ahmed[46] research, Emblic aqueous extract has superior antidiabetic efficacy to metformin. Their study compared the antidiabetic properties of metformin (600 mg/kg) with the aqueous fruit extract of Emblic (400 and 200 mg/kg) in STZ-induced diabetes in obese rats. After 5 and 6 weeks, the blood sugar of both plant extract-treated groups was significantly ($p<0.001$) lower than those of the metformin-administered rats. After 4, 5, and 6 weeks, there was a significant rise in body weight. This was more pronounced in the extract-treated group. Additionally, both extract doses significantly ($p<0.05$) decreased sugar levels, TC, and TG in a manner comparable to the metformin-treated rats.

The Emblic fruit pulp's aqueous extract exhibits potential antidiabetic and antioxidant properties. Oral administration of an aqueous extract of Emblic for four weeks to type2D rats

resulted in a significant ($p<0.01$) decrease in fasting blood glucose levels compared to baseline. TG dropped by 14%, but GSH content increased significantly ($p<0.05$).[47]

Emblic fruit hydroalcoholic extract was tested in a previously released study to determine how it affected type1D animals. STZ (45 mg/kg i.v.) induced experimental diabetes. For 28 days, Emblic fruit extract (100 mg/kg, p.o.) was given. Treatment with Emblic fruit extract reduced fasting serum glucose, $AUC_{glucose}$, TC, TG, LDL, and VLDL significantly. The extract also decreased lipid peroxidation and enhanced antioxidant characteristics in the hepatic homogenates of hyperglycemic rats. The portion of extract that was polyphenol-enriched significantly enhanced the dysfunctional lipid and carbohydrate metabolism. Its ability to promote cellular glucose utilization, raise insulin sensitivity, or have antioxidant activities is believed to be the mechanism underlying its antihyperglycemic and antihyperlipidemic effects [48].

According to findings from an earlier study, Emblic possesses antidiabetic properties and improves lipid profiles. Administration of Emblic fruit ethanolic extract (200 mg/kg) for 45 days led to a significantly lower blood glucose level and a significantly higher plasma insulin level in diabetic rats that had been induced with STZ (40 mg/kg). When given Emblic extract, diabetic rats had a significant decrease in TC, VLDL, LDL, free fatty acids (FFA), PL, and TG, as well as an increase in HDL.[49]

The impact of Emblic's aqueous fruit extract on type2D, TG, and the liver enzyme alanine transaminase (ALT) was investigated. After being administered i.p. to type2D rats (alloxan-induced), the fruit extract (200 mg/kg) significantly lowered blood glucose levels ($p<0.05$). Chlorpropamide (84 mg/kg) likewise caused a nearly same decline in glucose level. The extract also reduced TG levels in alloxan-induced rats at 0, 1, 2, and 4 hours ($p<0.05$). Additionally, it was observed that the extract normalized ALT level.[50]

Experimental studies documented Emblic fruits' activity against metabolic syndrome (MS)

The impact of Emblic ethyl acetate extract (a polyphe- nol-wealthy fraction, at 10 or 20 mg/kg/day for 2 weeks) on an excessive fructose diet (65%) (EFD)-triggered MS was investigated in rats. The Emblic extract ameliorated the EFD-triggered MS, inclusive of TG and TC. Also, hepatic triacylglycerol and TC had been drastically decreased (33.8% and 24.6 %, respectively; $p<0{\cdot}001$). Emblic extract (20 mg/kg) regulated the sterol regulatory element-binding protein (SREBP)-1 expression. In addition, Emblic extract (20 mg/kg) drastically inhibited serum and hepatic TBARS (21.1% and 43.1 %, respectively; $p<0{\cdot}001$). Furthermore, the Emblic extract inhibited the cyclo-oxygenase-2 with the regulation of NF-kB and bcl-2 proteins in the liver. It also drastically lowered the expression of bax at both doses.[51]

A study investigated the effects of ellagic acid (Ell) against MS induced by high-fat, high carbohydrat diet in rats. Rats divided into control, Ell, MS, MS+Ell. Ell and MS+Ell were given Ell (0.8g/kg diet) from the 8th to the 16th week. MS developed impairments in ventricular function, glucose tolerance, cardiovascular remodelling, with decreased proyein levels of CPT1 and Nrf2 and increased protein levels of NF-κB in the liver and the heart. In MS+Ell treated rats, Ell attenuated MS symptoms by suppressing inflammation and oxidative stress with normallised of protein levels of CPT1, Nrf2, and NF-κB.[52]

Another study compared the effects of gallic acid (GA) (20 mg/kg) and metformin (100 mg/kg) in MS rats fed high fructose diet (HFD) for 18 weeks. The GA and metformin were performed the last 4 weeks. Both GA and metformin normalized glucose tolerance, serum insulin, HOMA-IR score, blood pressure, plasma lipid and cholesterol levels.[53]

Clinical studies documented Emblic fruits' activity against hyperglycemia, hyperlipidemia, and MS

In a recent study by Kapoor et al.,[54] Emblic's preventative therapeutic properties and toxicity were investigated. Fifteen healthy adult volunteers were randomly assigned to receive either Emblic or a placebo (500 mg/day) for a period of 18 weeks. The Emblic intake showed significant improvements in the parameter of blood fluidity. Along with a considerable increase in HDL and a decrease in LDL, a reduction in von Willebrand factor, reduced 8-hydroxy-2′-deoxyguanosine, and thrombin, biomarkers of oxidative stress. After consuming Emblic, there were no discernible changes in hematological, urinalysis, or liver hepatotoxicity.

Another study examined the effectiveness of Emblic extract in treating individuals with hyperlipidemia. This extract has polyphenols, triterpenoids, and other compounds found in raw Emblic fruit. Ninety-eight hyperlipidemic individuals were included and split into the Emblic and placebo groups. 500 mg of the Emblic extract was given two times every day for 3 months. The patients were monitored for three months, and lipid profiles were tested to decide efficacy. The essential lipids consisting of TC, TG, LDL, and VLDL were significantly lowered in the Emblic group in comparison to the placebo group after 3 months ($p<0.001$). Furthermore, the Emblic group also showed a 39% decrease in plasma's atherogenic index ($p<0.05$) compared to the placebo group. The findings suggested that the Emblic extract utilized in the study may also have hypoglycaemic properties. Although there was a general trend toward lower FBS, only eight persons in the Emblic group could be categorized as belonging to the prediabetes and diabetes groups (FBS > 100 mg/dl)[55]

Fifty-nine patients (both sex) with endothelial dysfunction (ED) and MS and ages 30 to 68 were included. Capros 250 mg and 500 mg were the prescribed dosages. An aqueous extract of the Emblic fruit, containing emblicanin A, emblicanin B, pedunculagin, and punigluconin, was included in each Capros capsule. This extract was standardized to include not less than 60% of low-molecular-weight hydrolyzable tannins. One Capros (either 250 mg or 500 mg), or one placebo capsule were given to each study population at random to consume two times daily for a period of 3 months. The reflection index (RI), a predictor of ED, was calculated at each visit. Patients will be evaluated at baseline and after three months to assess lipids, hepatic and renal function markers, serum levels of the oxidative stress indicators nitric oxide (NO), MDA, GSH, and the proinflammatory mediator high-sensitivity C-reactive protein. Compared to baseline, the RIs of the two Capros groups at weeks 8 and 12 were significantly lower, indicating better endothelial

function ($p<0.001$). Compared to the Capros 250 mg group, the improvement was significantly better in the Capros 500 mg group ($p<0.05$). Reduction in oxidative stress and inflammatory markers were observed in both Capros groups at three months compared to baseline ($p<0.001$ values), with the Capros 500 mg group showing significantly more significant decreases than the Capros 250 mg group. Patients in the two Capros groups experienced significant reductions in blood lipids, with the Capros 500 mg group experiencing more significant decreases in TC ($p<0.05$), LDL ($p<0.001$), and TG levels ($p<0.01$) than the Capros 250 mg group.[56]

The glycemic and lipidemic profiles of the persons with Typ2D were improved by Emblic powder supplementation. This was confirmed in a study examining Emblic powder's effects on Type2D patients' blood glucose, HbA1c, lipid profiles, and hemoglobin (Hb) levels. 90 male and female patients with Typ2D were split into experimental and control groups (60 and 30, respectively). For 3 months, 10 g of Emblic powder each day was given to the test group. At baseline and three months later, all study parameters were evaluated. In comparison to the control group, the mean values for fasting, postprandial sugar levels, HbA1c, and serum lipids in the experimental group reduced significantly, while mean Hb levels increased.[19]

The effects of Emblic on type 2 diabetes were investigated in 60 type2D participants. The subjects were split into 2 equal groups: the intervention group and the control group. For six months, the intervention group administered a medium-sized fresh Emblic fruit (about 35 g) daily. They were instructed to eat the fruit every morning before breakfast. No dietary or pharmaceutical changes were made for the intervention and control groups. The biochemical markers FBS, postprandial blood sugar, HbA1c, and lipid profile were evaluated along with the anthropometric data. One medium-sized Emblic daily for six months caused a substantial decline in the intervention group›s FBS, postprandial blood sugar, HbA1c, and lipid profile values relative to control subjects.[57]

Patients with type 2 diabetes mellitus received atorvastatin 10 mg once daily, Emblic 250 mg twice daily, or Emblic 500 mg twice daily for 12 weeks. At the start of the experiment and twelve weeks later, laboratory parameters were assessed. Eighty patients finished the trial. After 12 weeks of treatment, atorvastatin 10 mg, Emblic 250 mg, or Emblica 500 mg significantly improved endothelial function relative to baseline. Compared to baseline and control, there was a significant reduction in oxidative stress and systemic inflammation indicators. In addition, compared to baseline and control, the therapies dramatically reduced HbA1c concentrations and improved dyslipidemia.[58]

In a previous study, the effectiveness of Emblic was assessed in people with type II dyslipidemia (T2Dys), and its hypolipidemic impact was compared to that of simvastatin. The study comprised 60 T2Dys patients of both sexes with plasma TC and LDL levels greater than 240 mg% and 130 mg%, respectively. Twenty patients received simvastatin (20 mg) capsules daily, while 40 individuals received Emblic (500 mg) capsules daily. Throughout the trial period (42-days), every patient received two follow-up visits. Therapy with Emblic resulted in statistically significant decreases in TC and LDL ($p<0.0001$), TG and VLDL ($p<0.0002$), and a statistically significant increase in HDL levels ($p<0.001$) [59].

In a study, healthy and diabetic volunteers were given Emblic fruit powder to assess its ability to lower blood sugar and lipids. The results showed that persons who received 1, 2, or 3 g of Emblic powder per day, whether they were normal or diabetic, experienced a substantial reduction ($p<0.05$) in fasting and 2-hour postprandial sugar levels after three weeks. Furthermore, post receiving either 2 or 3 g of Emblic powder/day, significant drops in TC and TG were also seen in both normal and diabetic individuals. TC levels did, however, significantly ($p<0.05$) decrease in diabetic subjects who had received 3 g of Emblic powder. Receiving 2 or 3 g of Emblic powder, healthy and diabetic individuals saw a significant ($p<0.05$) improvement in HDL and LDL.[60]

Amlamax is a dried extract of Emblic that has been purified and standardized to contain approximately 35% galloellagi tannins and other hydrolyzable tannins. Human participants were tested with two doses of the extract (500 mg and 1000 mg daily for 6 months). Blood tests in the third and sixth months indicated a decrease in total and LDL cholesterol and an increase in healthy HDL. Blood CRP levels, an index of inflammation, were also markedly decreased. These findings must be viewed as positive and show Amlamax's potential for treating heart conditions [61].

CONCLUSION

The current study provided evidence from experimental and clinical studies showing the fruit extract of the Emblic and several of its phytochemicals, including GA, Ell, pyrogallol, and beta-glucogallin, have antihyperglycemic, antihyperlipidemic, and protective actions against MS. Mechanistic research have found that Emblic and some of its phytochemicals enhance glucose uptake, preserve glucose homeostasis, enhance pancreatic insulin production, regenerate and restore pancreatic beta cells, and prevent its apoptosis. They also inhibit gluconeogenesis, combat free radicals and increase antioxidants, enhance adipogenesis, and inhibit the actions of the enzymes -gluco-α-glucosidase, α-amylase, and DPP-4 enzymes. The results of this review may be helpful for Emblic fruit clinical uses in people and may provide a new treatment approach.

Ethical approval

There is no need for ethical approval for this study.

Conflict of interest

There in no conflict of interest between authors

Authorship contributions

The author done this article alone.

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