Impact of *Emblica officinalis*: A Miracle Multipurpose Plants

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Abstract

Plants are a major source of nutrition and health care. *Emblica officinalis* (EO) is one of the most widely used in traditional Indian medicine in different forms and believed to alleviate against several diseases. This article summarizes the multipurpose and medicinal value of EO. I reviewed the application of EO in antioxidant, antidiabetic, anticancer, antiulcer, cardioprotective activity, cytoprotective, antitussive, immunomodualation, chelating agent, and respiratory problems.

Keywords: Antioxidant, Biological effect, *Emblica officinalis*, Pharmacological effect, Therapeutics

Introduction

Background

Plants have always been a major source of nutrition and health care for both humans and animals. The writings on nutritional and medicinal plants go way back to 1500 B.C in Egypt, 800–400 B.C. in Indo-Pakistan, and 500 B.C. in China. However, scientific research interest in medicinal plants received a thrust during the mid-1970s when the World Health Organization proposed the incorporation of traditional medicine into the health-care system.[1] Among the many medicinal plants of research interest, *Emblica officinalis* (EO) is the one.

EO is a plant genus of the family *Euphorbiaceae*. It is also named as amla, *Phyllanthus emblica,* or Indian gooseberry. The species is native to India and also grows in tropical and subtropical regions including Pakistan, Uzbekistan, Sri Lanka, South East Asia, China, and Malaysia and also found in Burma.[2] It is a deciduous tree of small to medium size up to 5.5 m with green-gray or red bark, peeling off scales, and long strips. The fruit is fleshly around 2.24 cm in diameter, 5.68 g in weight. Apart from the fruit, the leaves and bark are a good source of tannin.[3]

The fruit of EO is highly valued in traditional Indian medicine.[4] Thus, the dried fruits of amla are used to treat hemorrhage, diarrhea, and dysentery.[5] In addition, the fruit of EO is diuretic, hepatoprotective,[6,7] and antitumor.[8] Moreover, the fruits have potent antioxidant activity due to the presence of tannoids, tannins, Vitamin C, and flavonoids.[9] The pharmacological studies on EO have revealed that it has good antioxidant, cytoprotective, immunomodulatory, antidiabetic, hypolipidemic, and cardioprotective, antiulcerogenic.[10] EO has been widely consumed by humans for thousands of years, and it was found to be nontoxic to human and experimental animals.[11] No toxicity was observed in the toxicological results of the experimental models in the highest dose range.[12] The plant is very rich with different components [Table 1].

Preparations

The plant is used in many forms. One of the most popular is as a decoction and infusion of leaves and seeds. However, it is also used as liquor, a fixed, and an essential oil. It makes an astringent extract equal to catechu, which is prepared from the root by decoction and evaporation.[2]

Description of the plant

The green fruit is described as being exceedingly acid. The dried fruit is sour and astringent. The

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flowers are cooling and aperients. The bark is astringent.[14] There are two forms of amla, the wild one with smaller fruits and the cultivated form sometimes called "Banarasi" with larger fruits.[3] The plant is widely distributed and habitat in Asia and also used in different forms [Table 2].

Table 1: Average percentage composition of the fruit pulp of *Emblica officinalis*[13]

S. No.	Components	Percentage
1	Moisture	81.2
2	Protein	0.5
3	Fat	0.1
4	Mineral matter	3.4
5	Fiber	0.7
6	Carbohydrate	14.1
7	Calcium	0.05
8	Phosphorous	0.02
9	Iron	1.2 mg/100 g
10	Nicotinic acid	0.2 mg/100 g
11	Vitamin C	600 mg/100 g

Chemical constituents

The fruit is a very rich source of Vitamin C. it is mineral and vitamin contents include calcium, phosphorous, iron, carotene, thiamine, riboflavin, and niacin. The seed of the Indian gooseberry contains a fixed oil, phosphatides, and an essential oil. The fruits bark and the leaves of this tree are rich in tannin.[15]

The root contains ellagic acid and lupeol and bark contains leucodelphinidin. It has the following fatty acids: Linolenic 8.8%, oleic 28.4%, stearic 2.15%, palmitic 3.0%, and myristic 1.0%.[3]

Table 2: General description of *Emblica officinalis*[14]

No.	1. Habitat
1	Found in India, Pakistan, Uzbekistan, Sri Lanka, South East Asia, China, and Malaysia
	2. Used parts
1	Dried fruits, fresh fruit, seed, leaves, root bark, and flowers
	3. Fruits
1 2 3 4 5 6	Ripen from November to February Nearly spherical or globular, wider than long and with a small and slight conic depression on both apexes Fruit is 18–25 mm wide and 15–20 mm long Surface is smooth with six obscure vertical pointed furrow Mesocarp is yellow and endocarp is yellowish-brown in ripened condition In fresh fruit mesocarp is acidulous and in dried fruit, it is acidulous astringent
	4. Leaves
1 2	Leaf is 8–10 mm or more long and 2–3 mm broad, hairless light green outside, pale green, or often pubescent beneath It contains gallic acid, ellagic acid, chebulic acid, chebulinic acid, chebulagic acid, a gallantonic called amlic acid, alkaloids phyllantidine, and phyllantine
	5. Seed
1	Four-six, smooth a fixed oil, phosphatides, and a small quantity of essential oil. The fixed oil yield 16% and has the following physical and chemical characteristics: Acid value 12.7; saponification value 185; iodine value 139.5; acetyl value 2.03; unsaponifiable matter 3.81%; sterol 2.70%; saturated fatty acid 7%. Contains linolenic acid (8.78%), linoleic (44%). oleic (28.40%), stearic (2.15%), palmitic (2.99%), and myristic acid (0.95%)
	6. Barks
1 2	Thick to 12 mm, shining grayish-brown or grayish-green. Leukodelphinidin, tannin, and proanthocyanidin
	7. Roots
1	Ellagic acid and lupeol

Table 3: The biological effect of *Emblica officinalis*

Biological effect	References
Antimicrobial activity	[16]
Antioxidant activity	[7]
Enhancer of natural killer activity	[17]
Anti-inflammatory activity	[18]
Hypolipidemic	[3]

Therapeutic properties of EO

EO is a very rich source of Vitamin C, which is said to be the second-highest among all fruits.[19] The fruit, because of its high acidity and astringent taste, is not palatable for direct consumption but its excellent and therapeutic values offer enormous potentiality for processing.[20] Some of the therapeutic values are [Table 3]:

Antibacterial, antifungal, and antiviral

Medical studies conducted on amla fruit suggested that it has antiviral properties[21] and also functions as an antifungal agent.[22] EO has been reported for the antimicrobial activities.[16] The plant has been reported to possess potent antibacterial activity against *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella* Paratyphi A, *Salmonella* Paratyphi B, and *Serratia marcescens.*[23]

Antioxidant

The origin of disease of multi-factorial nature is being understood due to the vitiation in basic hemostatic balance phenomenon in the body. It is increasingly being realized now that majorities of the disease are mainly to the imbalance between pro-oxidant and anti-oxidant in the body.[10] Pro-oxidant condition dominates either due to increased generation of free radicals and/or their poor scavenging into the body. Free radicals are fundamental to any biochemical process and they are continuously produced by the body's normal use of oxygen such as respiration and some cell-mediated immune functions.[18] Free radicals play an important role in some pathogenesis of serious diseases such as cancer, neurodegenerative disorders, and cataracts; inflammation compounds that can scavenge free radicals have a great potential in ameliorating these disease.[4] It was reported that phenolic compounds in plants possess strong antioxidant activity and may help to protect cells against free radicals.[8]

Antidiabetic effect

Oral administration of the extracts (100 mg/kg body weight) reduced the blood sugar level within 4 h. EO and an enriched fraction of its tannoids are effective in delaying development of diabetic cataract in rats.[24] Aldose reductase (AR) has its involvement in the development of secondary complications of diabetes including cataract. EO is proved as an important inhibitor of AR.[24]

Anticancer activity

EO inhibits the growth and spread of various cancers, including breast, uterus, pancreas, stomach and liver cancers, and malignant ascites. It reduces the side effects of chemotherapy and radiotherapy.[25] EO has been reported to possess many medicinal properties including immune-stimulator and antitumor activities.[8] It enhances natural killer cell activity in various tumors.[26] Chemoprevention with food phytochemicals is presently considered as one of the most important strategies to control cancer.[27]

Antiulcer activities

A herbomineral formulation of the Ayurveda medicine named Pepticare, composed of EO, was tested for its antiulcer and antioxidant activity in rats. Reports were made that Pepticare exhibit antiulcer activity, which can be attributed to its antioxidant property.[28] Methanolic extract of EO was studied against ulcer and its healing effects due to its defensive mucosal factors.[29]

Cardioprotective activity

The effects of chronic oral administration of fresh fruit homogenate of amla on myocardial antioxidant system and oxidative stress induced by ischemic-reperfusion injury (IRI) were investigated on the heart in rats. Chronic EO administration produces myocardial adaptation by augmenting endogenous antioxidants and protects rat hearts from oxidative stress associated with IRI.[30]

Cytoprotective, antitussive, and gastroprotective activity

EO has been reported for its cytoprotective and immunomodulating properties against

chromium (VI) induced oxidative damage. It inhibited chromium induced immunosuppressant by macrophages and phagocytosis.[31]

EO was tested for its antitussive activity in conscious cats by mechanical stimulation of the laryngopharyngeal and tracheobronchial mucous areas of airways.[32] It was then reported that amla extract exhibits antisecretory, cytoprotective, and antiulcer properties.[33]

Immunomodulation activity

Immune activation is an effective as well as protective approach against emerging infectious diseases. Oral administration of Triphala appears to stimulate the neutrophil functions in the immunized rats, and stress-induced suppression in the neutrophil functions was significantly prevented by Triphala.[34] EO fruits have been reported to be used for hepatoprotection in Ayurveda.[35]

Chelating agent

Photoaging of the skin is a complex biologic process affecting various layers of the skin with major changes seen in the connective tissue within the dermis. *Emblica* was shown to reduce ultraviolet-induced erythema and had excellent free-radical scavenging ability, chelating ability to iron, and copper.[15]

Diarrhea

It is used medicinally for the treatment of diarrhea. As a fruit decoction, it is mixed with sour milk and given by the natives in cases of dysentery.[36] The bark partakes of the astringency of the fruit. A decoction and evaporation of the root solution produce an astringent extract equal to catechu.[16] An infusion of the leaves with fenugreek seed is given for chronic diarrhea.[37]

Respiratory problems

The fresh fruit is used inflammations of lungs the expressed juice of the fruit along with other ingredients is used to cure cough, asthma.[37]

Alcohol

The general chemical formula for alcohol is $C_nH_{2n+1}OH$. Alcohol is a psychoactive drug that has a depressant effect. Alcohol is a moderately good solvent for many fatty substances and essential oils. This attribute facilitates the use of flavoring and coloring compounds in alcoholic beverages, especially distilled beverages.[38]

Alcoholism

Alcohol can be addictive, and the state of addiction to alcohol is known as alcoholism. Alcoholism can lead to malnutrition because it can alter digestion and the metabolism of most nutrients. Alcoholism is also associated with a type of dementia called Wernicke-Korsakoff syndrome, which is caused by a deficiency in thiamine (Vitamin B_1). Muscle cramps, nausea, loss of appetite, nerve disorders, and depression are common symptoms of alcoholism.[39]

Effects of alcohol on health

Chronic excessive alcohol consumption is more prevalent all over the world and is associated with tissue and organ damage leading to coronary heart disease, alcohol liver disease, and several other manifestations, including neurological disorders for which therapeutic approaches are sought.[40] Enhanced oxidative stress and decreased antioxidant status induced by ethanol metabolism play a major role in the causation of alcohol toxicity and damage.[41] Chronic alcohol consumption has major effects on the absorption, elimination, and serum concentrations of many physiologically important electrolytes and minerals.[42]

Pathophysiology

Alcohol is metabolized by oxidative reactions to acetaldehyde and then converted to acetate through alcohol dehydrogenase (ADH) and acetaldehyde dehydrogenase (ALDH). ADH is quantitatively the most important enzyme capable of catalyzing the conversion of ethanol to acetaldehyde. Mechanisms implicated in alcohol-induced liver damage involve many biochemical reactions with different simultaneous pathways interacting with each other. These mechanisms involve enzymes, reactive oxygen species (ROS), endotoxins, cytokines, immune system cells, and genetic predisposition to develop alcoholic liver disease.[43]

Clinical Trails

Various studies have been done to examine the protective effects of EO against alcohol-induced oxidative stress. Most of these studies were done on animals using different doses of alcohol and EO. The length of the treatment period of most of the studies was also different in different groups.

In the study undertaken by Damodara Reddy,[44] the role of EO was investigated in the prevention of alcohol-induced hepatic injury. In this study,

2-month-old male albino Wistar rats, weighing about 120–140 g were used. The rats were randomly divided into four groups of eight rats in each group:

- Group I was the control group and received glucose instead of alcohol (i.e., caloric equivalent to alcohol)
- Group II was the alcohol-treated group, which received 20% (v/v) alcohol, at a dose of 5 g/kg body weight/day
- Group III was the alcohol plus EO treated group and was given 20% (v/v) alcohol (at a dose of 5 g/kg body weight/day) plus aqueous EO fruit extract (EFE), at a dose of 250 mg/kg body weight/day
- Group IV – Animals in this group received only the aqueous EFE, at a dose of 250 mg/kg body weight/day and glucose (iso-caloric equivalent to ethanol).

The extract and alcohol were administered daily for 60 days using an intragastric tube. Food and water intake of all the animals was recorded daily, and weight of the rats was measured on alternate days. At the end of the experimental period, the rats in each group were fasted overnight and then killed by cervical dislocation.

The liver tissues were dissected, weighed, and washed using ice-cold saline solution. Thiobarbituric acid reactive substances (TBARS) were measured by the formation of malondialdehyde. Protein carbonyls were determined using 2, 4-dinitrophenylhydrazine, and catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx) and were assessed based on the ability of a compound to scavenge the free radical.

A portion of the median lobe of the liver was dissected and fixed in 10% neutral buffered formalin solution for 24 h. The fixed tissues were processed routinely and were then embedded in paraffin, sectioned to 3–5 µm thickness. The extent of alcohol-induced necrosis was evaluated by assessing morphological changes in liver sections stained with hematoxylin and eosin, using standard techniques. The statistical significance of the difference between control and treatment groups in this study was determined by ANOVA. The data were expressed as mean and standard deviation (SD). The level of significance chosen was $P < 0.05$.

The results of this study also revealed that the mean levels of TBARS, protein carbonyls, nitrite, and nitrate levels were found to be significantly higher in alcohol-treated rats compared to the control group ($P < 0.05$). Mean activities of antioxidant enzymes, namely, SOD, CAT, GPx, and glutathione (GSH) levels, were found to be significantly decreased in the alcohol-treated group compared to the control group.

The investigators explained the adverse changes that occurred in the alcohol-treated group were as being the results of increased formation of lipid peroxides and associated ROS-mediated liver damage. Moreover, the improvement in the EFE treated group is because of the presence of a considerable amount of tannoids and polyphenolic compounds which have a radical scavenging activity and inhibits the lipid and protein oxidation of alcohol. The researchers concluded that administration of EFE in alcohol-induced oxidative stressed rats, increased the activity of enzymatic antioxidant, inhibits the effect of lipid peroxidation by its free radical scavenging nature, and also improves the histomorphology of the liver near to normal.

As stated by Yokozawa,[45] 21 of male Wistar strain rats were 2 months old (young rats) weighing 125 g and aged rats 10 months old weighing 476 g were used. The animals were divided into three groups.

- Group 1 was the control group and received water alone
- Group 2 was the alcohol-treated group, which received at dose of 10 mg/kg body weight/day
- Group 3 was the sun amla extract-treated group and was given at a dose of 40 mg/kg body weight/day.

The animals in all of the groups were treated for 100 days by gastric intubations. At 6 h after the last dose, all animals were decapitated to draw the blood. And they collected the serum and determined the levels of cholesterol, triacylglycerol (TAG), and peroxisome proliferator-activated receptor (PPAR) protein using commercial kit. They took liver, dried on tissue paper, weighed and stored at 80°C until analysis. Results were expressed as mean values with their standard errors (SE). The effect on each parameter was examined using one-way ANOVA. Individual differences between groups were evaluated. The level of significance chosen was $P < 0.05$.

The administration of amla significantly decreased the adverse effects of alcohol. The PPAR protein level in liver was reduced in aged alcohol-treated rats. The administration of amla significantly increased the hepatic PPAR protein level. The investigators explained the adverse changes that occurred in the alcohol-treated group were showed the total cholesterol and TAG levels in the serum of

aged rats (10 months old) were higher than those of young rats (2 months old). Administration of amla significantly decreased the adverse effect of alcohol in aged rats.

The researchers concluded that the age-related increases of lipids and oxidative stress were mediated by the reduction of hepatic PPAR protein expression. Administration of amla for 100 days to aged rats attenuates age-related dyslipidemia and oxidative stress by inhibiting increases in cholesterol and TAG levels in the serum and liver.

In another study by Reddy,[46] the protective effects of EO also were studied. Two-month-old male albino Wistar rats, weighing about 120–140 g were used. The animals were divided randomly into four groups each having eight members.

- Group I: Was the control group and received isocaloric amounts of glucose (18.6 g/kg of body weight/day), equal to that of alcohol
- Group II: Was the alcohol-treated group, which received 33% (v/v) alcohol at a dose of 10 g/kg of body weight/day.
- Group III: Was the alcohol plus EFE treated group and was given 33% (v/v) alcohol (at a dose of 10 g/kg of body weight/day) plus EFE, at a dose of 250 mg/kg of body weight/day
- Group IV: Animals in this group received only the EFE, at dose of 250 mg/kg of body weight/day.

The animals in all the groups were treated for 60 days by gastric intubations. Food and water intake of all the animals was recorded daily; and weight of the rats was measured on alternate days. At the end of the treatment, they took blood and determined the activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) using commercial kits. Liver tissues also were taken and determined the levels of SOD, GPx, reduced GSH, lipid peroxidation, and protein carbonyl content from freshly isolated mitochondria.

The results of this study also revealed that the mean levels of antioxidant enzymes such as SOD and GPx were found to be significantly decreased in alcohol-treated rats compared to the control group. The researchers concluded that administration of EFE at a dose of 250 mg/kg body weight/day to alcohol-treated rats offers protection by simultaneously lowering the carbonyl content and lipid peroxidation and elevating antioxidant enzyme activities.

In another study by Gopumadhavan,[47] 12–14 weeks old Wistar male rats weighing between 300 and 350 g were used. The rats were divided randomly into four groups of ten each.

- Group 1: Was the control group and received only the fish oil at a dose of 2.5 ml/kg/day
- Group 2: Was the ethanol-treated group, which received ethanol at a dose of 6 g/kg/day for 1st week along with 2.5 ml/kg of fish oil
- Rats of Groups 3 and 4: Were PartySmart (aqueous extract of *Phoenix dactylifera* [188 mg], *Cichorium intybus* [188 mg], *Andrographis paniculata* [188 mg], *Vitis vinifera* [188 mg], *Phyllanthus amarus* [124 mg], and EO [124 mg]) treated group and were received PartySmart as aqueous suspension at a dose of 250 and 500 mg/kg body weight/day, respectively.

The animals in all the groups were treated for 8 days orally. At the end of the treatment, they took blood and determined the levels of ALT, AST, and ALP. A portion of the liver was fixed in 10% neutral buffered formalin and processed for histopathological evaluation using hematoxylin and eosin. The values were expressed as mean ± SE and analyzed statistically using one-way ANOVA to find out the level of significance. The minimum level of significance was fixed at $P < 0.05$.

In this study, it was found that the administration of ethanol increases oxidative stress as manifested by a significant raise in the levels of ALT, AST, and ALP. They observed the changes found to be significant at 500 mg/kg body weight dose of PartySmart treatment. The researchers concluded that the administration of PartySmart in alcohol-induced oxidative stressed rats, increased the levels of serum parameters, involves in the prevention of cell membrane disturbance and reduction of oxidation stress by free radical scavenging and antioxidant activity. Further, they remind detailed studies on the liver are warranted to elucidate the precise mechanism of action. Liver section from rat treated suspension of PartySmart and ethanol-intoxicated with PartySmart and ethanol intoxicated group showed lesser vacuolar degeneration.[47] Rats showing marked improvement in glycogen.[47]

Amelioration of alcohol-induced oxidative stress by EO also was studied by Reddy.[48] Two-month-old male albino Wistar rats, weighing about 120–140 g were used. The rats were divided randomly into four groups of eight rats in each group.

- Group I: Was the control group and received glucose instead of alcohol (i.e., caloric equivalent to alcohol)
- Group II: Was the alcohol-treated group, which received 20% (v/v) alcohol at a dose of 5 g/kg body weight/day

- Group III: Was the alcohol plus EFE treated rats received aqueous EFE (AEFE) and was given 20% (v/v) alcohol (at a dose of 5 g/kg body weight/day plus AEFE, at a dose of 250 mg/kg body weight/day
- Group IV: Animals in this group received only the AEFE, at a dose of 250 mg/kg body weight daily.

The animals in all the groups were treated for 60 days by gastric intubations. The food and water intake recorded daily and weight of rats was followed on alternate days. At the end of the experimental period, they took blood and determined the levels of serum total protein, albumin to globulin (A/G) ratio, total bilirubin, creatinine, uric acid, and nitric oxide using commercial kits. Mean and SD values of all the parameters were determined for each group. The data were subjected to ANOVA. The level of significance was $P < 0.05$. Administration of EFE to alcohol-treated rats significantly decreased the levels of total bilirubin, creatinine, and nitric oxide, and increased the levels of plasma uric acid, total protein and A/G ratio when compared to alcohol alone treated group. The investigators explained that the toxicity is due to lipid peroxidation caused by the free radical generated in the form of ROS and inhibition of lipid peroxidation by EO ameliorates alcohol-induced oxidative stress. The researchers concluded that administration of EO plays a role in protecting hepatic, as well as renal function. The amelioration of alcohol-induced oxidative stress by EFE due to the polyphenols compounds.

In another study by Krushna,[49] the protective effect of EO was investigated in the prevention of alcohol-induced biochemical changes. Two-month-old male albino Wistar rats, weighing about 120–140 g were used. The animals were divided randomly into four groups each having eight members.

- Group I: Was the control group and received isocaloric amounts of glucose equal that of alcohol
- Group II: Was the alcohol-treated group, which received 33% (v/v) alcohol at a dose of 10 g/kg of body weight/day
- Group III: Was the alcohol plus AEFE treated group and was given 33% (v/v) alcohol (at a dose of 10 g/kg of body weight/day) plus EFE, at a dose of 250 mg/kg of body weight/day
- Group IV: Animals in this group received only the AEFE, at dose of 250 mg/kg of body weight/day.

The animals in all the groups were treated orally for 60 days. At the end the treatment, blood was collected and determined the activities of AST, ALT, ALP, and lactate dehydrogenase (LDH) using commercial kits. The statistical significance of the difference between control and treatment groups in this study was determined by ANOVA. The data were expressed as mean and SD. The level of significance chosen was $P < 0.05$.

The investigators explained the adverse effect of chronic alcohol feeding resulted in higher activities of the alcoholic plasma marker enzyme gamma-glutamyl transferase and abnormalities in plasma lipid and lipoproteins, as well as activities of plasma transaminases (AST and ALT), ALP, and LDH. Chronic alcohol administration significantly decreased the activities of SOD, CAT, and GPx with a fall in GSH content in erythrocytes activities. The AEFE supplementation to chronically alcohol-fed rats beneficially modulated plasma lipids and lipoprotein patterns and also corrected plasma enzyme activities and improved antioxidant and defense enzyme machinery status.

The researchers concluded that AEFE supplementation resulted in a significant increase in GSH content and the activities of SOD, CAT, and GPx. AEFE can contribute to the alleviation of alcohol-induced adverse effects by enhancing the status of the antioxidant defense system and by regulating lipid and mineral metabolism.

Discussion

In all of the researches conducted by various investigators confirm edit was that alcohol-induced oxidative stress caused damage of different organs and resulted in significant changes in all serum parameters, such as TBARS, nitrite/nitrates, and antioxidant enzymes. The parameters measured by the researchers were serum AST, ALT, and ALP and antioxidant enzymes SOD, CAT, and GPx.

In the investigation by Damodara Reddy,[44] alcohol treatment at a dose of 5 g/kg body weight administered by gastric intubation for 60 days resulted in increase in TBARS from 1.31 ± 0.18 nmole/mg (in the control) to 2.81 ± 0.29 nmole/mg (in the alcohol-treated) and nitrite/nitrates from 3.42 ± 0.21 nmole/mg (in the control) to 6.62 ± 0.53 nmole/mg (in the alcohol-treated). Coadministration of EO at dose of 250 mg/kg/day for 60 days decreased the changes TBARS and nitrite/nitrates to 1.7 ± 0.22 nmole/mg and 3.7 ± 0.34 nmole/mg, respectively, and also alcohol treatment caused CAT, SOD, and GPx decreased from 39.64 ± 1.17 U/mg, 22.02 ± 1.46 U/mg, and 9.44 ± 0.92 mole/mg (in the control) to 26.02 ± 2.51 U/

mg, 14.14 ± 1.57 U/mg, and 4.41 ± 0.51 U/mg (in the alcohol-treated) respectively. Coadministration of EO elevated the change to 35.11 ± 1.35 U/mg, 21.27 ± 1.07 U/mg, and 8.58 ± 0.56 U/mg, respectively. In this study, there were changes that occurred in the alcohol-treated group is because the increased formation of lipid peroxides and associated ROS leads to liver damage. Moreover, the administration of EFE used in alcohol-induced oxidative stress rats increases the activity of enzymatic antioxidants; inhibits the effect of lipid peroxidation by its free radical scavenging nature and improves the histomorphology of the liver to the normal.

In the study conducted by Yokozawa,[45] supplementation of animals with amla after treated with alcohol, resulted in amelioration of adverse effects of alcohol. For example, the level of lipids such as cholesterol and TAG were increased in serum and liver in aged rats as compared to the young rats. Administration of amla for 100 days to aged rats attenuates age-related dyslipidemia and oxidative stress by inhibiting increases in cholesterol and TAG levels in the serum and liver.

In the study conducted by Reddy,[46] administration of alcohol 33% (v/v) at a dose of 10 g/kg of body weight/day for 60 days caused AST to rise from 26.53 ± 3.16 IU/L (in the control) to 78.02 ± 6.31 IU/L (in the alcohol-treated). Coadministration of EFE 250 mg/kg of body weight/day decreased the change to 25.58 ± 3.67 IU/L, and ALT (26.30 ± 3.84 IU/L), (84.02 ± 11.38 IU/L), and (26.58 ± 3.67 IU/L), respectively, whereas alcohol treatment at dose of 10 g/kg for 60 days caused to lower SOD, GPx from 9.62 ± 0.12 IU/mg and 3.05 ± 0.20 mole (in the control) to 6.24 ± 0.16 IU/mg and 1.72 ± 0.22 mole (in the alcohol-treated). Administration of EFE at a dose of 250 mg/kg for 60 days raises the change to 9.68 ± 0.15 IU/L and 3.08 ± 0.13 mole/mg, respectively. The change seen in the administration of EFE at the dose of 250 mg/kg for 60 days can preserve the structural integrity of the liver from the adverse effects of ethanol.

In addition, the administration of ethanol at a dose of 6 mg/kg daily for 8 days in study of Krushna *et al*.,[49] caused AST, ALT, and ALP to raise from 119.60 ± 7.97 IU/L, 67.67 ± 2.85 IU/L, and 220.30 ± 14.2 IU/L (in the control) to 150.90 ± 8.43 IU/L, 86.5 ± 7.07 IU/L, and 319.20 ± 21.67 IU/L (in the ethanol-treated), respectively. Coadministration of polyherbal formulation PartySmart at the dose of 250 mg/kg and 500 mg/kg daily for 8 days decreased the changes to AST (135.50 ± 7.07 IU/L and 121.30 ± 5.01 IU/L), ALT (70.25 ± 3.91 IU/L and 7.50 ± 2.18 IU/L), and ALP (274.30 ± 22.7 IU/L and 243.00 ± 13.34 IU/L), respectively. The changes found to be significant at dose of 500 mg/kg body weight/day PartySmart treatment. When we compare these researches, the administration of PartySmart in the study of Gopumadhavan *et al*.[47] caused the decrease of the values closest to the normal level as compared to the study of Reddy *et al.* (2009). These may be the high dose of PartySmart, 500 mg/kg and lower dose of ethanol 6 g/kg for 8 days treatment, whereas in the study of Reddy *et al*.,[46] the lower dose of EO, 250 mg/kg as compared to Nandi *et al*.[13] and high dose alcohol, 10 g/kg.

In the study conducted by Reddy,[48] supplementation of animals with amla after treated with alcohol, resulted in amelioration of adverse effects of alcohol. For example, the levels of total bilirubin, creatinine, and nitric oxide increased from 0.61 ± 0.03 mg/dl, 0.84 ± 0.02 mg/dl, and 27.29 ± 1.93 µmole/L (in the control) to 1.02 ± 0.06 mg/dl, 0.81 ± 0.06 mg/dl, and 43.44 ± 3.37 µmole/L (in the alcohol treated), and decreased in uric acid, total protein, and A/G ratio from 2.46 ± 0.14 mg/dl, 6.92 ± 0.29 g/dl, and 1.48 ± 0.07 (in the control) to 1.72 ± 0.15 mg/dl, 5.77 ± 0.41 g/dl, and 1.13 ± 0.06 (in the alcohol-treated), respectively. Administration of 250 mg/kg EFE to alcohol-treated rats significantly decreased the levels of total bilirubin, creatinine, and nitric oxide from 1.02 ± 0.06 mg/dl, 0.81 ± 0.06 mg/dl, and 43.44 ± 3.37 µmole/L (in the alcohol treated) to 0.64 ± 0.07 mg/dl, 0.46 ± 0.05 mg/dl, and 27.0 ± 32.24 µmole/L (in the EFE treated), and raised the levels of uric acid, total protein and A/G ratio from 1.77 ± 0.15 mg/dl, 5.77 ± 0.41 g/dl, and 1.13 ± 0.06 (in the alcohol-treated) to 2.51 ± 0.11 mg/dl, 6.98 ± 0.43 g/dl, and 1.51 ± 0.083 (in the EFE treated), respectively. This is because of inhibition of lipid peroxidation by EO ameliorates alcohol-induced oxidation stress.

Histological section of the liver in majority of the investigators has similar results[44] and has stated that histologically the liver of alcohol treated rats showed fibrosis, atrophy and nucleus is degenerated. The same thing is said by Gopumadhavan[47] that in the histological study animals treated with ethanol (6 g/kgb.wt/day) showed ballooning of hepatocytes with vacuolar degeneration, necrosis, and flattened nuclei in the hepatic sinusoids. This effect was significantly decreased in animals treated with amla in both studies. EO treatment markedly ameliorates the severity of hepatic alternations.

In all of the studies by different investigators albino Wistar rats were used. In majority of the studies, 2-month-old rats weighing 120–140 g were used,

except in the study conducted by Gopumadhavan,[47] 12–14 weeks old weighing 300–350 g and,[49] 2 months old weighing 125 g and 10 months old weighing 476 g were used. The rats were randomly divided into different groups in all studies except in.[45] In the study conducted by Damodara Reddy[44] and Reddy[48] 20% (v/v) alcohol at a dose of 5 g/kg body weight/day was used and 33% (v/v) alcohol at a dose of 10 g/kg body weight/day was used in the study of Krushna *et al*.[49] and Reddy *et al*.[46] However, in the study of Gopumadhavan *et al*.[47] and Yokozawa *et al*.,[45] alcohol at a dose of 6 g/kg body weight/day and 10 mg/kg body weight/day were used, respectively. In all of the studies, EFE was used at the same dose of 250 mg/kg body weight/day, except in the study of Yokozawa *et al*.,[45] the extract used at a dose of 40 mg/kg body weight/day. The animals in majority of studies were treated for 60 days, except in Gopumadhavan *et al*.[47] and Yokozawa *et al*.,[45] treated for 8 and 100 days, respectively. The alcohol and extract were administered in majority of studies by gastric intubations, whereas, in Krushna *et al*.,[49] administered orally. However, different methods were used by different researchers and the levels of different parameters were determined using different techniques, in all of the studies by different investigators the same results were obtained.

Conclusion

In all studies, the toxicity of alcohol is confirmed, so avoidance of unnecessary exposure has to be considered. Ethanol-induced oxidative stress is the result of the combined impairment of antioxidant defenses and the production of ROS. As clearly established by the various researches, EO ameliorates the toxic effect of the alcohol on liver and other organs by lowering free radical-mediated oxidative stress. Ongoing research should provide additional insight into the biological mechanisms underlying liver and other organ damage and new approaches to treating the problem in alcoholic patients.

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