Hepatoprotective Activity of Phoenix Dactylifera Fruits Aqueous Extract against Ethanol Induced Hepatotoxicity in Albino Rats

Vivek Kumar Tiwari*, K. V. Akhil and B. Sindhu Varshini

Department of pharmacy, Gokaraju Rangaraju College of Pharmacy, Bachupally, India

Abstract

In rats, the ameliorative effect of aqueous extracts of the mesocarp (fesh) of dates (*Phoenix dactylifera L*.) was studied using ethanol-induced hepatotoxicity. The rats were divided into six groups and among them; three groups received the mesocarp extract of Phoenix dactylifera (10mg, 20mg, and 40 mg/kg) and ethanol 20% (3.76 gm/kg/day) orally. Two groups were considered controls and one group received the ethanol intervention while another received distilled water and the last group was treated with the Standard drug Silymarin (100 mg/kg).

In both treated and untreated groups, the change in the biochemical markers like SGPT (Serum glutamic pyruvic transaminase) and SGOT (Serum oxaloacetic transaminase) were determined to assess the hepatic injury. The group which received the ethanol treatment exhibited enhanced levels of SGPT and SGOT. The intervention with the fruit extract in a dose-dependent way has restored the altered levels of the biomarkers to near normal levels which were evident from the marked reduction in serum enzymes, SGOT and, SGPT. Hence, it was concluded that the extract from the mesocarp of Phoenix dactylifera exhibits hepatoprotective activity against ethanol-induced hepatotoxicity in the rat model.

Phoenix dactylifera L.) reduced the ethanol-induced elevated plasma enzyme concentration and ameliorated morphological and histological liver damage signifcantly. This study proposes that ethanol-induced liver damage can be ameliorated by administering *P. dactylifera* fesh extract.

§ : Phoenix dactylifera; Silymarin; SGOT; SGPT

e key organ for regulating body homeostasis is the liver. It is involved with almost all the biochemical pathways related to growth, ght against disease, nutrient supply, energy production, and reproduction1. e liver is intended to protect against the dangers of toxic medications and substances in addition to performing physiological duties. Despite signi cant scienti c progress in the eld of hematology in recent years, liver disease is on the rise. Hepatitis and jaundice are two major liver illnesses with a signi cant mortality rate.

Modern medicine is still grappling with how to treat liver illness. Presently only a few hepatoprotective drugs and that too from natural sources (there is not a single e ective allopathic medication), are available for the treatment of the liver disorder. In an assessment by the WHO in 2005, 4% of the burden of disease and 3.2% of all deaths globally were attributable to alcohol. ALD is the foremost health risk

dehydrogenase [5]. e altered ratio of NAD/NADH causes the inhibition of gluconeogenesis and fatty acid oxidation resulting in fatty liver. CYP 2E1, which is upregulated in chronic alcohol use, oxidizes Nicotinamide adenine dinucleotide phosphate (NADPH) to NADP[18] generating free radicals. Chronic alcohol exposure also activates hepatic macrophages to produce tumor necrosis factor α (TNF- α) [19] to increase the production of reactive oxygen species. is oxidative stress promotes hepatocyte necrosis and apoptosis, which is huge in alcoholics who are de cient in antioxidants like glutathione and Vitamin E. In ammation and brosis, is caused due to lipid peroxidation initiated by free radicals [6]. In ammation is also induced by acetaldehyde that, when bound covalently to cellular proteins, forms adducts that are antigenic (Figure 1).

C ` § §

ere are many causes of Fatty Liver Disease, some of them are:

- Drinking too much alcohol is termed Alcoholic Liver Disease (ALD).
- Type 2 Diabetes
- e rise in cholesterol level and triglyceride fats in the blood
- Overweight and obesity: this factor is one of the most

Table 1: Classification of hepatotoxins.

Category of agent	Mechanism	Histological lesion	Examples
1.Intrinsic toxicity			
a.Direct	Membrane injury destruction of the structural basis of cell metabolism	Necrosis (zonal) and/ or steatosis	CCl_4,$CHCl_3$,Phosphorus
b. Indirect Cytotoxic	Interference with the specifc metabolic pathway leads to structural injury	Steatosis or Necrosis	Ethionine,Thioacetamide,Paracetamol, Ethanol
b. Cholestatic	Interference with hepatic excretory pathway leads to cholestasis	Bile duct injury	Rifampicin, Steroids
2.Host idiosyncrasy			
a.Hypersensitivity	Drug allergy	Necrosis or Cholestasis	Sulfonamides, Halothane
b.Metabolic abnormality	Production of hepatotoxic metabolites	Necrosis or Cholestasis	Isoniazid

cigarette smoking, and increasing exercise.

Withdrawals from alcohol intake and nutrition modi cation form the backbone in the management of ALD. Symptom treatment can include corticosteroids for severe cases, anti-cytokines (in iximab and pentoxifylline), Propylthiouracils to modify metabolism, and colchicine to inhibit hepatic brosis.

It is widely believed that alcohol-induced liver damage occurs via the generation of oxidants. us, natural antioxidant supplements like milk thistle are routinely recommended by alternative health care practitioners. Unfortunately, there is no valid clinical data to show the e ect of milk thistle [11]. “Milk thistle for alcoholic and/ or hepatitis B or C liver diseases—a systematic Cochrane hepato-biliary group review with meta-analyses of randomized clinical trials”.

When everything fails and the liver is damaged beyond repair, the only alternative is liver transplantation. While this is a valid option, liver transplant donors are scarce. One of the criteria to become eligible for liver transplantation is to cease alcohol consumption for a minimum of six months.

Phoenix dactylifera L (Date palm) vernacularly known as ‘Nakhla’ and the ‘Tree of Life’ by the Arabs, is considered as one of the oldest cultivated fruit trees. It is believed to be indigenous to the Arabian Gulf countries [12]. Many Middle Easterners believe that consuming date fruits, especially in the morning on an empty stomach, can reverse the actions of any toxic material that the subject may have been exposed to. Di erent parts of this plant are traditionally claimed to be used for the treatment of a broad spectrum of ailments including memory disturbances, fever, and loss of consciousness, in ammation, paralysis, and nervous disorders. e fruits of *Phoenix dactilyfera* are used as an astringent in intestinal troubles, treatment for sore throat, colds, bronchial asthma, to relieve fever, cystitis, gonorrhea, edema, liver, and abdominal troubles, and to counteract alcohol intoxication.

e date palm (*Phoenix dactylifera*) is a dioeciously, medium-sized tree with pinnate leaves and small yellowish owers which develop into fruits called dates (Figure 2).

Kingdom: Plantae

Division: Magnoliolphyta

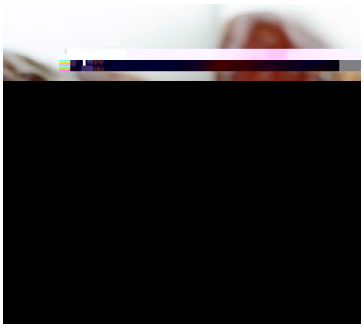

Figure 2: Fruits of *Phoenix dactylifera L*.

Class: Liliopsida

Order: Arecales

Family: Arecaceae

Genus: *Phoenix*

Species: *dactylifera*

Binomial name: *Phoenix dactylifera*

A total of 36 animals were equally divided into 6 groups (n=6), All the test drugs were administered orally (Table 2)

On the 18th day rats were treated with ether and blood samples were collected by retro-orbital puncture in sterilized centrifuge tubes. Blood was allowed to coagulate at 37 for 30 min and the serum was used for the assay of marker enzymes i.e. serum glutamic oxaloacetate transaminases (SGOT), serum glutamic pyruvic transaminase (SGPT), which re ected the functional state of the liver analyzed according to the method of Reitman and Frankel (1957).

Each rat was laprotomized to obtain the liver immediately a er collecting blood under ether anesthesia. Small fragments of the liver were xed in 10% formalin solution [13], dehydrated with ethanol solution from 50% to 100% embedded in para n, and cut into 5µm thick sections which were stained using hematoxylin eosin dye for photo microscopic observation including necrosis, steatosis and fatty change of hepatic cells.

All the data was expressed as Mean ± S.D and analyzed using

one way analysis of variance (ANNOVA) followed by Dunnet test and compared with respective control group. A value of P<0.05 was considered signi cant.

S S S SS

e Phytochemical screening revealed the presence of Alkaloids, Carbohydrates, Steroids, Tannins, Saponins, Flavonoids, and Glycosides in *Phoenix dactylifera.* e Hepatoprotective studies of *Phoenix dactylifera* extract did not show any signi cant decrease in the AST and ALT levels in concentrations 10mg/kg and 20mg/kg and reduced the elevated levels of AST and ALT at 40mg/kg as shown in the (Table 3).

All the values were expressed as Mean ± SD

Oral administration of ethanol at a dose of 3.76 g/kg/day caused signi cant (P<0.0001) rise in level of serum marker enzymes such as AST and ALT [14], compared with the control group Silymarin (100mg/kg) signi cantly (P<0.0001) reduced AST and ALT levels near to normal. A signi cant (P<0.0001) decrease was observed in the AST and ALT of animals treated with di erent doses (10 mg/kg, 20 mg/kg, 40 mg/kg) of *P. dactylifera* fruits aqueous extract and showed dose dependent activity. At the dose of 40mg/kg *P. dactylifera* fruits aqueous extract showed comparable activity with standard drug silymarin.

In Control animals, the liver sections showed normal hepatic cells with well-preserved cytoplasm, prominent nucleus, and normal liver parenchymal cells. Ethanol (3.76 g/kg/day, *p.o*) induced hepatic injury produced liver cell necrosis. Aqueous extract of *P. dactylifera* treated liver showed di use areas of liver cells necrosis and isolated liver cells and focal areas of liver cells showed evidence of regeneration. Silymarin treated liver histopathology also showed di use areas of liver cells necrosis and focal areas of liver cells regeneration.

Liver damage induced by ethanol is perhaps the best studied model of liver cirrhosis. e reduction of ethanol induced elevated plasma levels of AST and ALT when treated with the aqueous extract of *P. dactylifera* shows their ability to restore the normal functional status of poison liver and also to protect against subsequent ethanol toxicity [15].

e mechanism by which *P. dactylifera* induces its hepatoprotective activity is not certain. However, it is possible that β-sitosterol, a constituent of *P. dactylifera,* is at least partly responsible for the protective activity against ethanol induced hepatotoxicity. Flavonoids in *P. dactylifera* could be a factor in contributing to its hepato protective ability through inhibiting the Cytochrome P 450 aromatase.

C S

is study clearly demonstrates that aqueous extract of *Phoenix dactylifera* (40mg/kg) signi cantly decreased SGOT and SGOT in the animals treated with ethanol. Comparative studies were obtained with standard drug Silymarin.

e data suggest that the daily oral consumption of an aqueous extract of the esh of *P. dactylifera* as a part of the daily diet was prophylactic to ethanol poisoning.

References

1. Stewart S, Jones D, Day CP (2003) Alcoholic liver disease: new insights into mechanisms and preventative strategies. Trends Mol Med 7:408-413.

2.

12. Ziouti A, El Modafar C, Fleuriet A, El Boustani S, Macheix JJ(1996)