Research Article [Saxena *et al.*, 7(2): Feb, 2016:4895-4899]
CODEN (USA): IJPLCP ISSN: 0976-7126

INTERNATIONAL JOURNAL OF PHARMACY & LIFE SCIENCES
(Int. J. of Pharm. Life Sci.)

Antihepatotoxic Effect of *Artocarpus heterophyllus* Leaves against Paracetamol induced Hepatic Damage in Albino rats

***Khushboo Saxena, R. Irchhaiya and K.K Chagti**
Uttar Pradesh Technical University, (UP) - India

Abstract

The objective of this study was to investigate the hepatoprotective activity of ethanolic extract of leaves of *Artocarpus heterophyllu*s .againt paracetamol induce hepatic damage. There are lack of reliable hepatoprotective drugs in modern medicine to prevent and treat paracetamol induce liver damage. The ethanolic extract showed presence of flavonoid and steroids. The plant material was dried in shade, powdered and extracted with ethanol. The hepatoprotective activity of the ethanolic extract was assessed in paracetamol induced hepatotoxic rats. Biochemical parameters like SGOT, SGPT, ALP and Bilirubin were tested in drug induced and untreated groups of rats. Treatment of ethanolic extract of *Artocarpus heterophyllus* .leaves has brought back the altered level of biochemical parameter to the normal level in the dose dependent manner and also compared with silymarin used as standard drug.

Key-Words: *Hepatoprotective, ethanol, leaves. paracetamol,silymarin*

Introduction

The *Artocarpus heterophyllus* is a species of tree of the mulberry family (Moraceae) is known by other names jackfrui, Kathal, Panas, Kanthal, Palaa, Phanas & Chakka. It is native to Western Ghats of India, Malaysia and also found in central and eastern Africa, south-eastern Asia, the Caribbean, Florida, Brazil, Australia, Puerto Rico and many Pacific Islands. It is a large, evergreen tree, 10-15m in height, indigenous to the evergreen forests at altitude of 450-1,200m and cultivated throughout the hotter parts of India. Stem of this plant is straight rough whereas bark is green or black, 1.25cm thick, exuding milky latex, leaves broad obovate, elliptic, decurrent, glabrous, entire inflorescencesolitary axillaries, cauliforous and ramflours on short leafy shoots.[1] Male head is sessile or on short peduncles receptacles, sometimes born on the ultimate twing, Female head are oblong ovoid receptacle, syncarpus, cylindrics . Seeds are separated horny endocarpus enclosed by sub-gelatinous exocarpus (1mm thick) oblong ellipsoid in nature.

*** Corresponding Author**
E.mail: khushbusaxena1987@gmail.com

Taxonomical classification

- Kingdom : Plantae
- Subkingdom : Tracheobionta
- Division : Magnoliophyta
- Class: Magnoliopsida
- Subclass: Hamamelidae
- Order: Urticales
- Family : Moraceae
- Genus : Artocarpus
- Species : Artoca*ip*us heterophyllus Lam.

Material and Methods

Drugs and Chemicals:

All the chemicals were analytical grade. Paracetamol was obtained from Amol Pharma Jaipur (Rajasthan).and silymarin from kypton pharma.

Plant collection and authentication

The leaves of *Artocarpus heterophyllus* was collected from Jhansi (U.P), and Identified and authenticated by National vrkshayurveda research institute Jhansi. The accession no. is NVRI/05582/2015. The leaves was dried in shade, and finally grounded in powdered form in and electronic grinder and stored in cellophane bags at 4^{o}C until use.

Preparation of Extract:

The air dried and coarsely powdered leaves (350 g) were first extracted with 1ltr petroleum ether about 40-80^{o}C to remove all fatty acids and again it is extracted with ethanol (95%) in a soxhlet apparatus for 70 hr .The extract were concentrated to dryness under

reduced pressure and controlled temperature (30-50ºC).The yield value of both the leaves extract is recorded.

Animals:

Healthy Wistar-albino rats weighing about (180-250gm) of either sex were obtained from animal house, Institute of Pharmacy, Bundelkhand University, Jhansi. The animals were housed in specific standard laboratory conditions. The conditions were kept in a temperature-controlled environment (25±1^{0}C) and with a regular 12h light/12h dark cycle. All animals were fed with commercial diet & water *ad libitum*, during the experiment. All protocols of the study was approved by the Institutional Animal Ethical Committee with reference no. **BU/Pharm/IAEC/14/022**.The IAEC is approved by Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) with registration no. **716/02/a/CPCSEA Dose and Treatments:** Rats were divided into different groups (n=6). Silymarin syrup (0.5ml/100gm), Paracetamol (2gm/kg) & AHEE (and mg/kg) were administered orally. The control group received 1.5% Tween 80 in distilled water as vehicle (10ml/kg B.W.).

Experimental Design: The general principle involved in the evaluation of Hepatoprotective activity is to induce liver toxicity or infection with the help of hepatotoxin in the liver of experimental animals. The magnitude of the protective activity is measured *in-vivo* by estimating the following parameters:

Biochemical Parameters: These are the most reliable parameter in the *in-vivo* study & include the estimation of different enzyme like SGOT or Aspartate transferase & Alanine transferase or SGPT & Serum alkaline phosphate (SALP). It also includes estimation serum bilirubin (SBLN) & estimation of Hydroxyproline fat & protein content of Livers.

Groups of Animals: The animals were divided into five groups of six animals each.

- **Group I:** served as control & received 1.5% Tween 80 in distilled water as vehicle (10ml/kg B.W.) for 7 days**.**
- **Group II:** received vehicle for 7 days followed by Hepatotoxin (2gm/kg B.W.).
- **GroupIII:** received silymarin (0.5ml/100gm B.W. per day) simultaneously 7 days followed by Hepatotoxin.
- **Group IV:** received AHEE (200mg/kg/day) simultaneously 7 days followed by Hepatotoxin.
- **Group V:** received AHEE (400mg/kg/day) simultaneously 7 days followed by Hepatotoxin.**[38]**

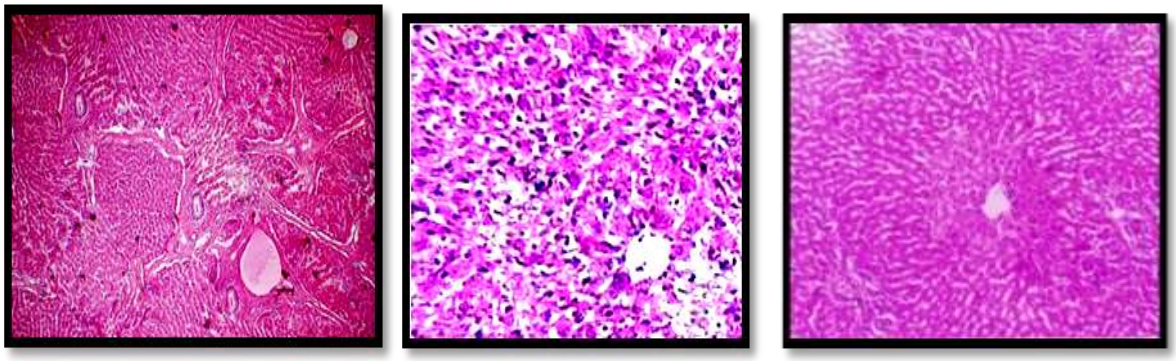
Paracetamol was administered to animals of Groups II, III, IV & V in single dose (2gm/day B.W.) as suspension of 1.5% tween 80.

Table1: Effect of *Artocarpus heterophyllus* Extract on Biochemical Parameters in Rats Subjected to Paracetamol Induced Hepatotoxicity.

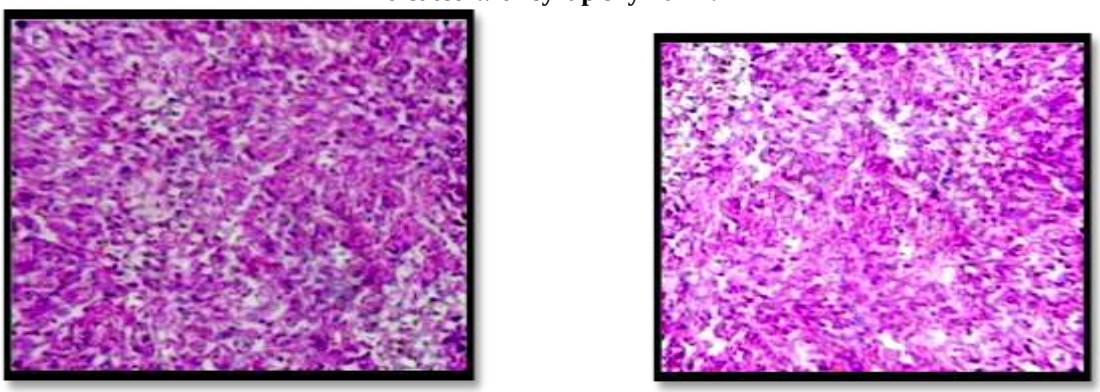
Enzyme group	SGOT	SGPT	SALP	Bilirubin
Control group	**28.30±0.089**	**28.222±0.085**	**87.23±1.5**	**0.52±0.06**
PCM treated group	**68.29±1.25**	**40.350±0.250**	**2516.25±26.03**	**1.895±0.006**
Standard group	**66.20±0.103**	**34.282±0.160**	**1556.20±0.839**	**1.417±0.006**
AHEE(200mg/kg B.W.)	**48.283±1.22**	**32.283±0.054**	**425.100±0.052**	**1.16±1.696**
AHEE(400mg/kg B.W).	**29.243±0.060**	**21.383±0.145**	**116.211±0.122**	**1.168±0.012**

Statistical Analysis The results were expressed as mean ± SEM of six animals from each group. The statistical analysis were carried out by one way analysis of variance (ANOVA) P values < 0.05 were considered significant.

Histopathological Examination: Small pieces of liver tissue were collected in 10% formaldehyde solution for histopathological study. The pieces of liver were processed and
embedded in paraffin wax sections were made about 4-6µm in thickness. They were stained with hematoxylin and photographed.



Photograph:1,2,3 Liver of rat treated with vehicle, 2)Liver of rat treated with paracetamol. 3) Liver of rat treated with syrup silymarin.



Photograph: 4,5 Liver of rat treated with HIEE (200mg/kg bodyweight.5) Liver of rat treated with AHEE (400mg/kg bodyweight)

Results and Discussion

The present work was to carried out with the objective of ethanolic extract of leaves of *Artocarpus heterophyllus*. Phytochemical investigation, evaluation of the Hepatoprotective activity (*in-vivo*) against PCM induced Hepatotoxicity model .Liver is a versatile organ in the body concerned with regulation of internal chemical environment. Therefore damage to the liver inflicted by a hepatotoxic agent is of grave consequence. In the present study, the ethanolic extract of *Artocarpus heterophyllus.* Paracetamol is a well known antipyretic & analgesic agent, which is safe in therapeutic doses but can produce fatal necrosis in experimental animals & humans & is employed as an experimental hepatotoxic agent. A sign of hepatic injury is the leaking of cellular enzymes into the plasma due to the disturbances caused in the transport functions of hepatocytes. The estimation of enzymes in the serum is a useful quantitative marker of the extent & type of hepatocellular damag$_{e}$[15]**.** The mode of action of paracetamol on the liver is by covalent binding of its metabolite, n-acetyl-p-benzoquinone-amine to sulfhydryl group of protein resulting in cell necrosis and lipid peroxidation **.**Due to liver injury caused by PCM overdose, the transport function of the hepatocytes gets disturbed resulting in the leakage of plasma membrane [5] thus causing an increase in serum enzyme levels. Assay of the activities of these serum marker enzymes and AHEE helps to assess the liver function [5]**.**

Herbal Silymarin is a unique, all natural, complex multi-ingredient formula. It helps in protecting the liver from harmful toxins & regulates levels of enzymes and optimizes assimilation. Herbal Silymarin has been found to be associated with an increase in serum albumin & restores the functional efficiency of the liver by promoting the hepatocellular regeneration. Silymarin is believed to be the first multi-herb remedy

granted regulatory approval as a drug, Silymarin, the well known hepatoprotective product. Silymarin is a favoured drug for different liver diseases because of its oral effectiveness, good safety profile, avaialvility in India and importantly affordable [35].

In this experiment, it is observed that the level of hepatic biochemical markers i.e. SGOT, SGPT, SALP & Bilirubin is increased due to PCM in comparison to the control group. This clearly indicates that there is significant hepatic damage due to the paracetamol. The toxic effect of PCM was controlled in animals treated with ethanolic extract of *Artocarpus heterophyllus*. 400 mg/kg/day by way of restoration of the markers levels in the liver with comparison to positive control Silymarin. Hepatoprotective effect of AHEE was further confirmed by histopathological studies of the liver, which basically supported the results from the serum assay. AHEE administration resulted in bringing about an almost normal histological architecture of the liver. The preliminary phytochemical screening of *Artocarpus heterophyllus* leaves shows the presence of flavonoids and Steroids compounds as major active principle in ethanolic extract of *Artocarpus vheterophyllus*. leaves. Many of flavonoids and steroids(Beta- steroid) compounds have been reported for hepatoprotective activity.

References

1. A.M. Rahman, N. Nahar, AJ. Mian and M. Mosihuzzaman. Variation of carbohydrate composition of two forms of fruit from jack tree*(Artocarpus heterophyllus L)* with maturity and climatic conditions. *Food Chem.* 65: 91-97 (1999).
2. P. Rowe-Dutton. *Artocarpus heterophyllus*- jackfruit. In: The propagation of tropical fruit trees (Garner RJ and Chaudhri SA, eds.). FAO, Rome (Italy); Commonwealth Bureau of Horticulture and Plantation Crops, Maidstone, 269-290 (1985).
3. E. T. Arung, K. Shimizu and R. Kondo. Inhibitory effect of artocarpanone from *Artocarpus heterophyllus* on melanin biosynthesis. Biol.*Pharm.* Bull. 29: 1966-1969 (2006).
4. S. Shyamalamma, S.B.C. Chandra, M. Hegde and P. Naryanswamy. Evaluation of genetic diversity in jackfruit *(Artocarpus heterophyllus* Lam.) based on amplified fragment length polymorphism markers. *Genet. Mol. Res.* 7(3): 645-656 (2008).
5. Roy, S.K., P.K. Royand and R.G. Brumfield, *In vitro* propagation and establishment of a new cultivar of jackfruit *(Artocarpus heterophyllus* lam.) bearing fruits twice yearly. *Acta Hort.*, 429: 497-502 (1996).
6. M. Kamaluddin, M. Ali and M.K. Bhuiyan. Effect of auxin on rooting of cuttings and growth of stecklings of jackfruit *(Artocarpus heterophyllus* lam.). *Chittagong Univ. Stud. Sci.* 20(1): 71-75(1997).
7. A.V. Rama Rao, Mala Varadan and Venkataraman. Colouring matter of the *A. hetetophyllus. Indian J. Chem.* 11: 298-299 (1973).
8. Perkin and Cope. The constituents of *Artocarpus integrifolia. J. Chem. Soc.* 67: 937-944 (1895).
9. G. Pavanasasivam, M. Uvais and S. Sultanbawa. Cycloartenyl acetate, cycloartenol and cycloartenone in the bark of *Artocarpus species. Phytochemistry*, 12(11): 2725-2726 (1973).
10. F.A. Chawdhary, M.A. Raman. Distribution of free sugars and Fatty acids in Jackfruit. *Food chemistry.* 60(1): 25-28 (1997).
11. B.R. Barik, T. Bhaumik, A.K. and A.B. Kundu. Triterpenoids of *Artocarpus heterophyllus, J. Indian Chemical Soc.* 74: 163-164 (1997).
12. Chun-Nan Lin and Chai-Ming Lu. Heterophylol, a phenolic compound with novel skeleton from *Artocarpus heterophyllus, Tetrahedron letters.* 34(17): 8249-8250 (1993).
13. R. Dayal and T.R. Seshadri. Colourless compounds of the roots of *Artocarpus heterophyllus.* Isolation of new compound artoflavone.*Indian J Chem.* 12: 895-896 (1974).
14. Chai-Ming Lu and Chun-Nan Lin. Two 2~, 4', 6'--trioxygenated flavanones from *Artocarpus heterophyllus. Natural Products Research Center* 33(4): 909-911 (1993).
15. K. Hedge ,A .Joshi. Hepatoprotective effect of Carissa carandas root extract againt CCl4 nad paracetamol –induce hepatic oxidative stress, *Indian Journal of Experimental Biology*, Vol 47,Aug2009,pp660-667.

How to cite this article
Saxena K., Irchhaiya R. and Chagti K.K. (2016). Antihepatotoxic Effect of *Artocarpus heterophyllus* Leaves against Paracetamol induced Hepatic Damage in Albino rats. *Int. J. Pharm. Life Sci.*, 7(2):4895-4899.
Source of Support: Nil; Conflict of Interest: None declared

Received: 30.12.15; Revised: 21.01.16; Accepted: 01.02.16