

## Hepatoprotective Effect of Ethanolic Extract of *Artocarpus Heterophyllus* Leaves against Rifampicin Induced Hepatic Damage in Albino Rats

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Submitted: 01-06-2022

Revised: 14-06-2022

Accepted: 16-06-2022

### ABSTRACT

The liver has 2 massive sections, referred to as the left and right lobes. The gall bladder is found underneath the liver, in conjunction with elements of the duct gland and viscus. The liver and these organs work along to digest, absorb and method food. The main task of the liver is to filter the blood from the GI tract before sending it to the remainder of the body. The liver conjointly detoxifies chemicals and metabolizes medication. The liver secretes the gall that lands up within the viscus. Rifampicine is a type of antibiotics which is used in the treatment of mycobacterial infection. It is also used in treatment of leprosy and Tuberculosis. *Artocarpus Heterophyllus* is also known as Jack fruit or Jack fruit tree. The length of *Artocarpus Heterophyllus* is 8-25 Meters. The diameters of *Artocarpus Heterophyllus* is grow upto 6 meters within 5 years. Fruits of *Artocarpus Heterophyllus* is about 4-30 kg. Jackfruits are help to control flood and soil erosion.

**KEYWORDS:** *Artocarpus Heterophyllus*, Rifampicine, Jackfruits, Tuberculosis, Liver

### I. INTRODUCTION

#### LIVER

- ❖ The liver may be a massive, fleshy organ that's settled on the proper aspect of the belly. a person's liver typically weighs one.44-1.66 kg (3.2-3.7 pounds) and is fifteen cm wide, the liver is burnt sienna and feels sticky to the bit. ordinarily you can not feel the liver, as a result of it's protected by the skeletal structure .
- ❖ The liver has 2 massive sections, referred to as the left and right lobes. The gall bladder is found underneath the liver, in conjunction with elements of the duct gland and viscus. The liver and these organs work along to digest, absorb and method food .
- ❖ The main task of nthe liver is to filter the blood from the GI tract before sending it to the

remainder of the body. The liver conjointly detoxifies chemicals and metabolizes medication. The liver secretes the gall that lands up within the viscus.

- ❖ Liver diseases area unit classified as chronic liver disease (inflammatory liver disease), liver disease (non-inflammatory disease) and cirrhosis of the liver, i.e. disorder that causes liver fibrosis<sup>1</sup>. Liver cirrhosis of the liver has become a significant pathological state because of the broader use of pharmaceuticals with adverse reactions in trendy life or misuse.

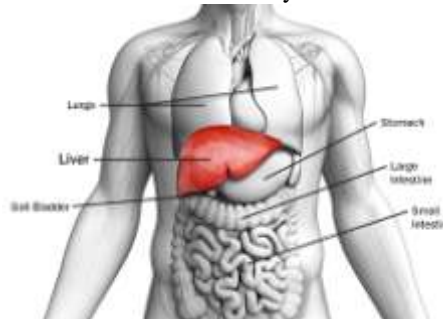


Fig1- LIVER

#### FUNCTION

**The main functions of the liver include:**

- ❖ **Gall production:** gall helps the tiny gut to disintegrate and absorb fats, cholesterol and a few vitamins. gall consists of gall salts, cholesterol, bilirubin, electrolytes and water.
- ❖ **Absorb and metabolise animal pigment:** bilirubin is created by the breakdown of haemoprotein. The iron free from haemoprotein is hold on within the liver or bone marrow and is employed to supply succeeding generation of blood cells.
- ❖ **Blood support:** antihemorrhagic factor is important for the creation of some coagulants that facilitate to coagulate the blood. gall is important for the absorption of

antihemorrhagic factor and is formed within the liver. If the liver doesn't turn out enough gall, action factors can't be created.

**Fat metabolism:** gall breaks down fats and makes them easier to digest.

**Metabolise carbohydrates:** carbohydrates are held on within the liver, where they're lessened into aldohexose and extracted into the blood to keep up traditional aldohexose levels. {they are|they're} held on as polysaccharide and are free whenever a fast discharge of energy is required.

**Preservation of vitamins and minerals:** the liver stores vitamins A, D, E, K and B12. It keeps vital amounts of those held on vitamins. In some cases, many years of vitamins are held on as backups. The liver stores iron from haemoprotein within the type of protein, able to turn out new red blood cells. It conjointly stores and releases copper.

**Filter the blood:** the liver filters and eliminates the body's compounds, as well as hormones, like oestrogen and mineralocorticoid, and compounds external to the body, like alcohol and alternative medicine.

**Angiotensinogen synthesis:** this internal secretion will increase pressure by narrowing blood vessels once alerted by the assembly of associate catalyst known as protease within the kidneys [2].

#### Detoxification

The liver plays a vital role in detoxifying substances harmful to the body, like alcohol, drugs, solvents, pesticides and serious metals. Once someone is exposed to high levels of those chemicals, the liver might feel inundated. Toxins are sent to the liver from the portal. The liver processes these chemicals and excretes them into the gall.

#### Liver Diseases

Liver sickness is any alteration in liver operation that causes the disease. Liver disease may be a broad term that covers all the potential issues that cause the liver to fail to perform its selected functions.

The liver is that the largest solid organ within the body; and it's conjointly thought-about a organ as a result of among its several functions it produces and secretes gall.



Fig2: stages of liver diseases

#### SYMPTOMS OF LIVER DISEASES [15]

- ❖ Fatigue
- ❖ weakness
- ❖ Nausea, less frequent vomiting.
- ❖ Poor appetite
- ❖ jaundice
- ❖ Dark urine, light stools
- ❖ temperature
- ❖ Anorexia, weight loss.
- ❖ Abdominal pain
- ❖ abdominal inflammation (ascites)
- ❖ change in sleep pattern and behaviour.

**Main Risk Factors Of Liver Diseases:-** Some liver diseases are undoubtedly preventable and related to fashion decisions. Alcohol-related disease is thanks to excessive consumption and is that the most typical preventable explanation for disease.

Hepatitis B may be an infection that's typically transmitted through the exchange of body fluids (for example, unprotected sex, sharing of apparatus for the injection of non-sterile medication, use of non-sterile instrumentation for tattoos or piercings). Hereditary diseases are often genetically transmitted from generation to generation. Chemicals like anabolic steroids, vinyl chloride and dissolver will cause cancer of the liver.

Overdose of paracetamol (Tylenol) may be a common explanation for liver failure. It's necessary to review the indefinite quantity pointers for all over-the-counter medications and raise your doctor or apothecary for steering on the number of medicines which will be taken safely. Whereas over-the-counter medication area unit comparatively safe, they'll cause complications

directly or as associate interaction with a prescribed drug.

Medications will irritate the blood vessels of the liver and cause narrowing or formation of blood clots (thrombosis). contraception pills will cause internal organ phlebothrombosis, particularly in smokers.

#### Test for the identification of disease.

There are 3 main styles of tests that are performed within the identification of liver diseases:

##### 1. Lab test

- a) Blood
- b) Humor enzymes
- c) Pathology fluid

##### 2. Radiological studies

- a) USG
- b) CT scan
- c) MRI
- d) ERCP

#### TREATMENT AND PREVENTION

There is no specific treatment for acute liver disease. Bed rest isn't continually essential, though you'll feel higher if you limit the quantity of physical activity. it's necessary to take care of adequate calorie intake. Your doctor will suggest tiny, frequent and high-calorie meals with many fluids. the employment of alcohol should be avoided or restricted to assist the recovery of the liver. If you cannot eat or drink, you'll be able to be hospitalized.

To prevent the unfold of hepatitis, hand laundry by medical personnel returning into contact with contaminated tools, bedding or article of clothing is crucial. health care professionals ought to be immunized, as they need AN inflated risk of infection because of exposure to infected folks.

#### LIVER COMPLICATIONS

- Disease is that the most typical liver complication of IBD and is commonly reversible and affects folks with colitis and regional ileitis within the same method. this is often a condition within which excess fat is deposited within the liver and squeezes the traditional liver cells.
- Liver disease may be a generic term for inflammation of the liver. It will be caused by medication like methotrexate sodium, medication, 6-mercaptopurine (6 MP) or, rarely, anti-TNF agents.

#### TYPES OF LIVER DISEASES

##### 1. Viral hepatitis

- A, B, C, D, E, other (EBV, CMV), cryptogenic

##### 2. Immune and autoimmune liver diseases

- Primary biliary cirrhosis (PBC)
- Autoimmune hepatitis (CAH)
- Sclerosing cholangitis (PSC)
- Graft-versus-host disease (GVHD)
- Allograft rejection

##### 3. Liver involvement in systemic diseases

- Sarcoidosis
- Amyloidosis
- Glycogen storage diseases
- Celiac disease
- Tuberculosis

##### 4. Genetic liver diseases

- $\alpha$ 1-antitrypsin deficiency
- Hemochromatosis
- Wilson's disease
- Benign recurrent intrahepatic cholestasis (BRIC)
- Progressive familial intrahepatic cholestasis (PFIC) types I-III
- Others (galactosemia tyrosinemia, cystic fibrosis, Newman-Pick disease, Gaucher's disease)

##### 5. Alcoholic liver diseases

- Acute fatty liver
- Acute alcoholic hepatitis
- Laënnec's cirrhosis
- Nonalcoholic fatty liver
- Steatosis
- Steatohepatitis (NASH)

##### 6. Drug-induced liver disease

- Hepatocellular (INH, acetaminophen)
- Cholestatic (methyltestosterone)
- Mixed (sulphonamides, phenytoin)
- Micro- and macrovesicular steatosis (MTX, fialuridine)
- Vascular injury

#### Causes of Hepatitis

Hepatitis A: - it's transmitted by water and spreads principally through waste water and contaminated food and water.

Hepatitis B: transmitted by contact with infected bodily fluid, blood or channel secretions and from the mother to the new-born. serum hepatitis is most frequently transmitted through unprotected sex and sharing of infected needles (including those used for tattoos, treatment and ear piercing).

Hepatitis C: - It spreads through direct blood contact with blood.

Hepatitis D: - it's transmitted by infected needles and blood transfusions.

- ❖ Excessive semipermanent alcohol consumption

- ❖ Chronic infection with serum hepatitis virus
- ❖ Hereditary disorders of iron and copper metabolism.
- ❖ severe reactions to sure medicine
- ❖ liver disease caused by blubber

### Symptoms Of Hepatitis

The signs and symptoms of acute infectious disease seem quickly. They include:

- ❖ Tiredness
- ❖ Flu-like symptoms
- ❖ Dark urine
- ❖ unexplained weight loss
- ❖ Yellow skin and eyes, which may be signs of jaundice.

### Complication of Hepatitis

Chronic hepatitis B or C will typically cause a lot of serious health issues. as a result of the virus affects the liver, folks with chronic hepatitis B or C ar in danger of:

- Chronic liver disease
- cirrhosis
- liver cancer

### Liver Cirrhosis

Cirrhosis could be a condition during which the liver isn't functioning properly thanks to long harm. Liver cirrhosis of the liver merely suggests that scarring of the liver. This method happens slowly and is usually irreversible and may cause hardening of the liver and healing and shrinking.

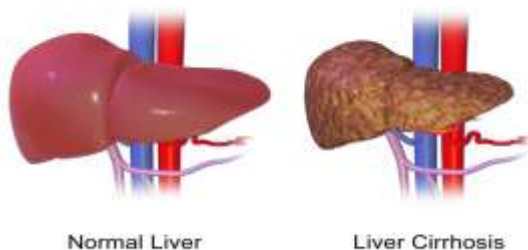
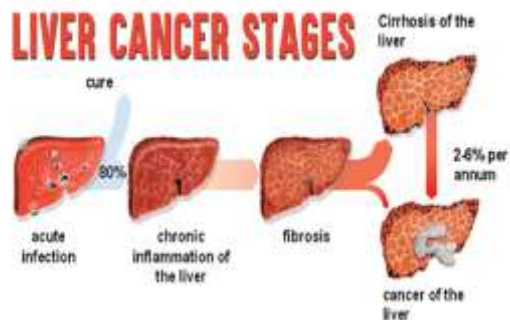


Fig9: Liver Cirrhosis

### Liver Cancer

Cancer begins once healthy cells amendment and grow out of management, forming a mass known as a growth. A growth will be cancerous or benign. A cancerous growth is malignant, which implies that it will grow and unfold to alternative components of the body. A nonmalignant tumour will grow however won't unfold. Primary cancer of the liver is cancer that starts within the liver. regarding eightieth of primary cancer of the liver is carcinoma (HCC). alternative kinds of primary cancer of the liver

embody duct ancer and malignant tumor, a cancer of the blood vessels within the liver.



### Causes of liver cancer

There area unit many risk factors for liver cancer

- ❖ serum hepatitis and long viral hepatitis infection area unit associated with liver disease as a result of they typically cause liver disease. serum hepatitis will cause liver disease while not liver disease.
- ❖ Excessive alcohol use.
- ❖ fatness and polygenic disorder area unit closely related to a sort of liver abnormality known as "non-alcoholic liver disease disease" (NAFLD) which may increase the danger of liver disease, notably those that drink a great deal or have hepatitis.
- ❖ Some hereditary metabolic diseases.
- ❖ Environmental exposure to aflatoxins.

### Treatment

- ❖ Transplantation, if the cancer has not unfold, for a few patients, a liver transplant (liver replacement) could also be AN choice.
- ❖ Surgery If the growth has been detected early and therefore the remainder of the liver is healthy, doctors will perform surgery to get rid of the liver growth (partial hepatectomy).
- ❖ Radiofrequency ablation Radiofrequency ablation uses a special probe to destroy cancer cells with heat.
- ❖ Other treatment choices if surgery and transplantation aren't potential include:
- ❖ Take measures to stop exposure to serum hepatitis and viral hepatitis.
- ❖ Treatment for serum hepatitis and C.

### Hepatectomy

An hepatectomy is performed to get rid of a little of the liver or the whole liver. This surgery is sometimes performed once the cancer is restricted to the liver. Over time, the remaining healthy tissue can grow back and replace the missing half.

### Liver transplantation

A liver transplant involves exchange the whole unhealthy liver with a healthy liver from an acceptable donor. A transplant will be done provided that the neoplasm has not unfold to alternative organs. medicine ar administered to stop rejection once transplantation.

### Ablation

Ablation involves the utilization of warmth or ethyl alcohol injections to destroy cancer cells. it's created with anaesthesia. This numbs the world to stay you from feeling pain. Ablation will facilitate those who don't seem to be candidates for surgery or transplantation.

### Chemotherapy

Chemotherapy is associate aggressive type of drug medical aid that destroys cancer cells. The medicine ar injected intravenously or intravenously. In most cases, therapy will be given as associate patient treatment. therapy could also be effective in treating carcinoma, however many folks have aspect effects throughout treatment, like reflex, shrivelled craving and chills. therapy can even increase the chance of infection.

### Radiotherapy

Radiation therapy involves the utilization of high-energy radiation beams to kill cancer cells. It will be administered by external radiation or internal radiation. In external beam radiation, radiation is directed towards the abdomen and chest. Internal radiation involves the utilization of a tubing to inject tiny radioactive spheres into the arteria. The radiation then destroys the arteria, a vas that provides blood to the liver. This reduces the quantity of blood flowing into the neoplasm. once the arteria is closed, the vein continues to nourish the liver.

### Direct therapy

Targeted medical aid involves the utilization of medicine designed to attack cancer cells wherever they're vulnerable. They cut back the expansion of the neoplasm and facilitate to shut the blood provide to the neoplasm. Sorafenib (Nexavar) has been approved as a targeted medical aid for individuals with carcinoma. Targeted medical aid could also be helpful for those who don't seem to be candidates for hepatectomy or liver transplantation. However, targeted medical aid will have vital aspect effects.

### TYPES OF LIVER CANCER

#### Primary Liver Cancer: -

The different kinds of primary carcinoma come back from the varied cells that conjure the liver. Primitive liver cancer will begin as one bump

that develops within the liver or can begin in several places on the liver at the same time. individuals with severe liver harm ar a lot of possible to possess a lot of cancer growth sites.

### Diagnosis of Liver Cancer

Diagnostic tests and procedures for cancer of the liver embody the following:

- Liver operate tests facilitate the doctor confirm liver health by measure the amount of proteins, liver enzymes and haematoidin within the blood.
- The presence of alpha-fetoprotein (AFP) within the blood may be a proof of cancer of the liver. This supermolecule is typically created solely within the liver and vitellus sac of youngsters before they're born. AFP production typically stops when birth.
- Abdominal X-radiation or resonance imaging (MRI) produces careful pictures of the liver and different organs within the abdomen. they'll permit the doctor to work out wherever a neoplasm is developing, confirm its size and assess whether or not it's unfold to different organs.

### Liver biopsy

Another offered assay may be a liver diagnostic test. A liver diagnostic test involves the removal of alittle portion of liver tissue. it's invariably through with physiological condition to avoid feeling pain throughout the procedure.

If cancer of the liver is found, the doctor can confirm the stage of the neoplasm. Staging describes the severity or extent of the neoplasm. you'll be able to facilitate your doctor confirm treatment choices and your perspective. section four is that the most advanced stage of cancer of the liver.

### STAGES OF LIVER CANCER[111]

The staging of a cancer permits the doctor to come to a decision the course of treatment.

Liver cancer is classed into four phases:

**Stage I:** the tumor is found within the liver and has not spread to a different organ or place.

**Stage II:** there are many small tumors that remain within the liver or a tumor that has reached a vas.

**Stage III:** there are several large tumors or a tumor that has reached the main blood vessels. The cancer may even have reached the gall bladder.

**Stage IV:** the tumor has metastasized. This means that it has spread to other parts of the body.

### PREVENTION OF LIVER CANCER [105]

Moderate alcohol consumption

Limiting tobacco use can also help prevent liver cancer and other organs.

Vaccination against hepatitis B: the following people should consider receiving the hepatitis vaccine:

- People with drug addiction who share needles.

**EPIDEMIOLOGY**

Chronic liver disease occurs worldwide, regardless of age, gender, region or race. Cirrhosis is the end result of a variety of liver diseases characterized by fibrosis and architectural distortions of the liver with the formation of regenerative nodules and can have various manifestations and clinical complications.

According to the WHO, about 46% of global diseases and 59% of mortality are due to chronic diseases and nearly 35 million people worldwide die from chronic diseases. The rates of liver disease have been steadily increasing over the years. According to national statistics in the United Kingdom, liver diseases have been classified as the fifth most common cause of death [183]. Liver diseases are recognized as the second leading cause of mortality among all digestive diseases in the United States. UU.

Table 1: Cancer incidence (thousands) by site, by WHO region, 2004 [201]

	World	Africa	The Americas	Eastern Mediterranean	Europe	South-East Asia	Western Pacific
Lung cancer	1 448	27	264	34	401	164	558
Stomach cancer	933	38	89	25	182	78	521
Colon and rectum cancers	1 080	32	217	23	409	106	293
Liver cancer	632	65	38	13	67	64	386
Cervix cancer	489	95	95	15	81	180	73
Breast cancer	1 100	72	310	54	326	154	184
Prostate cancer	605	77	236	13	180	45	54
Lymphomas and multiple myeloma	479	56	102	39	113	91	79
Leukaemia	375	20	68	28	86	72	101
Other cancers	5 187	234	874	226	1 214	773	919
All sites (excluding non-melanoma skin cancer)	11 474	716	2 294	470	3 058	1 726	3 166

**PLANT PROFILE**

**Taxonomical Classification**

Kingdom: Plantae  
 Subkingdom: Tracheobionta  
 Division: Magnoliophyta  
 Class: Magnoliopsida  
 Subclass: Hamamelidae  
 Order: Urticales  
 Family: Moraceae  
 Genus: Artocarpus  
 Species: Artocarpus heterophyllus Linn

**II. MATERIALS AND METHODS**

**Plant collection and authentication**

The leaves of jackfruit was collected from native space of Varanasi, state, Bharat within the month of Gregorian calendar month and known and genuine by Sheat faculty of pharmacy, Varanasi. The recent leaves were washed with water, followed by water so dried beneath shade at temperature. when drying properly, the scale of

leaves was reduced so grounded in fine-grained type and hold on during a plastic wrap bag.

**Drugs and Chemicals:**

All the chemicals were collected from our faculty Sheat faculty of Pharmacy, Varanasi, state, India. Rifampicin (2 gramme /kg) was obtained from Alkem laboratory and silymarin(0.5ml/100gm) from celestial point nutrition laboratory.

**Animals**

Healthy Wistar-albino rats deliberation concerning 150-200 gramme of either sex were obtained from animal house, Sheat faculty of Pharmacy, Varanasi, state. The animals were housed in specific customary laboratory conditions. The conditions were unbroken during a temperature-controlled surroundings and with an everyday 12h light/12h dark cycle. throughout the experiments all animals were fed with industrial diet and water. All the experiments were administered as per CPCSEA (Committee for the

aim of management and superintendence of Experimental on Animals) pointers. All protocols of the study were approved by the institutional Animal moral Committee with reference no 1229/PO/RE/S/11/CPCSEA.

Dose and Treatment: Rats were divided into completely different groups(n=6). Rifampicin(2gm/kg) and AHEE were administered orally. The management cluster received one.5% Tween eighty in water as a vehicle (10ml/kg).

#### Preparation of Plant Extract

The air dried and coarsely fine-grained leaves (300g) were initial extracted with crude oil ether concerning 40-50c to get rid of all fatty acids and once more it's extracted with fermentation alcohol (99%) during a soxhlet equipment for 72hr.

#### Experimental Design

##### Group of Animals

The animals were divided into four teams of 5 animals every.

Group I: Served as traditional management cluster and received one.5% Tween eighty in water as vehicle (10ml/kg) for fifteen days.

Group II: Received vehicle for fifteen days followed by Rifampicin as toxin.

Group III: customary drug cluster received Rifampicin (2 gm/kg) and Silymarin (0.5ml/100gm).

Group IV: Received Rifampicin and alcohol extract of plant jackfruit leaves (300mg/kg/day) at the same time fifteen days followed by toxin.

#### Estimation of Biochemical Parameters:

These square measure the foremost reliable parameters within the in-vivo study and embrace the estimation of various enzymes like SGOT or Aspartate enzyme and amino acid enzyme or SGPT and humor alkalescent phosphate (SALP). It conjointly includes estimation humor hematoidin (SBLN).

### III. RESULT AND DISCUSSION

#### Effect of Ethanolic Extract of Leaves of Artocarpus Heterophyllus (EELA) on Rifampicin induced hepatotoxic rats.

Animal group	SGOT(IU/L)	SGPT (IU/L)	ALP( IU/L)	Bilirubin (mg/dl)
Control group( Vehicle treatment)	41.4±2.22	43.5±1.57	67.0±1.26	0.36±0.03
Toxic control (Rifampicin treated group)	163.0±4.19*	67.0±2.92*	430±5.11*	0.96±0.07*
Standard drug (Silymarin 0.5ml/100gm)	90.52±3.73 <sup>a</sup>	47.12±1.66 <sup>a</sup>	228.56±4.87 <sup>a</sup>	0.61±0.05 <sup>a</sup>
EELA (300 mg/kg)	120.56±0.22 <sup>a</sup>	51.68±1.36 <sup>a</sup>	343.67±5.52 <sup>a</sup>	0.73±0.03 <sup>a</sup>

\*Group II compared with Group I.

<sup>a</sup> Group III and Group IV compared with Group II.

\*P <0.05–Significant; values: Mean ±SEM. SEM–Standard Error of Mean, n–Number of animals in each group (6)

#### Statistical analysis

Data were statistically analyzed victimisation unidirectional analysis of variance and expressed as mean ± S.E.M. followed by Dennett's t-test.

### IV. DISCUSSION

Liver disease may be a broad term that covers all the potential issues that cause the liver to fail to perform its selected functions. In general, it's necessary that quite seventy fifth or 3 quarters of the liver tissue is affected before a decrease in perform happens.

The present work was meted out with the aim of evaluating the result of ethanolic extract of leaves of Artocarpus heterophyllus against the rifampicin-induced hepatotoxicity model. The liver may be a versatile organ within the body that

regulates the inner chemical atmosphere. Therefore, liver injury caused by a toxic agent is of great importance. Rifampicin is associate antitubercular drug, that is safe in therapeutic doses, however will turn out fatal gangrene in experimental associateimals and in humans and is employed as an experimental toxic agent. a symbol of liver injury is that the filtration of cellular enzymes within the plasma because of alterations caused within the hepatocytes transport functions.

In this experiment it absolutely was determined that the extent of internal organ organic chemistry markers like SGOT, SGPT, tunicate and hematoidin will increase in rifampicin treated teams compared to the management cluster. This clearly indicates that there's vital liver injury because of rifampicin. The venomous result of rifampicin was controlled in animals treated with *Artocarpus heterophyllus* fermentation alcohol extract within the dose of three hundred mg / weight unit / day.

It contains many active constituents like Morin, dihydromorin, cynomacurin, artocarpin, cycloartocarpin, cycloheterophyllin, artocarpetin, betulinic acid and heterophylol. The plant additionally contains fatty acids, ellagic acid and a few essential amino acids like essential amino acid, Cystine, histidine, leucine, essential amino acid etc.

## V. CONCLUSION

It contains many active constituents like Morin, dihydromorin, cynomacurin, artocarpin, cycloartocarpin, cycloheterophyllin, artocarpetin, betulinic acid and heterophylol. The plant additionally contains fatty acids, ellagic acid and a few essential amino acids like essential amino acid, Cystine, histidine, leucine, tryptophane etc. The leaves of jackfruit additionally contain flavonoids and steroid compounds. several flavonoids, steroid, amino acids ar reported to possess hepatoprotective activity and inhibitor activity. therefore the hepatoprotective activity could also be thanks to the active biomolecule gift within the extract. any histopathological studies and clinical evaluations ar needed for future therapeutic use for personalities.

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