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EVALUATION OF HEPATOPROTECTIVE ACTIVITY OF AMALAKYADI LEHA ON PARACETAMOL - INDUCED LIVER DAMAGE IN ALBINO RATS

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ABSTRACT

The liver, the biggest and most intricate internal organ in the body, plays an essential part in maintaining the body's internal environment. Despite advancements in contemporary treatment,the prevalence of liver diseases remains a global issue. The scarcity of efficacious therapies for hepatic disorders in modern medicine underscore s the necessity f o r hepatoprotective medication. The Liver is regarded as *yakrit* according to the *Ayurveda. Yakrit* and *Pleeha* are regarded as the *moola sthana* of *raktavaha srotas.* Thus, medications that pacify *pitha* and *rakta* can be used to treat y*akrit vikaras. Amalakyadi leha,* mentioned in *Kamala chikitsa prakaranam* of *Vaidya chinthamani* has indications like *Halimaka, Pandu, and Kamala*. Hence in this study, hepatoprotective activity of *Amalakyadi leha,* mentioned in *Vaidya chinthamani*, was evaluated. The present study was conducted at the College of Veterinary and Animal Sciences, Pookode, Wayand. 36 male Wistar albino rats were randomly divided into 6 groups. *Amalakyadi leha* was given in Low doses, Therapeutic dose, and High dose for 14 days and Silymarin was the standard drug. Paracetamol was given to all groups except the normal group on the 14th day to induce hepatotoxicity. On the 15th day, animals were sacrificed in a diethyl ether chamber, and blood samples were collected for analyzing blood parameters. Liver tissues were collected a n d preserved f o r performing histopathological studies. Estimating blood parameters shows that the Low dose and Therapeutic dose of *Amalakyadi leha* have hepatoprotective action as that of silymarin. Even though High dose exhibited hepatoprotective action, the effect was not as much as silymarin and other doses of *Amalakyadi leha*. The hepatoprotective effects of the drug were also confirmed by histopathological examination of the liver section of standard drug, paracetamol, and *Amalakyadi leha* treated groups of rats. The study established that *Amalakyadi leha* possesses significant Hepatoprotective activity comparable to silymarin in Paracetamol-induced liver damage.

Keywords*: Amalakyadi leha*; Hepatotoxicity; Paracetamol; Silymarin.

INTRODUCTION

Ayurveda promotes a comprehensive approach to both the prevention and treatment of human illness. The major goal of *Ayurveda* is to use a methodical approach to uphold a healthy lifestyle to enhance people's mental, physical, and spiritual capacities. Chronic degenerative diseases, heart diseases, and liver diseases are major global health concerns for people today. In these circumstances, the research in *Ayurveda* combined with advanced scientific techniques may give a better outcome in the treatment.

The liver plays a crucial role in breaking down and detoxifying drugs, still, ironically, drugs and their byproducts can harm the liver, leading to drug induced liver damage that can mimic natural liver conditions[1]. Common symptoms of liver damage or disease include yellowing of the skin and eyes (jaundice), exhaustion, itching, pain in the upper right abdomen, nausea, loss of appetite, bloating, and intestinal bleeding. The metabolism of carbohydrates, proteins, lipids, hormones, bilirubin, porphyrin, bile salts, and many other drugs is largely controlled by the liver. Drug induced injury to the liver is of 2 types. The first type is predictable and dose-dependent and the other type is due to the idiosyncrasy of the drug which is unpredictable and independent of the dose[2]. Liver injury is a possible consequence of ingestion of any xenobiotic industrial toxins and pharmacologic agents. Drug-induced liver injury is the leading cause of acute liver failure among patients, accounting for the majority of cases[3].

Liver can be considered as *Yakrit* according to *Ayurvedic* concepts. One *Nirukti* of *Yakrit* is "*yathaa tathaa karoti yakrit* [4]. It means that it can function as per the needs of the body. According to the demands of the system, it performs metabolic as well as detoxification processes. *Yakrit* is mentioned as the root of *Rakta vaha srotas* and *Kamala* is a disease of *raktavaha srotas.* Furthermore, *Kamala* is classified as a *pithaja vyadhi*, with *ranjaka pitha* being the specific subtype of *pitha* involved in its development. Given that the liver is the primary site of *ranjaka pitha*, it is clear that *Kamala* is a liverrelated condition. To treat *Yakrit vikaras,* medications that alleviate *Pitha* and *Raktha are* used. *Amalakyadi leha*, mentioned in *Kamala* chikitsa *prakaranam* of *Vaidya chinthamani* contains drugs that show hepatoprotective effects in various in-vivo studies. This *leha* is indicated mainly in *Halimaka, Pandu,* and *Kamala.* Hepatotoxicity is one of the main reasons behind the withdrawal of certain medicines from the market. The study on drugs with hepatoprotective effects will be helpful to humanity. Protecting the liver is essential because it is the organ where detoxifying activities are carried out. As the prevalence rates for liver disorders are increasing day by day, the study will be beneficial to mankind.

MATERIALS AND METHOD

Ingredients and useful part of *Amalakyadi leha*[5]

Sl no	Name of drug	Botanical name	Malayalam name	Useful part	Quantity
1	*Amalaki*	*Emblica officinalis*	*Nellikka*	Fruit	128 parts
2	*Pippali*	*Piper longum*	*Thippali*	Fruit	8 parts
3	*Yashtimadhu*	*Glycyrrhiza glabra*	*Irattimadhuram*	Stem	1 part
4	*Draksha*	*Vitis vinifera*	*Unakkamunthiri*	Fruit	8 parts
5	*Sunti*	*Zingiber officinale*	*Chukku*	Rhizome	1part
6	*Tugakshiri*	*Maranta arundinaceae*	*Koovanooru*	Rhizome	1part
7	*Sarkara*	Sugar	*Panchasara*		25 parts
8	*Madhu*	Honey	*Thenu*		8 parts




Amalaki ***Sunti*** ***Pippali*** ***Draksha***

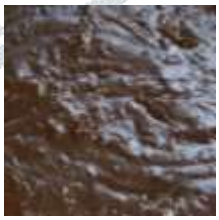



Tugaksheeri **Honey** **Sugar** ***Yashtimadhu***

METHOD OF PREPARATION OF *AMALAKYADI LEHA*

This was prepared in a wide-mouthed vessel and a spatula was used for mixing the medicine. 640 ml of filtered *Amalaki swarasa* was taken in a clean dry stainless steel vessel, to this *swarasa* 125g of prepared *sarkara* was dissolved. This was filtered through a double-folded cloth to remove the physical impurities. The mixture was then transferred to a clean, dry, wide-mouthed bronze container. Mild heat was given throughout the procedure and continuous stirring was maintained till it attained a thick consistency and a two-thread structure were formed, when one or two drops of this were kept over the thumb and tried to stretch index finger, at this stage, 40 g of *draksha kalka* along with *prakshepaka dravya* (40g *Pippali,*5g *Yashti madhu*,5g *Sunti*,5g *Tugakshsiri)* were added slowly with continuous stirring and processed into *lehyapaka.* Once *paka lakshanas* were observed gas was turned off. Once cooled, 125g of honey was added to the mixture at this stage. The contents were stirred continuously till the blend became homogenous and semisolid mass. 412 g of *Avaleha* was obtained. This prepared *avaleha* was stored in an airtight plastic container.



(a) **(b)** **(c)** **(d)**

(a)Sieving of *Prakshepaka dravya (b)Amalaki swarasa (c)* Boiling of *Amalaki swarasa* (d) Finished product

EXPERIMENTAL STUDY

Objective: To investigate the in-vivo study on the Hepatoprotective activity of *Amalakyadi leha* in Paracetamol-induced hepatotoxicity in male Wistar albino rats.

Locale of the study: The Experimental trial was conducted in the Animal House of the College of Veterinary and Animal Sciences, Pookode, Wayanad.

Chemicals and requirements: Distilled water, Diethyl ether, Equipment, and Glassware, Glass beakers and stirrers, Feeding tube, Disposable syringe Weighing machine,Camera, Hand gloves, Cotton roll, Vacutainer, Eppendorf tube, UV-visible spectrophotometer, Precision balance, Refrigerator, Mortar and pestle, Centrifuge, Semi auto analyzer, Micropipette

Route of administration: Oral route with a tuberculin syringe tube to prevent oral injury.

METHOD

Selection of Animal species: Rats are the preferred rodent species.

Housing conditions: The animals were housed in cages made of polypropylene, with paddy husk used as bedding material to line the bottom of the cages. The temperature in the experimental room was around 24^0 C (+/- 3^0 C). Lighting was natural, the sequence being a 12-hour dark/light cycle.

Feeding schedule: Animals were provided standard food pellets and purified water ad libtum.

Preparation of cages: All the cages used for the experiment were cleaned before the commencement and during the experimentation.

Preparation of animals: Before the experiment, the animals were randomly chosen and acclimated to their laboratory cages for a minimum of 7 days. Before the study began, all Wistar albino rats underwent a thorough examination, which included:

- Verification of sex and weight.
- Evaluation for any abnormal behaviour or health issues.

IN-VIVO STUDY

- Estimation of liver function
- Histopathology study

EXPERIMENTAL ANIMALS

Studies were carried out after receiving requisite approval from IAEC (Approval no: IAEC NO: CVAS/MTY/IAEC/24/61). The weight of rats used in this study was between 150 to 200g, hence the dose of paracetamol, silymarin, and the trial drug were fixed accordingly. Each cage contained 3 rats. Total animals were maintained in 12 cages.

Grouping of Animals

Group No:	Group name	No: of rats
1	Normal	6
2	Control (Paracetamol only)	6
3	Low dose *Amalakyadi leha* + Paracetamol	6
4	Therapeutic dose of *Amalakyadi leha* + Paracetamol	6
5	High dose *Amalakyadi leha*+ Paracetamol	6
6	Silymarin + Paracetamol	6

DOSE FIXATION:

The dose for the study was confirmed by referring to the table of Paget and Barnes (1964). The human dose was converted to the animal dose based on the body surface area ratio. Human dose × conversion factor (0.018) for rat = 'x' g /200g. According to AFI the human dose of *Leha* is 10g/day

Rat dose = 10×0.018 = 0.18g/200 g.

The dose calculated as per Paget and Barnes equation

TD-180 mg/200g

HD-360 mg/200g

LD-90mg/200g

Dose fixation of Silymarin: Silymarin is used as a standard Hepatoprotective drug. It was dissolved in distilled water for the administration of animals. Silymarin Dose – 100 mg/kg body weight orally .

EXPERIMENTAL PROTOCOL

The appropriate dose of paracetamol was dissolved in water and the suspension was given to experimental animals according to their body weight. Silymarin was available in powder form for research purposes. Powdered Silymarin was dissolved in distilled water.The experimental animals were given the resulting suspension taking into account their body weight. The trial drug administration had been fixed for 14 days followed by paracetamol intake after overnight fasting. Based on the trials the paracetamol administration was fixed for one day. A total of 36 Wistar rats were separated into 6 groups, each with 6 animals. G1 served as the normal group and G2 as a control group and received 3g/kg of paracetamol. *Amalakyadi leha* was given orally to G3, G4, and G5 for 14 days at doses, of 90 mg (low dose), 180 mg (therapeutic dose), and 360 mg (high dose) respectively. Silymarin (100 mg /kg b.wt.) was continuously administered to animals in group 6 for 14 days. On the 14th day paracetamol (3g/kg body weight) was given to all groups except the normal group, one hour after the administration of *Amalakyadi leha*. On the 15th day, all the animals were sacrificed by anesthetic overdosage. Blood was collected from the tail vein. The serum was separated after centrifuging the blood sample for 10 minutes at 3000 rpm. The liver was collected, packed, and stored at -80 ^{0} C. A section of the liver sample was put in 10% formalin solution and sent for histopathological study.

Animals used for Experimental study

Oral administration

Blood collection

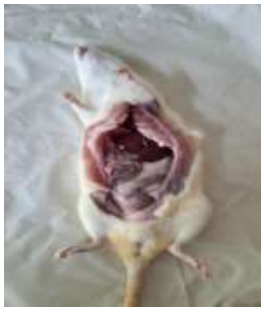
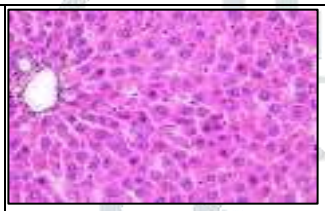
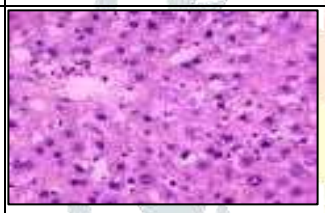
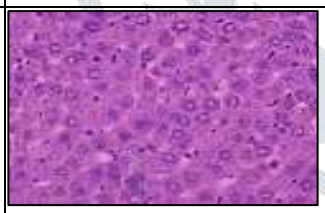
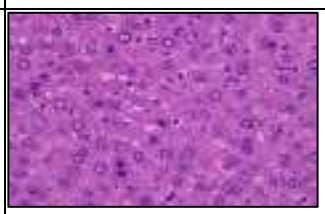
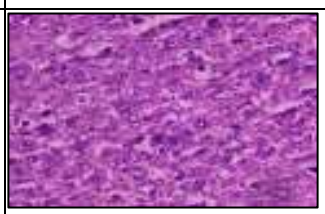


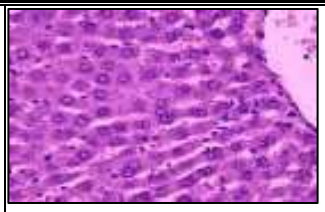
Fig no: 26 (a, b, c): Dissection of rat

EXPERIMENTAL STUDY

GROUP	DOSE	SGOT	SGPT	ALP	Albu min	Total protein	Total bilirubin
I	**Normal group**	22.688	26.190	18.33	5.485	6.262	0.583
II	**Paracetamol control group**	260.19	138.55	341.7	4.168	8.367	1.133
III	**Half dose**	122.66	58.723	146.46	3.853	6.865	0.515
IV	**Therapeutic dose**	41.812	61.275	171.1 2	4.188	7.063	0.672
V	**Double dose**	201.30	67.790	307.6	3.458	5.475	0.737
VI	**Silymarin treated group**	128.04	52.690	255.21	4.015	10.31 0	0.533

HISTOPATHOLOGY

Normal group		It shows liver tissue with normal portal triads and venous systems. Hepatocytes are normal and they are arranged in cords. Kupffer cells and sinusoidal spaces are normal.
Paracetamol treated group		Extensive multifocal areas of vacuolar degenerative changes can be seen in hepatocytes. Increased number of mononuclear cells in the portal area. Mild congestion is noticed in the central vein and hepatic sinusoids.
LD of *Amalakyadi leha* + Paracetamol Treated Group		Hepatocytes which are arranged in cords. Focal areas of vacuolar degenerative changes can be seen. A small number of erythrocytes are noticed in the hepatic sinusoids. Portal triad, sinusoidal space, and Kupffer cells appear normal.
TD of *Amalakyadi leha* + Paracetamol		Hepatocytes which are arranged in cords. Intracytoplasmic vacuoles can be seen in some hepatocytes. Mild congestion in the central vein. A small number of erythrocytes noticed in the hepatic sinusoids. Portal triad and Kupffer cells appear normal.
HD of *Amalakyadi leha*+ Paracetamol		Hepatocellular degenerative changes. Diffuse areas of varying degrees of vacuolar degeneration are noticed in the hepatocytes. Pyknotic nuclei can be seen in some hepatocytes. Mild congestion is noticed in the central vein and hepatic sinusoids.

Silymarin+ Paracetamol group		Liver tissue with normal architecture. Mild congestion was noticed in the central vein. Normal hepatocytes which are arranged in cords and a small number of erythrocytes are noticed in the hepatic sinusoids. Portal triad, sinusoidal space, and Kupffer cells appear normal.

DISCUSSION

The Liver can be considered *yakrit* according to the *Ayurvedic* concept. In the etiopathogenesis of *Yakrit rogas, Vidahi annapana* leads to *pitha prakopa* and thereby *rakta pradoshaja rogas* like *yakrit pleeha roga* and *kamala*. In dealing with problems of the liver, the primary goal is to enhance liver detoxification processes and help to protect against further liver damage. *Amalakyadi leha* mentioned in *Vaidya chinthamani Kamala chikitsa prakaranam* contains medicines that show a liver protective effect in various in vivo studies.

Sl no:	**NAME OF DRUG**	***RASA***	***GUNA***	***VIRYA***	***VIPAKA***	***KARMA***
1	*Amalaki*	*Lavana varjita pancha rasa*	*Laghu, Ruksha*	*Seeta*	*Madhura*	*Tridosha hara*
2	*Pippali*	*Katu*	*Laghu, Snigdha Tikshana*	*Anushna seeta*	*Madhura*	*Kapha vataghna*
3	*Yashtimadhu*	*Madhura*	*Guru, Snigdha*	*Seeta*	*Madhura*	*Pitha vata hara*
4	*Draksha*	*Madhura*	*Guru,Snigdha, Mrdu*	*Seeta*	*Madhura*	*Vata pitha samaka*
5	*Sunti*	*Katu*	*Laghu,Snigdha*	*Ushna*	*Madhura*	*Kapha vata hara*
6	*Tugakshiri*	*Madhura*	*Ruksha, Laghu*	*Seeta*	*Madhura*	*Pithahara*
7	*Sarkara*	*Madhura*	*Guru, Snigdha*	*Seeta*	*Madhura*	*Pitha hara*
8	*Madhu*	*Madhura ,Kashaya*	*Laghu, Ruksha*	*Ushna*	*Katu*	*Tridoshaghna*

Amalakyadi leha predominantly having *Madhura rasa, Laghu snigdha guna, seeta veerya, madhura vipaka,* and mainly *vata pitha hara* property. In this formulation, *Amalaki* is the main ingredient. It has *lavana varjitha pancha rasa, laghu ruksha guna, madhura vipaka* and *tridosha hara* property. Most of the drugs shows *deepana, pachana,*and *ruchya* property. So the formulation augments *jatharagni* as well as *dhatwagni* up to optimum level. *Pippali* is said to be an enhancer of bioavailability as it increases intestinal absorption and subsequently absorption of other drugs. *Draksha* having *snigdha guna* decreases the *ruksha guna* of *vata dosha* and diminishes the vitiated *pitha doshas. Amalaki* which is considered as best *rasayana* drug, improves general health and immunity. *Yashtimadhu* being *Madhura* in *rasa* and *vipaka*, acts to minimize the effect of elevated *pitta dosha. Shunti* is one of the good appetizers which also has *aamahara* property and therefore it enhances *agnideepana karma. Tugakshiri* is *deepana pachana* and *madhu* is *yogavahi* and *tridosha samaka*. It also shows the action of *chedhana, sandhana, ropana, and krimighna*. *Sita* has *vata pithahara* property. In brief, most of the drugs possess *madhura rasa,laghu snigdha guna,seeta veerya, madhura vipaka* and *pitha samana* properties. So *Amalakyadi leha* can be effectively used in *Yakrit rogas.*

Paracetamol overdose results in liver damage and failure due to excessive formation of NAPQI, which occurs when the usual metabolic pathways of glucuronidation and sulfonation are affected. It results in mitochondrial dysfunction and severe liver cell death.

Ingredients like *Amalaki* and *sunti* have hypolipidemic effects which prevent the free fatty acid formation and thus repress the further fatty acid accumulation in the liver. *Amalaki* and *Pippali* have hypoglycemic properties which decrease glycogenesis and necessitate usage of accumulated fat. *Amalaki* has hepatoprotective activity and *sunti* has anti-inflammatory activity that inhibits the pathogenesis which leads to hepatitis. As per previous studies, the phytochemicals in *amalaki* such as gallic acid, ellagic acid, quercetin, and corillagin have hepatoprotective properties against a variety of xenobiotic substances. It is also known that *Pippali* contains various alkaloids like piperine, piper longumine, and piper longuminine, which help in the regeneration of hepatocytes. *Pippali* shows an antihepatotoxicity effect due to an increase in SOD and a decrease in lipid peroxidation. It is proven that *Vitis vinifera* is a stupendous source of vitamins, minerals, and other active ingredients. Grape juice and seeds are rich sources of flavonoids, such as catechins, epicatechins, anthocyanidins, proanthocyanidins, and resveratrol. It is capable of reducing carbonyl and lipid peroxidation levels in the plasma and liver. It has anti-oxidant activity for the prevention of oxidative damage to tissues, by reducing lipoperoxidation or inhibiting the production of free radicals. About the grape's phytochemicals, resveratrol has been the most studied of these compounds as a possible hepatoprotective agent. As we know, honey is rich in phenolic acids, flavonoids, bioactive compounds, and phenol contents, which contribute to its antioxidant and potential health benefits. Phenolic acids and flavonoids could ameliorate NAFLD by activating the adiponectin /AMPK pathway. *Yashtimadhu* contains glycyrrhizin and glycyrrhetic acid which decreases serum bilirubin and promotes its excretion in urine. *Sunti* acts as hepatoprotective, due to the presence of volatile oils. Gingerol 1 has various pharmacological and physiological effects including anti -inflammatory and anti-hepatotoxic activities.

HEPATIC PARAMETERS

The liver sustains the greatest degree of tissue injury by certain drugs and its metabolites because it is the primary site of metabolism. The study of different enzyme activities has great value in the assessment of clinical and experimental liver damage. Elevation in serum enzyme levels and decrease in serum protein levels were taken as indicators of liver damage. The rise in liver enzyme levels in serum is due to the deterioration of the structural framework of the liver as they are cytoplasmic in location and released into circulation after cellular damage.

SGOT (AST)

SGOT level elevated significantly in the Paracetamol alone treated group when compared to the normal group. An increase in serum concentrations of SGOT level suggested disruption of plasma membrane integrity, which finally led to the escape of the enzyme into the blood circulation. Compared to the paracetamol control group, *Amalakyadi leha,* and Silymarin-treated groups showed major decline in SGOT. The Therapeutic dose and Low dose of *the Amalakyadi leha* treated group showed significant hepatoprotection than Silymarin treated group. However a high dose of *Amalakydi leha* treated group had higher levels of SGOT than that of Silymarin treated group, but low as compared to Paracetamol alone treated group. So Therapeutic dose and low dose of *Amalakyadi leha* were found to be more effective than Silymarin. Restoration of SGOT level suggested that *Amalakyadi leha* could potentially restore hepatic cells, or more specifically the integrity of cell membrane and the normalization of hepatocytes into their normal tissue architecture.

SGPT (ALT)

SGPT has a significant role in amino acid metabolism and gluconeogenesis. Normal levels are in the range of 5-50 IU/L. Estimation of SGPT is a more specific test for detecting liver abnormalities since it is primarily found in the liver. SGPT levels are very high in patients of viral hepatitis, hepatic necrosis, post hepatic jaundice, intrahepatic cholestasis, cirrhosis, and alcoholic hepatitis. In the present study, the Paracetamol alone treated group showed an exceptional increase in SGPT value, which is a clear indicator of liver damage. It is a sensitive indicator of acute liver damage and elevation of this enzyme in non-hepatic diseases is usually unusual. It is more selectively a liver parenchymal enzyme than AST. A lowering of SGPT was found by the *Amalakyadi leha* treatment at high, therapeutic, and low doses (67.790+/-12.024,61.275+/-6.076 and 58.723+/-17.618 IU/L, respectively). These results were significant in the restoration of SGPT level when

compared to the paracetamol alone group but not as much as in the Silymarin-treated animals (52.690+/-24.493 IU/L). Liver damage was significantly corrected in *Amalakyadi leha*-treated groups. Restoration of SGPT level suggested that *Amalakyadi leha* could potentially restore hepatic cells, or more specifically the integrity of cell membrane and the normalization of hepatocytes into their normal tissue architecture.

ALP

It is also found in bone, placenta, kidney, and intestines, besides its main location. Normal levels are in the range of 20-120 IU/L. The increase in serum ALP levels in the paracetamol-induced liver damage group is likely due to increased synthesis caused by elevated biliary pressure, indicating pathological changes in biliary flow. Additionally, Paracetamol-induced toxicity in rats may disrupt liver membrane structure and function, as well as lipid metabolism, leading to changes in membrane fluidity, permeability, enzyme activity, and transport systems, ultimately affecting lipid transport in the liver. In the study, the paracetamol-alone treated group showed a significant increase in ALP levels. Paracetamol consumption causes both plasma and organelle membrane damage. Due to damage to the structural integrity of the hepatic cells by paracetamol, the enzymes ALP located in the cytoplasm may be released into the circulation. That causes an increase in ALP values in the control group. Compared to the paracetamol control group, *Amalakyadi leha,* and Silymarin-treated groups showed significant reduction in ALP. Therapeutic dose and low-dose treated groups of *Amalakyadi leha* had also shown decreased ALP activity showing moderate restoration. Here hepatoprotection provided by *Amalakyadi leha* on a therapeutic dose and low dose were more than that of the standard drug Silymarin. *Amalakyadi leha* in double dose provides hepatoprotection though, it is less than that of the standard drug silymarin. In brief *Amalakyadi leha* has shown decreased ALP activity which may be due to the high antioxidant potential of *Amalakyadi leha.*

BILIRUBIN

Bilirubin is an endogenous anion derived from the regular degradation of hemoglobin from the red blood cells and excreted from the liver in bile. It is normally present in blood in small amounts and used by the liver to produce bile. Normal level ranges from 0.2-1.2 mg/dL. When the liver cells are damaged, they may not be able to excrete bilirubin in the normal way, causing a build-up of bilirubin in the blood and extracellular fluid. In acute human hepatic injury, total bilirubin can be a better indicator of disease severity compared to ALT. An increase in total bilirubin concentration in the serum of Paracetamol-induced Wistar rats might reflect increased hemolysis, decreased conjugation, or defects in bilirubin transport. Normal, standard, and *Amalakyadi leha* treated (LD, TD, HD) groups show a substantial decrease in total bilirubin as compared to the paracetamol control group.

TOTAL PROTEIN

It helps differentiate between normal and damaged liver function as the majority of plasma proteins like albumin and globulin are produced in the liver. Total protein is often reduced slightly but the albumin globulin ratio shows a sharp decline during hepatocellular injury. Its normal range is 6-8 g/dL.A low total protein level can suggest a liver disorder, a kidney disorder, or a disorder in which protein is not digested or absorbed properly. Generally, in hepatotoxicity, levels of total proteins are decreased, but in this study, these levels are increased compared to the normal group after hepatotoxicity induction. Compared to the normal group, the high-dose treated group showed a remarkable reduction in total protein level. Here dose and therapeutic dose treated group showed protective action. The high dose of *Amalakyadi leha* treated group shows a low mean total protein level as compared to the normal group.

ALBUMIN

Albumin is the most prevalent protein in plasma, comprising approximately 50% of the total protein concentration in healthy individuals, with levels ranging from 3.5 to 5 g/dL. The liver's hepatocytes produce albumin, which is then rapidly released into the circulation at a daily rate of 10-15 grams. Notably, the liver stores minimal amounts of albumin, with the majority being quickly secreted into the bloodstream.

Serum albumin plays a crucial role in transporting both endogenous and exogenous substances, including drugs, and significantly influences plasma oncotic pressure. In this study, no significant changes in albumin

levels were witnessed in groups treated with paracetamol alone, *Amalakyadi leha,* or Silymarin. This is because the liver stores a limited amount of albumin, and significant changes in albumin levels only occur when the liver is severely damaged. As a result, acute liver injuries or infections may not immediately affect albumin levels, as the liver's stored albumin is only released when the damage is extensive**.**

HISTOPATHOLOGY

The liver section histology of the normal groups displays liver tissue with normal portal triads and venous systems. Hepatocytes are normal and they are arranged in cords. Kupffer cells and sinusoidal spaces are normal. However, the group treated only with paracetamol showed extensive multifocal areas of vacuolar degenerative changes in hepatocytes. Increased number of mononuclear cells in the portal area. Mild congestion is noticed in the central vein and hepatic sinusoids. In the group treated with a low drug dose, hepatocytes are arranged in cords. Focal areas of vacuolar degenerative changes can be seen. A small number of erythrocytes are noticed in the hepatic sinusoids. Portal triad, sinusoidal space, and Kupffer cells appear normal. In the group treated with a therapeutic dose hepatocytes are arranged in cords. Intracytoplasmic vacuoles can be seen in some hepatocytes. Mild congestion in the central vein. A small number of erythrocytes noticed in the hepatic sinusoids. Portal triad and Kupffer cells appear normal. In the group treated with a double dose of *Amalakyadi leha,* the section shows liver tissue with diffuse areas of hepatocellular degenerative changes. Diffuse areas of varying degrees of vacuolar degeneration are noticed in the hepatocytes. Pyknotic nuclei can be seen in some hepatocytes. Mild congestion is noticed in the central vein and hepatic sinusoids. In Silymarin-treated groups, the section shows liver tissue with normal architecture. Mild congestion noticed in the central vein. Normal hepatocytes which are arranged in cords and small number of erythrocytes noticed in the hepatic sinusoids. Portal triad, sinusoidal space and Kupffer cells appear normal.

CONCLUSION

The study established that *Amalakyadi leha* possesses significant Hepatoprotective activity comparable to silymarin in Paracetamol-induced liver damage

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