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EXPERIMENTAL STUDY ON HEPATOPROTECTIVE ACTIVITY OF SHIRISHADI YOGA IN ACETAMINOPHEN INDUCED HEPATOTOXICITY IN SD (SPRAGUE-DAWLEY) RATS

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ABSTRACT

The liver, a critical organ for metabolism, detoxification, and homeostasis, is vulnerable to damage from toxins, including acetaminophen, a widely used analgesic and antipyretic drug. Excessive or prolonged acetaminophen use can induce severe hepatotoxicity, marked by oxidative stress, inflammation, and hepatic necrosis. Traditional medicinal systems like *Ayurveda* provide potential remedies for liver disorders. *Shirishadi Yoga*, a polyherbal *Ayurvedic* formulation, incorporates herbs such as *Shirisha* (Albizia lebbeck) and *Haridra* (Curcuma longa), celebrated for their hepatoprotective, detoxifying, and antioxidant effects. These herbs are thought to alleviate liver damage by reducing inflammation, neutralizing oxidative stress, and promoting tissue regeneration. This study investigates the hepatoprotective efficacy of *Shirishadi Yoga* against acetaminophen-induced liver injury. It assesses the formulation's ability to mitigate oxidative damage, normalize liver enzyme levels, and prevent histopathological changes in the liver. By leveraging its natural therapeutic properties, *Shirishadi Yoga* could emerge as a viable alternative for managing drug-induced hepatotoxicity, offering a holistic approach to liver health restoration and protection.

Keywords: Hepatotoxicty, *Shirishadi Yoga*, Liver, Acetaminophen

INTRODUCTION

The liver, as a vital organ, plays a central role in metabolic processes, detoxification, and maintaining homeostasis. However, it is highly susceptible to damage from various toxins, including drugs such as acetaminophen (paracetamol). Acetaminophen is widely used for its analgesic and antipyretic properties, but its overdose or chronic use can lead to severe hepatotoxicity, characterized by oxidative stress, inflammation, and liver cell necrosis. *Ayurveda* traditional systems of medicine offer promising therapeutic approaches for managing liver disorders. *Shirishadi Yoga,* an *Ayurvedic* polyherbal formulation, has been traditionally recognized for its hepatoprotective, detoxifying, and antioxidant properties. Comprising a combination of herbs like *Shirisha* (*Albizia lebbeck*), *Haridra* (*Curcuma longa*), and others, this formulation is believed to mitigate liver damage through its anti-inflammatory, antioxidant, and regenerative properties.

This study focuses on evaluating the hepatoprotective effect of *Shirishadi Yoga* against acetaminophen-induced hepatotoxicity. By exploring its potential to reduce oxidative stress, restore liver enzyme balance, and prevent histopathological damage, *Shirishadi Yoga* may offer a natural and effective alternative for managing drug-induced liver injuries.

Aims and Objectives of Research Work:

- To assess the hepatoprotective effect of *Shirishadi Yoga*
- To compare the hepatoprotective effect of *Shirishadi Yoga* in comparison to Silymarin as standard on Acetaminophen induced hepatotoxicity.

Materials and Methods

Materials

1) Trial Drug *(Shirishadi Yoga)*
2) Standard Drug (Silymarin)
3) Animals –36 males SD (Sprague-Dawley) rats
4) Toxicity drug (Acetaminophen)

Study Design: Animal Experimentation

- **Settings:** Toxicology Lab, CSIR-IHBT Palampur, HP
- The materials and techniques used in the present work are described in the following pages. Drugs (with information on sources) used for hepatoprotective evaluation are as follows:

1. Test Drug: *Shirishadi Yoga*

Shirishadi Yoga is the formulation which contains the drugs having *Vishghana* properties mentioned in different *Ayurvedic Samhitas.* This yoga contains *Shirisha (Ch. Su. 4/16), Haridra (Ch. Su. 4/16), Daruharidra (Raj Nighantu Pippalyadi Varg 202) , Nimba (Kaidev Nighantu Aushada Varga 883) , Manjistha (Ch. Su. 4/16)* in combined decoction form.

Table No. 1: a. Ingredients of *Shirishadi Yoga*

Ingredients	Scientific name	Family	Part used
Shirisha	*Albizzia lebbeck Benth*	*Leguminosae*	Bark
Haridra	*Curcuma longa* Linn.	*Zingiberaceae*	Rhizome
Daruharidra	*Berberis lycium* DC.	*Beberidaceae*	Root
Manjishtha	*Rubia cordifolia* Linn.	*Rubiaceae*	Root
Nimba	*Azadirachta indica A. Jugs*	*Meliaceae*	Leaf

b. Collection and Authentication of Ingredients of *Shirishadi Yoga:*

- All the drugs of *Shirishadi Yoga* were collected from Baijnath Pharmaceuticals Paprola, Distt. Kangra, Himachal Pradesh.

- All the drugs were authenticated from Department of Dravya Guna, R.G.G.P.G. Ayurvedic College & Hospital Paprola, Distt. Kangra (H.P)

c. Preparation of *Shirishadi Yoga:*

In *Shirishadi Yoga*, no *pramana* (proportion) of contents are mentioned, hence according to *Sharangadhara Samhita* "where no proportions are mentioned all contents of *yoga* is to be taken in same proportion"[1].

All the ingredients are taken in equal quantity. They are powdered separately; the fine powders of the ingredients are mixed well to form a homogenous mixture.

Preparation for *Shirishadi Yoga Kwatha:*

- *F*ine powder of *Shirishadi Yoga* is made. One *pala* of *dravya churna* mixed with sixteen parts of water in pan and boiled over *Mridu Agni* till the liquid reduced to one eighth part.[2]

Standard Drug:

Silymarin was kept as the standard drug. It was administered at a concentration of 100mg/kg body wt. It was obtained from Pharmacology and Toxicology lab CSIR-IHBT, Palampur.

Toxicants:

The toxicant used to induce hepatic injury in respective protocol was Acetaminophen =500mg/ kg Body wt I.P and was obtained from Pharmacology and Toxicology lab CSIR-IHBT, Palampur.

Dose Fixation:

a. Dose calculation of *Shirishadi Yoga Kwatha:*

Dose of *Kwatha* in *Sharangadhara Samhita* was given as 2 *Pala* i.e 96 ml.

So, Human dose of *Shirishadi Yoga* = 96 ml.

Conversion factor of rat (200g) = 0.018[3]

Dose of *Shirishadi Yoga Kwatha* in rat = 96 ml X 0.018. i.e. dose in rat = 1.728 ml/200g body weight (8.65 ml/kg body wt.)

b. Reference Standard

Silymarin - Rat dose =100mg/kg Body wt. mixed in Dimethyl Sulfoxide (DMSO)[4]

c. Toxicant

Acetaminophen(Paracetamol)- Rat dose = 500mg/ kg Body wt I.P.[5]

Route of Administration

The test drug *Shirishadi Yoga Kwatha* , Standard drug was administered orally by using rat feeding tube fixed to the syringe and toxicants were administered intraperitoneally by using syringe.

Drug Dosing Schedule:

In Acetaminophen induced hepatotoxicity model, test drug, reference standard and toxicants were administered simultaneously between 10 to 11am morning and between 5 to 6 pm evening for 6 days. Both treatment and disease were induced simultaneously.

Acetaminophen Induced Hepatotoxicity

Experimental protocol was approved by the Institutional Animal Ethics Committee of CPCSEA. All the animals used in this study received human care in compliance with CPCSEA guidelines.

Table No: 2 Experimental protocols

Group	Treatment	Number of animals/ Group
Group 1	Normal Control	6
Group 2	Acetaminophen Induced Hepatoxicity	6
Group 3	Acetaminophen Induced Hepatotoxicity + Silymarin (two times a day)	6
Group 4	**Acetaminophen** Induced Hepatotoxicity + *Shirishadi Yoga* (Low Dose) = 1 Pala (48ml)/(24gm) in the form of *Kwath* = 0.864ml/200 gm body weight	6
Group 5	**Acetaminophen** Induced Hepatotoxicity + *Shirishadi Yoga* (Normal Dose) =2 Pala (96ml)/(48gm) in the form of *Kwath* = 1.728ml/200 gm body weight	6
Group 6	**Acetaminophen** Induced Hepatotoxicity + *Shirishadi Yoga* (High Dose) =	6

	3 Pala (144ml)/(72gm) in the form of *Kwath* = 2.592ml/200 gm body weight	

The Test drug *Shirishadi Yoga* , reference drug silymarin, and the toxicant (acetaminophen) were administered for 6 consecutive days to each group except the control group. After 24hrs animals were made too fast overnight and sacrificed by CO_2 hypoxia and blood samples of animals were collected through retro orbital route for serum bio-chemical evaluations. All the animals were sacrificed by cervical dislocation. Liver was dissected out, cleaned to remove extraneous tissues, blotted to remove blood stain and weighed. A piece of liver tissue was preserved in 10% formalin for histopathological processing. Serum was separated and serum level of biochemical parameters namely Bilirubin, Protein, SGOT, SGPT, ALP, etc. were estimated as per standard procedure.

Analysis of Biochemical parameters:

The blood samples were collected into micro centrifuge tube (2ml) and were kept at room temperature for 2 hours. Then the samples were centrifuged at 5000rpm for 10 minutes. Now serum was aspirated and frozen at -80°C. The concentration of biochemical parameters was estimated by using automated biochemical analyser. The following parameters were assessed:

- SGOT
- SGPT
- Alkaline Phosphatase
- Total Bilirubin
- Direct Bilirubin
- Total Protein
- Albumin

Histopathology

A branch of pathology concerned with tissue changes characteristic of disease. It is a microscopic examination of tissue in order to study the manifestation of disease. Compound of three Greek words (histos- tissue, pathos- suffering, and logia- study of) refers to the microscopic examination of tissue to study the manifestation of disease.

Procedure followed to prepare histopathological slides fixation.

Animals were sacrificed at the end of the treatment schedule. Liver was isolated from animals and then stored in 10% formalin solution for fixation. The tissue sample was processed to make paraffin block which was then sectioned with microtome. The section was then stained with hematoxylin and eosin. Histology was then analyzed under microscope at magnification of 100x-400x.

Assessment Criteria:

All the observations were analysed statistically. Mean, standard deviation and standard error for each group was calculated. Statistical evaluation of the data was done by one way ANOVA and Tuckey's Multiple Comparison Test (post hoc). All the groups were compared with Normal Control, Diseased group and Standard Drug (Silymarin).

One way ANOVA and the Tuckey's Multiple Comparison Test were done with the help of Sigmastat 3 software package. The Multiple Comparison Test was performed only if the P value obtained from one way ANOVA was less than 0.05. If p value>0.05 means not significant.

DISCUSSION

The whole study has discussed under the following points –

1. Discussion on conceptual study
2. Discussion on drug review
3. Discussion on observation and results

1. Discussion on Literature

Toxic chemicals in the body can cause significant harm, impacting various organs, systems, and overall health. These substances can lead to cellular damage, disrupt metabolic functions, and increase the risk of diseases such as cancer, neurological disorders, and liver diseases. Liver plays an important role in maintaining the internal environment of the human body. The liver is crucial for metabolism and detoxification,

acting as a central hub for processing nutrients and neutralizing harmful substances. Metabolically, it converts carbohydrates, proteins, and fats into energy and essential compounds, regulates blood sugar levels, synthesizes proteins like albumin and clotting factors, and produces bile for fat digestion. In detoxification, the liver removes toxins, drugs, and waste products via a two-phase enzymatic process: Phase I makes toxins more reactive, and Phase II makes them water-soluble for excretion.

Acetaminophen (APAP), a common pain reliever, can cause liver damage (hepatotoxicity) in excessive doses. Normally, its toxic metabolite, N-acetyl-p-benzoquinone imine (NAPQI), is neutralized by glutathione. In overdose cases, glutathione depletion leads to NAPQI accumulation, causing severe liver damage. APAP hepatotoxicity remains a global concern, involving predictable pathways within hepatocytes but variable clinical presentations.

Agada Tantra is the branch of *Ashtanga Ayurveda* that addresses all toxicological issues. One of its distinctive contributions is *Gara Visha*. *Gara Visha,* also known as "concocted poison," is a synthetic poison that is made by mixing different inanimate and animated poisons. Food adulteration, incompatible food, various medicines etc., are a few examples of this. Modern lifestyle, eating, and other changes have led to a number of grave health problems. The idea of *Gara Visha,* as it is described in the classics, has many applications in modern culture. *Gara Visha* is associated with the majority of toxins that enter our bodies on a regular basis. They are known as "*Kalantaravipaki"* because they do not meet normally.

They attain the property of *Visha* and fiinally result in *Srotorodha* and *Agnimandya*. Any toxin that enters our body can hamper *Agni* which in turn alters the process of *Dhatuparinama*. *Yakrita* and *Pliha* are considered to be the *Moolasthana* of *Raktavaha Srotas*. It is a site of *pita* as well. Thus, it is the controller of many *Paittika* and enzymatic activities of the body.

In the present study, paracetamol induced hepatotoxicity is compared with *Gara Visha.*

Discussion on Drug Review & Probable Mode of Action

Table 3: Pharmacodynamics of the ingredients of *Shirishadi Yoga*

Sr No.	Drug	*Rasa*	*Guna*	*Virya*	*Vipaka*	*Karma*
1.	*Shirisha* [6]	*Tikta* (Bitter), *Katu* (Pungent), *Kashaya*,	*Laghu* (Light)	*Anusna*	*Katu*	*Vishaghna* (Antipoisonous), *Tvagdosha (For* skin disorder*), Tridoshara (*Balance *Vatta Kapha Pitta* humor, *Sothahra* (Antiinflammatory), *Varnya* (Complexion promoter)
2.	*Haridra*[7]	*Tikta* (Bitter), *Katu* (Pungent)	*Laghu* (Light), *Ruksha* (Dry)	*Ushna* (Hot)	*Katu*	*Kushthaghna (*Antileprotic), *Kandughna* (Antipruritic), *Vishaghna* (Antipoisonous), *Lekhaniya* (Aids in reducing corpulency), *Krimighna* (Antihelmentic), *Kaphavatarakta doshahara* (Balance *Kapha Vata* and *Rakta* humor)
3.	*Daruharidra*[8]	*Tikta* (Bitter), *Kashaya* (Astringent)	*Laghu* (Light), *Ruksha* (Dry)	*Ushna* (Hot)	*Katu*	*Kandughna* (Antipruritic), *Vishahara* (Antipoisonous), *Shophahara* (Anti-inflammatory), *Kaphapittahara* (Balance *Kapha Pitta* humor)
4.	*Manjishtha*[9]	*Tikta* (Bitter),	*Guru*	*Ushna*	*Katu*	*Shothahara* (Antioedematous,

		Kashaya (Astringent), *Madhura* (Sweet)	(Heavy, *Ruksha* (Dry)	(Hot)		*Vranaropana* (Wound healing), *Kushthaghna* (Antileprotic), *Deepana* (Gastrostimulant), *Pachana* (Digestive), *Stambhana* (Antihemorrhagi), *Krimighna* (Antihelmentic), *Raktashodhaka* (Blood purifier), *Varnya* (Complexion promoter), *Rasayana* (Rejuvenant), *Kapha-Pittashamana* (Balance *Kapha Pitta* humor)
7.	*Nimba*[10]	*Tikta* (Bitter), *Kashaya* (Astringent),	*Laghu* (Light),	*Shita* (Cold)	*Katu* (Pungent)	*Kaphapittahara* (Balance *Kapha Pitta* humor), *Kandughna* (Antipruritic), *Kushthaghna (*Antileprotic), *Varanpachna, Vranshodhna (*wound purification), *Rochan(appetiser), Grahi, Dahprashman* (Relieving burning sensation*)* , *Raktvikar shodhna* (Blood purifier), *Vednasthapna* (Analgesic*), Jwarghan* (antipyretic), *Krimighna* (Antihelmentic), *Vishahara* (Antipoisonous),

An antitoxic medicine should have properties like *Deepana, Pachana, Srotoshodhana, Raktashodhaka*, and *Vishahara* etc. Together, this formulation has *Katu Tikta, Kashaya* and *Madhura rasa, Katu Vipaka, Ushna Virya,* and *Laghu Ruksha Teekshna Guna*. The composition of the individual medications in *Shirishadi Yoga* may have been influenced by the properties of *Vishaghna, Shothaghna, Krimighna, Deepana, Pachana, Vranahara, Garanashaka,* and *Raktashodhaka.* Therefore, *Shirishadi Yoga* is thus capable to take action due to its *Vishaghna Guna.* Literature reveals that various ingredients of *Shirishadi Yoga* have antioxidants, immuno-modulatory, anti-inflammatory, anti-ulcerative & hepatoprotective actions.

Previous studies have also proved the hepatoprotective and antioxidant effect of most of the ingredients of *Shirishadi Yoga. Shirishadi Yoga* may act by – 1. Prevent synthesis of prostaglandins, which may help as anti-inflammatory. 2. It may suppress CYP450, which plays important role in producing toxic metabolite (NAPQI). 3. May be by increasing synthesis of Glutathione (GSH). Thus, the above said actions of *Shirishadi Yoga* may contribute towards its hepatoprotective activity.

Discussion on observation and results

Table No. 4 Biochemical parameters

Group	**SGOT(IU/L) [Mean±SD]**	**SGPT(IU/L) [Mean± SD]**	**Total Bilirubin BIT (mg/dl) [Mean ± SD]**	**Direct Bilirubin BID (mg/dl) [Mean±SD]**	**Alkaline Phosphate ALP (IU/l) [Mean ± SD]**	**Albumin (g/l) [Mean±SD]**
Normal Control (NG)	156.6±5.785	110.56±6.33	0.07±0.02	0.09±0.03	168.4±46.83	2.77±0.807
Acetaminophen alone (DG)	186.6±5.785	148.83±8.91	0.13±0.02	0.68±0.22	290±33.8	4.81±0.508
Shirishadi Yoga (low dose)	171.6±5.574	137.11±3.91	0.076±0.02	0.15±0.03	153.3±24.7	2.6±0.22

Shirishadi Yoga (normal dose)	166.6±5.785	118.96±3.00	0.073±0.02	0.10±0.04	132.5±22.25	2.87±0.24
Shirishadi Yoga (high dose)	151.0±12.744	96.88±20.72	0.08±0.01	0.10±0.01	163.0±46.16	2.83±0.15
Silymarin (SIL)	166.8±5.913	121.61±2.92	0.09±0.03	0.12±0.04	215.8±132.9	3.19±0.49

Discussion on serum biochemical parameters, Liver Function Test

Any rise in liver enzyme levels suggest damage of structural integrity of liver. The assessment of enzyme activities like SGOT, SGPT, ALP, Total bilirubin etc. have been found to be of great value in assessment of liver damage.

Discussion on SGPT values:

SGPT is the enzyme produced by liver responsible for metabolism and release of energy from nutrients. Increased SGPT level indicates pathological conditions of liver cell including inflammation and necrosis of hepatocytes.

In this study test results shows standard group and test groups (all the three *Shirishadi Yoga* (LD), *Shirishadi Yoga* (ND) and *Shirishadi Yoga* (HD) got prevented from acetaminophen induced liver toxicity. In case of disease control group, there is significant increase in SGPT level due to acetaminophen induced toxicity. Test drug *Shirishadi Yoga* (ND) shows reversal of hepatotoxicity.

Discussion on SGOT values:

There is a significant rise of SGOT level in disease group, indicates inflammation of liver tissue due to acetaminophen toxicity. But in the case of standard group and test groups there is a significant decrease in the level of SGOT which shows reduced hepatotoxicity, at the same time test drug *Shirishadi Yoga (ND)* shows values almost equal to the standard drug Silymarin.

Discussion on Total Bilirubin:

Bilirubin level increases in blood due to several conditions such as disease of hepatocytes, obstruction to the biliary excretion into the duodenum, in hemolysis and defect of hepatic intake and conjugation of bilirubin pigment such as Gilbert's disease.

Bilirubin a breakdown product of porphyrin ring of heme containing protein are found in the blood in two fractions- conjugated and unconjugated. Conjugated bilirubin is water soluble. In conjugated hyper bilirubinemia the rate of secretion of conjugated bilirubin into the bile or the flow of bile into the intestine reduces. Due to the reflex of conjugates back into the plasma elevated level of conjugated bilirubin level usually indicates hepatobiliary disease.

In the present study disease control group shows a significant increase in the bilirubin value after inducing acetaminophen, In test groups *Shirishadi Yoga* (LD), *Shirishadi Yoga* (ND), *Shirishadi Yoga* (HD) there is significant decrease in the values and the decrease is more evident in test groups, while standard group shows no evident decrease in total bilirubin levels.

Discussion on Direct Bilirubin:

There is a significant rise of direct bilirubin level in disease group, but in the case of standard group and test group *Shirishadi Yoga* (LD), *Shirishadi Yoga* (ND), *Shirishadi Yoga* (HD) there is a significant decrease in the level of Direct Bilirubin which shows reduced hepatotoxicity.

Discussion on Alkaline Phosphatase (ALP) values.

Alkaline phosphatase mainly produced by bones, liver, intestine and placenta and excreted through bile. Increased level of ALP in blood indicates diseases of bone, liver or in pregnancy. If we exclude diseases of bone and pregnancy, an increased level of ALP generally indicates hepatobiliary disease.

In the present study, ALP values showed significant increase in acetaminophen group when compared to control group. All the three groups of test drug *Shirishadi Yoga* (LD), *Shirishadi Yoga* (ND), *Shirishadi Yoga* (HD) and standard drug silymarin show decrease in ALP values. But the decrease is more evident in *Shirishadi Yoga* (ND) than standard drug silymarin.

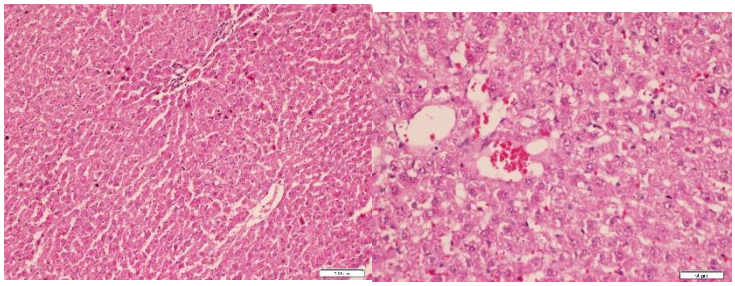
Discussion on Albumin:

The liver plays a vital role in protein metabolism, including deamination and transamination of amino acids, plasma protein synthesis, and removal of ammonia to urea in the urine. Several of the enzymes used in the amino acid metabolism pathways (for example, ALT/AST) are commonly assayed in serum to assess liver damage since they are present at much higher concentrations in the liver than in other organs. Total protein is often reduced slightly but the albumin globulin ratio shows decline during hepatocellular injury. Albumin, which is the main protein in human blood, plays a major role in maintaining plasma osmotic pressure as well as transportation of lipids and hormones. Some liver injury can affect the concentrations of plasma albumin, and the clinical presentations are hypoalbuminemia and hyperglobulinemia.

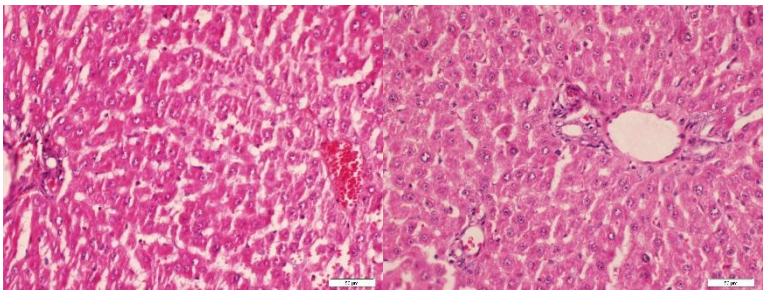
In the present study, albumin concentration increased significantly in acetaminophen group as compared to control. All the three groups of test drug *Shirishadi Yoga* (LD, ND, HD) and standard drug silymarin was effective in normalizing the levels of albumin. Silymarin shows higher hepatoprotection when compared to all doses of *Shirishadi Yoga*

Discussion on histopathology report

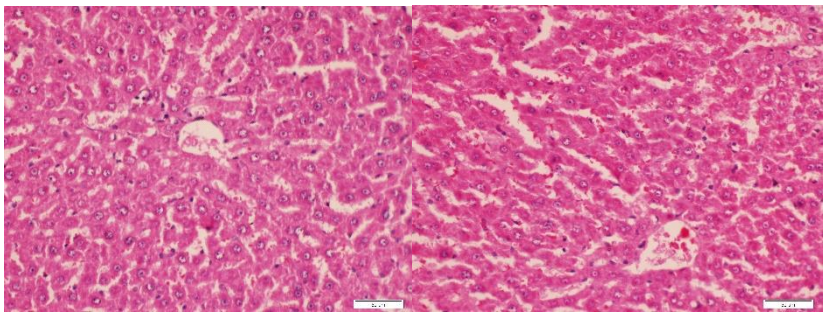
Histopathological Analysis



Normal Control ***Disease Group***



Silymarin ***Shirishadi Yoga (Low Dose)***



Shirishadi Yoga (Normal Dose) ***Shirishadi Yoga (High Dose)***

While observing the histopathological findings in the present study, there is no abnormality detected in the case of normal group. Examination reveals normal cellular features of hepatocyte with normal vascular tissue in the hepatic parenchyma also there was not any inflammatory or degenerative pathological changes.

At the same time, in the disease control group moderate changes are observed. Degenerative changes were seen in the hepatoparenchyma with cellular swelling. Hepatic necrotic changes with loss of nucleus were noted. Focal vascular congestion with hemorrhages in hepatic parenchyma.

When was administered in *Shirishadi Yoga (*low dose) section shows normal portal triads and central venous system. Many hepatocytes are normal. Sinusoidal spaces cells show mild increase, no inflamatory changes are seen. *At Shirishadi Yoga* (Normal dose) section shows normal portal triad and hepatic veins. Hepatocytes look normal in structure but mild inflamtory changes were there. When administered in *Shirishadi Yoga* (High dose*)* no inflamation is seen and hepatocytes are normal no swelling is seen.

In the case of silymarin, liver section showed marks of injury. The hepatocytes are not radially arranged, and also mild infiltrations of inflammatory cells were also seen.

All these features show the efficacy of *Shirishadi Yoga* in counteracting in acetaminophen induced hepatotoxicity. From there it is clearly revealed that the drug is useful in both preventive as well as curative aspect of drug induced liver damage.

CONCLUSION

After evaluating the observations and taking into consideration the statistical analysis and literary review of the study, conclusion drawn as follows:

- The study proved that *Shirishadi Yoga* and silymarin both possess hepatoprotective and antioxidant activities.
- Overall discussion regarding the efficacy of *Shirishadi Yoga* in acetaminophen induced liver damage, can conclude that *Shirishadi Yoga* is effective in acetaminophen induced hepatotoxicity.
- Laboratory investigations regarding liver function test (LFT) shows that *Shirishadi Yoga* minimized the drug induced liver damage. *Shirishadi Yoga* (ND) is more effective than the LD and HD and silymarin.
- From the histopathological examination of liver tissue, it is noticed that *Shirishadi Yoga* minimized the inflammation, congestion and necrosis of hepatocytes and blood vessels associated with it.
- There were no adverse effects observed among the albino rats in the form of signs and symptoms during the study.
- Finally, from the statistical analysis it is clear that hepatoprotective activity of *Shirishadi Yoga* (ND) is more effective than the standard drug silymarin in acetaminophen induced liver damage.

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