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# Phytochemical And Pharmacological Evaluation Of Vitex Peduncularis For Management Of Liver Dysfunction

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***Abstract***
*Liver illnesses are still the serious problem of human health. Paracetamol is a common analgesic and antipyretic drug. Several studies have demonstrated the induction of hepatocellular damage or necrosis by acetaminophen higher doses in experimental animals and humans. Vitex Peduncularis is a moderate sized tree found in Bangladesh, India and many other countries. The plants are known to produce certain bioactive molecules which react with other organisms in the environment and in turn cause the inhibition of bacterial or fungal growth. Vitex Peduncularis will be useful for different types of diseases like inflammation, ulcer, wound, diabetic wound. The objective of the present study is to establish efficacy of Vitex Peduncularis for treatment of liver dysfunctioning. From our results, it can be concluded that decrease levels of catalase, and increased serum marker enzymes and lipid peroxidation level in paracetamol treated animals was due to hepatocellular damage. Methanol extract of Vitex Peduncularis afforded protection from such paracetamol induced liver damage, and has shown the most pronounced hepatoprotective effect.*
***Keywords:*** *Vitex Peduncularis, Liver Dysfunction, Paracetamol, Hepatotoxicity*

**INTRODUCTION:** Human liver is the most essential visceral organ in body concerned with synthesis, excretion, metabolism and detoxification of diverse exogenous and endogenous substances such as drugs [1]. Because of these multi-dimensional functions, it is prone to many diseases. Death of hepatocytes is the main feature of liver diseases and liver disease is a worldwide major health issue. Causative agents include diseases that interfere with liver functions; chemicals (ethanol, CCl4, thioacetamide, d-galactosamine; environmental toxins) and drugs such as paracetamol [2].

Liver damage caused by inhalation or ingestion of hepatotoxin like drugs is increasing worldwide, and conventional drugs for this drug induced liver damage management are generally insufficient and show serious adverse effects. Drug- induced liver damage accounts for more than 50% of acute liver damage according to the United States Acute Liver Failure Study Group. Drug-induced liver damage caused by overdose of paracetamol, PILD, accounts for about 13% of the hospitalization [3]. A 0.08% of the UK people each year are found in hospital with paracetamol poisoning and only 0.6% of them develop acute liver damage. Paracetamol overdose is a significant clinical problem in USA, Denmark and Australia although less common than in the UK, and is the commonest cause of acute liver damage in USA. Each year, approximately 0.02% of the Australian and 0.01% of the US population are found with paracetamol poisoning in hospital [4]. So, paracetamol toxicity is the second most common cause of liver transplantation worldwide. Several already approved drugs were withdrawn from the market due to common reason, the drug induced liver damage. It is, hence, necessary to explore the herbal drugs in the management of drug induced liver damage to replace the drugs of low safety and efficacy [5].

Natural resources such as medicinal plants are constantly being searched to find new molecules as drugs. Several plants and their formulations are being utilized for drug induced liver damage in traditional systems of medicine and in ethnomedical practice in India. Plant-derived medicinal agents such as silymarin extracted from the seeds of milk thistle (Silybum marianum)) are utilized globally as hepatoprotective agent. Commercially, about 40 polyherbal formulations reputed to possess hepatoprotective activity are being utilized in India. Extracts from 25 medicinal plants have been reported to treat drug induced liver damage. Natural remedy by utilizing medicinal plants is considered a safe and an effective alternative management of drug induced liver damage [6].

Vitex Peduncularis is a moderate sized tree found in Bangladesh, India and many other countries. The plants are known to produce certain bioactive molecules which react with other organisms in the environment and in turn cause the inhibition of bacterial or fungal growth. Medicinal plants that have been traditionally used to produce a variety of compounds with known therapeutic properties. These kinds of plants are used as antipyretic. The bark is used for the external application of the chest pain [7].

The plants of this genus have an overabundance of ethanopharmacological usage for treating a range of human ailments related to insects, bacteria, fungi, snakes and poisonous spiders and diseases associated with gynecological problems. Traditionally, the boiled bark extract of Vitex peduncularis is used as a drink to treat the joint ache. Leaves of Vitex peduncularis contain the compounds like peduncularaside, iridoid, anguside, vitexin, triterpenoids and flavonoids which act as anti-inflammatory properties. It is also known to promote the cardiovascular health by improving blood and nutrient flow of the heart muscles [8]. Although this plant is used as a traditional system of medicine for a long period of time, they have some lack of the scientific documentation, particularly in the light of modern scientific knowledge. The demand for more and more drugs from this kind of plants sources are continuously increasing. Therefore, it is essential for a systematic evaluation of these plants for using in the traditional medicine in various ailments. Earlier studies on different parts of the plant reported the isolation of flavonoids vitexin, pachypodol, peduncularism, ursolic acid and 2α-hydroxyursolic. Vitex Peduncularis will be useful for different types of diseases like inflammation, ulcer, wound, diabetic wound [9-11]. The objective of the present study is to establish efficacy of Vitex Peduncularis for treatment of liver dysfunction Ing.

## MATERIAL AND METHODS

*Vitex Peduncularis* herbs along with inflorescence were collected from tribal region of Bhopal and Plant material were identified and authenticated. The plant materials were dried in shade, powdered moderately and pass-through sieve No. 10.

**Extraction of plant material**

The crude plant materials leave of *Vitex Peduncularis* was often subjected to the selective extraction comprised of treating the moderately coarse powder of plant material with non-polar solvent in succession to extract various plant constituents according to their solubility.

The powdered plant material (250 gm) was successively extracted in a soxhlet apparatus with petroleum ether (60-80°C), Chloroform, Ethyl acetate, methanol and finally with water (by maceration process). After each extraction test was performed to see whether the drug had been completely exhausted or not. The completion of extract was confirmed by evaporating a few drops of the extract on the watch glass and ensuring that no residue remained after evaporating the solvent. After ethanol extraction the marc obtained was dried and macerated with chloroform water for 24 hrs repeatedly two to three times. The liquid extracts were collected in a tare conical flask. The solvent removed by distillation method. The last traces of solvent being removed under vacuum. The extract obtained with each solvent was weighed to a constant weight and percentage w/w yield was calculated

**Animal Housing and environmental condition**

Animals wistar rats weighing between 180-200 gm were selected for hepatoprotective activity of extracts of Vitex Peduncularis leaves extracts. All the animals were segregated into groups of six animal rats each. All animals were housed in air-conditioned rooms with 10-15 air circulation cycles per hour. The relative humidity was maintained between 30-70%, temperature between 22- 25°C and illumination cycle set to 12 hours artificial fluorescent light and 12 hours dark. In each of the polypropylene cages with stainless steel grill top (32.5cm x 21cm), facilities for food and water bottle and bedding of clean paddy husk, the animals were kept in the groups of five. Standard pelleted basal diet and purified water were provided ad libitum to the animals. All the animals were acclamitized to the laboratory conditions before they were used in the experiments. Experimental protocol was approved by Institutional Animal Ethics Committee

**Hepatoprotective effect of Vitex Peduncularis**

Methanol and aqueous extract of dried leaf of Vitex Peduncularis were found to have higher amount of total phenolic and total flavanoid content than chloroform extract so Methanol and aqueous extract were selected for hepatoprotective activity. The over-usage of analgesic, antipyretic and certain medicines that is easily available across the counter in pharmaceutical outlets, overdrinking of alcohol has producing toxicity. Though all drugs have been found to be safe when used within limit of therapeutic dose, it may produce a fatal condition i.e. centrilobular hepatic necrosis when consumed in larger doses and/or over prolonged periods. While the biochemical and metabolic events that arise in the initial stages of toxicity have been described, the exact culprit of hepatocyte death is still not known. Here, necrosis is found to be a major cause of cell death while the involvement of apoptosis has been eliminated. The elevated levels of ROS, primerily superoxide ions may result in the formation of hydrogen peroxide and subsequently

leads to lipid perioxidation reaction by Fenton type mechanism. It has also been reported that, NAPQI reacts rapidly with glutathione, the naturally occurring non-catalytic antioxidant. Additionally, there are varieties of key mechanisms that have been thought to play an important role. In the present study, hepatoprotective activity of the extracts of Vitex Peduncularis leaves were carried out using model of paracetamol induced hepatotoxicity in experimental animals [12-15].

**Study Design:** Animals of group I were treated with 1 ml/kg bw of saline (0.85%) intraperitoneally twice a week for four weeks. Rats of group 2 to 7 were treated with (Paracetamol 1000 mg/kg p.o. for 7 days) intraperitoneally. Animals of group III serve as standard treated with silymarin suspension (10 mg/kg body weight, IP). Remaining group animals received extracts of Vitex Peduncularis leaves. After 24 h of the last treatment, all the animals were weighted, sacrificed, collected the blood while liver was removed, weighted and perfuse in ice-cold saline solution. Liver samples were treated with liquid nitrogen and stored at −70 °C for further studies.

**Table 1: Experimental design for hepatoprotective effect of Vitex Peduncularis extracts**

| S No. | Group | Treatment |
|---|---|---|
| 1 | Normal control | Normal Saline |
| 2 | Disease control | (Paracetamol 1000 mg/kg p.o. for 7 days) |
| 3 | Standard | Standard (silymarin) + Paracetamol (1000 mg/kg p.o.) |
| 4 | MVP 150 | Methanol extract of Vitex Peduncularis leaves (150 mg/kg ) |
| 5 | MVP 300 | Methanol extract of Vitex Peduncularis leaves (300 mg/kg ) |
| 6 | AVP 150 | Aqueous extract of Vitex Peduncularis leaves (150 mg/kg ) |
| 7 | AVP 300 | Aqueous extract of Vitex Peduncularis leaves (300 mg/kg ) |

The preparation of test extract Vitex Peduncularis leaves was done freshly prior to dosing. The animals were dosed by intraperitoneally approximately at the same time each day. The dosage volume administered to individual rat was adjusted according to its recently recorded body weight. All the animals were treated with test drugs (extracts) and standard drug, (Silymarin) for 7 days. After this, the food supply was withdrawn and drinking water was provided ad libitum. Next day, the animals were sacrificed.

**Mortality and Clinical Signs**

All the animals were observed twice daily (morning and evening) for morbidity and mortality, throughout the acclimatization and period of study. After test item administration, individual animals were observed for abnormal clinical signs, due to treatment, throughout the study period. The clinical observations included changes in skin and fur, in the eyes and mucosal membrane in the respiratory, circulatory, central nervous and autonomous system and behaviour.

**Body weight:** Body weight was recorded on day 0 (prior to dosing) and day 8. Change in body weight (%) was calculated on day 8 based on previous body weight

**Biochemical Analysis:** Using rat capillaries, blood was drawn from retro-orbital plexus and was transferred to the in heparinised eppendorf tubes. It was then centrifuged at 3000 RPM for 10 minutes to separate plasma, which was collected using clean pipette. After collection, plasma samples were subjected to biochemical analysis. Biochemical analysis was performed on blood of animals fasted overnight. The major reason for this is the increased variability that would inevitably result from feeding and would mask more subtle effects and make interpretation difficult.

**Histopathology Evaluations:** Histopathology of liver tissues of all animals was performed to evaluate the alteration incurred due to treatment of CCl4 and reversal effect of this by various extracts of Vitex Peduncularis leaves as well as by a known hepatoprotective compound silymarin, at microscopic level. To evaluate the parameters of oxidative stress and histopathology of liver tissue, portions of liver tissue were taken from each animal separately.

## RESULT AND DISCUSSION

**Macroscopic evaluation**

Macroscopic evaluation was carried out on fresh leaves and dried seeds of Vitex Peduncularis size, colour and taste. Vitex Peduncularis leaves are palmately compound, typically with 3 leaflets (rarely 4). The leaflets are lanceolate-oblong or lanceolate-elliptic, with the central leaflet measuring 10-22 cm in length

and 2-5 cm in width, while the lateral leaflets are slightly smaller. The leaf margins are entire or slightly undulate, and the apex is acuminate. The leaflets are generally lanceolate (shaped like a lance head) or elliptic (oval). The central leaflet is typically 10-22 cm long and 2-5 cm wide, while the lateral leaflets are 8-16 cm long and 2-4.5 cm wide. The leaves are palmately compound, meaning the leaflets radiate from a central point, like fingers from a palm.

**Hepatoprotective effect of extracts of the *Vitex Peduncularis* leaves:** The results of body weight, biochemical analysis, oxidative stress analysis and organ weight, were presented as the mean ± SD of six rats per group. Graph Pad Prism 6.01 software was used for Statistical Analysis. Descriptive statistics and comparisons between groups were analyzed using one way analysis of variance (one way ANOVA).

**Clinical signs and mortality:** Administration of paracetamol and different extracts of *Vitex Peduncularis* leaves showed no mortality or morbidity in the animals during the period of study. Cage side observations did not show any observable clinical signs related to the compound toxicity. No tremors, convulsions, salivation, diarrhoea, lethargy, or unusual behaviors were observed in extract treated animals throughout the study period. Administration of paracetamol and different extracts showed no mortality or morbidity in the animals during the period of study.

**Effect on body weight:** The recorded body weights of the animals at day 0 and day 8 of the experiment. The change in the body weights of the experimental animals from day 0 to day 8. Treatment with paracetamol induce hepatotoxicity caused significant reduction ($P<0.01$) in body weight

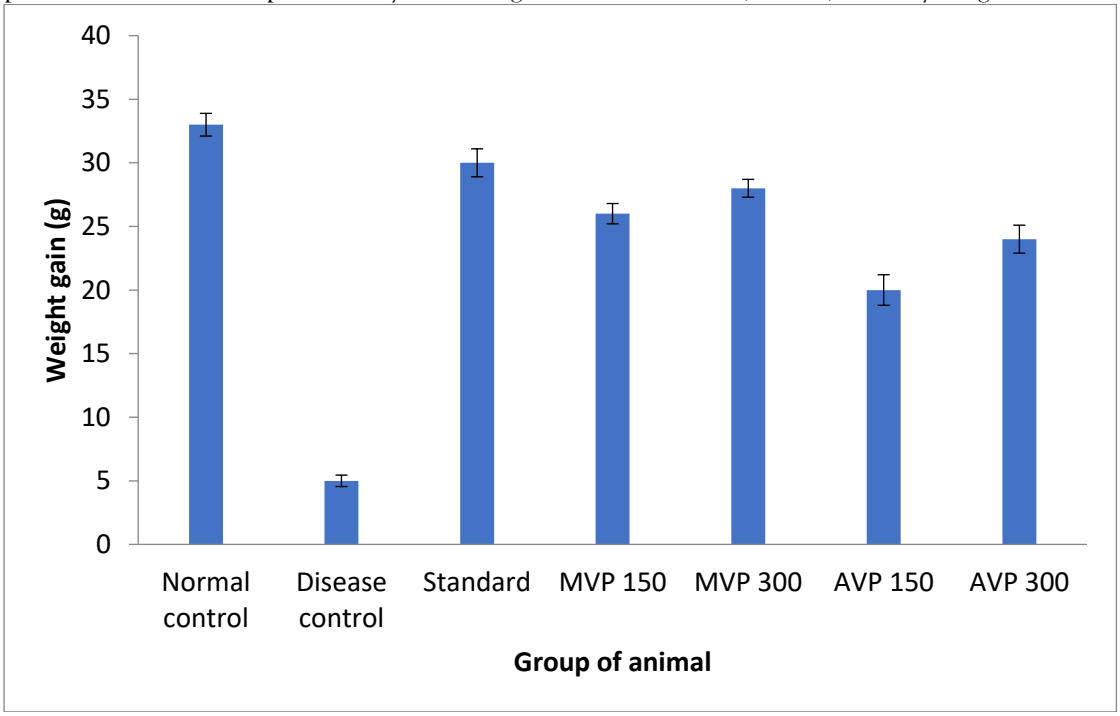


**Figure 1: Effect of *Vitex Peduncularis* leaves extracts on body weight**

The initial (day 0) to day 8 body weight of animals from various experimental groups of animals were recorded and gain in body weight has been calculated. In the disease control group, the weight gain was lesser than all group. Treatment with *Vitex Peduncularis* leaves extract apparently took the animals towards normalcy since the weight gain in animals that of control animals. In the animals that received silymarin a hepatoprotective compound, resulted in a weight gain that was greater than disease control. The maximum weight gain was found in the group received 300 mg/kg of the methanolic extract of *Vitex Peduncularis* than aqueous extract.

**Biochemical Analysis**

**Effect on the levels of AST in blood plasma**

AST (Aspartate Aminotransferase), is an enzyme found in the liver, heart, muscles, and other tissues. An AST blood test measures the amount of this enzyme in the blood. Elevated AST levels in the blood can indicate damage to these tissues, with liver damage being a primary concern.

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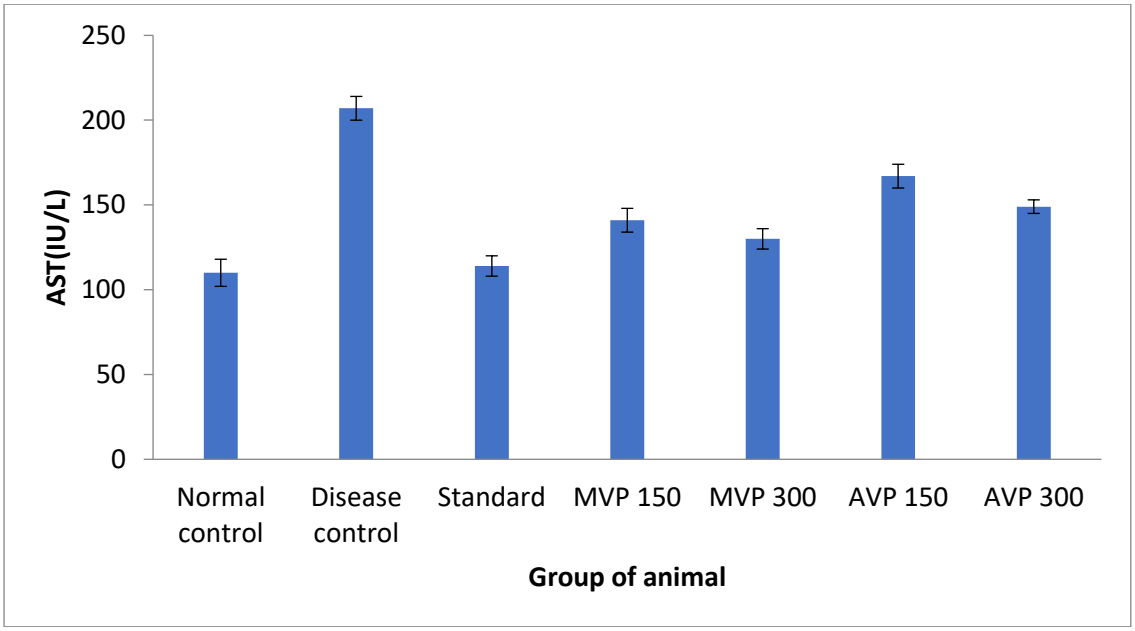


**Figure 2: Effect of *Vitex Peduncularis* leaves extract on AST levels in blood plasma of animals**

The levels of AST activity in the blood plasma of animals in different experimental groups were performed. In the animals from disease control AST level were increased in comparison to normal control group. Animals that received the dose of 300 mg/kg methanol extract of *Vitex Peduncularis* leaves, the levels of AST was found to be 141.96±09.23 IU/L, (150 mg/kg), while it was found 130.96±13.78 IU/L, (300 mg/kg). Methanol extract showed dose dependent activity on AST levels in blood plasma of animals. Methanol extract were found more active than aqueous extract. Methanol extract showed maximum control than aqueous extract.

**Effect on ALT levels in blood plasma of animals**

ALT (Alanine Aminotransferase) is an enzyme primarily found in the liver, and its levels in blood plasma can indicate liver health in animals. Elevated ALT levels can suggest liver damage or disease, while normal levels generally indicate healthy liver function. The levels of ALT activity in the blood plasma of animals in different experimental groups were performed. In the animals from disease control ALT level were increased in comparison to normal control group. Animals that received the dose of 300 mg/kg methanol extract of *Vitex Peduncularis* leaves, the levels of ALT was found to be 93.34±5.18 IU/L, (150 mg/kg), while it was found 76.96±6.78 IU/L, (300 mg/kg).

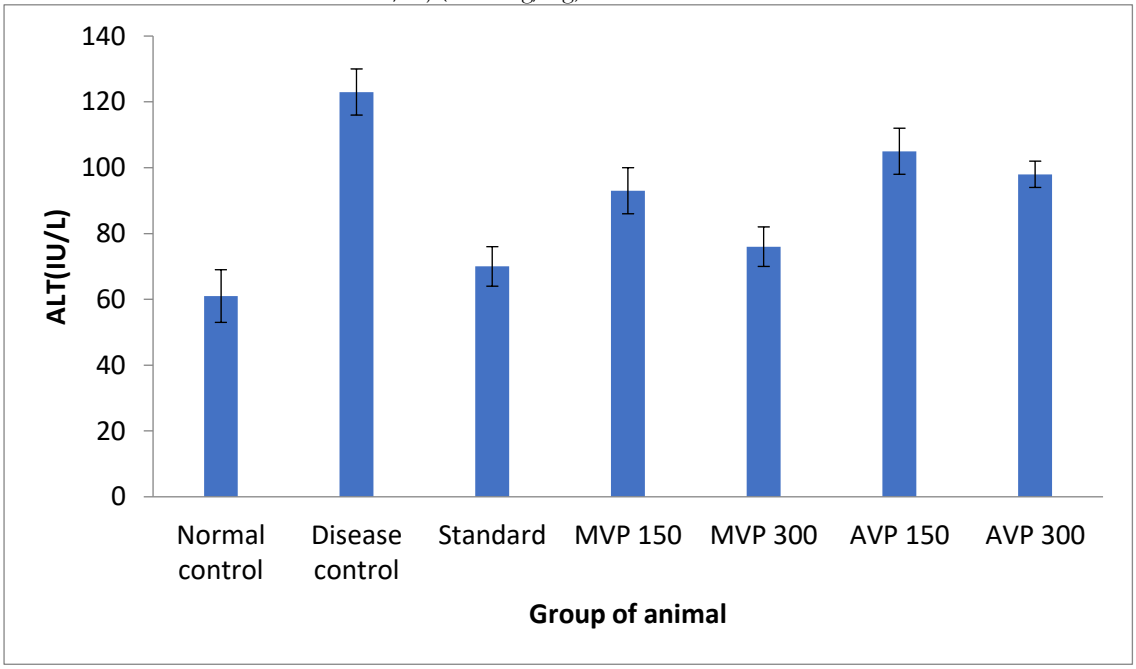


**Figure 3: Effect of *Vitex Peduncularis* leaves extract on ALT levels in blood plasma of animals**

**Effect on ALP levels in blood plasma:**

Alkaline phosphatase (ALP) is an enzyme found in various tissues, including the liver, bones, and intestines. Elevated ALP levels can indicate liver or bone disorders, while low levels can suggest other conditions like hypothyroidism or deficiencies. Disease control animal level of ALP was much higher, than normal control. The difference in normal control and disease group was quite significant. The methanol extracts *Vitex Peduncularis* showed reduced levels of ALP activity, at both dose level. Administration of standard (Silymarin), the level of ALP activity was found to be significant reduction and close normal control animals. Methanol extract showed maximum control than aqueous extract.

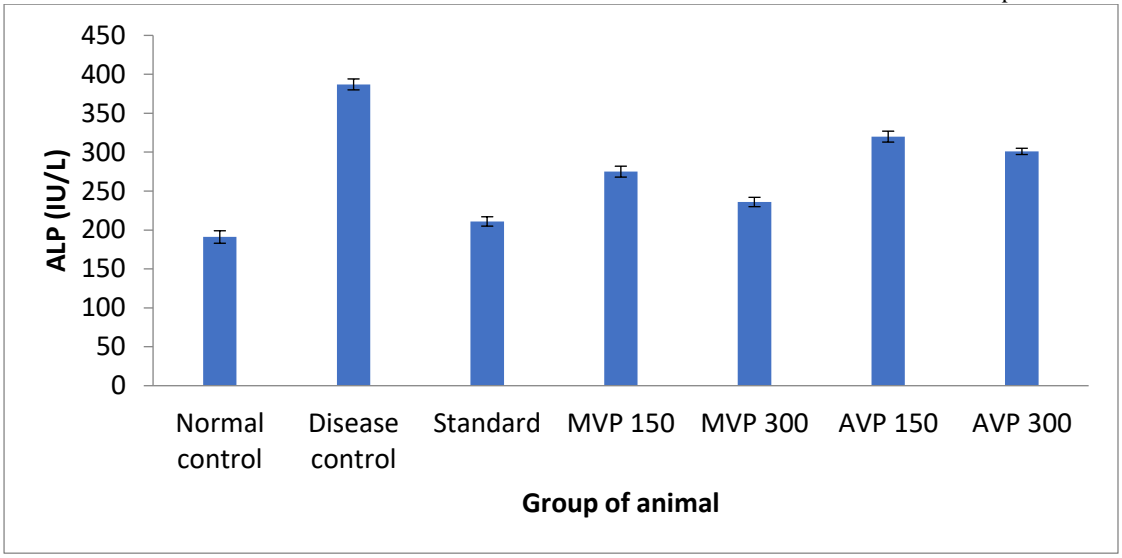


**Figure 4: Effect of the *Vitex Peduncularis* leaves extract on ALP levels in blood plasma**

**Effect on Bilirubin level of animals**

Paracetamol (acetaminophen) can increase bilirubin levels, particularly in cases of overdose. This is because paracetamol can cause liver damage, leading to impaired bilirubin processing and elevated bilirubin levels in the blood. Elevated bilirubin levels can indicate liver problems. Bilirubin is a waste product of heme breakdown, primarily from hemoglobin, and is processed by the liver. High bilirubin levels, often seen in jaundice, can signify liver damage or disease, as the liver may not be properly clearing it.In the normal control animals the concentration of bilirubin was 0.35 ±0.013 mg/dL and that in disease induced group was 0.70±0.027 mg/dL, Animals that received methanol extract of *Vitex Peduncularis* at the dose of 150 mg/kg, the concentration of bilirubin was 0.54±0.009 mg/dL, while at dose 300 mg/kg bilirubin was 0.49±0.012mg/dL showed maximum level of recovery. Standard treated animal showed bilirubin content of 0.42±0.017 mg/dL. This too suggests that the methanol extract of *Vitex Peduncularis* at the dose of 300 mg/kg are able to normalize the Bilirubin level in animals.

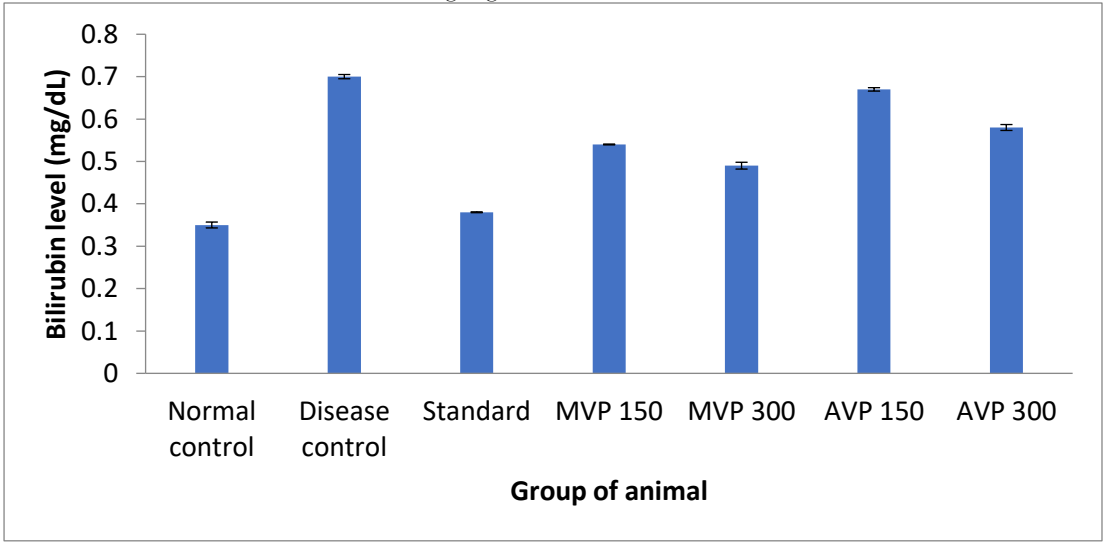


**Figure 5: Bilirubin level of animals treated with *Vitex Peduncularis* leaves extract**

**Effect on Total-Albumin level of animals**

Albumin is a major protein in the blood, and it's primarily produced by the liver. It plays a crucial role in maintaining fluid balance, transporting hormones, vitamins, and other molecules, and acting as an antioxidant. Low albumin levels can be a sign of liver or kidney disease, or other medical conditions. Albumin has been shown to protect the liver from damage caused by various factors, including alcohol, toxins, and diseases. Some studies suggest that albumin can inhibit inflammation and oxidative stress in the liver, which are common mechanisms of liver damage. Albumin may also play a role in promoting liver cell regeneration, further contributing to its hepatoprotective effects.

The methanol extracts *Vitex Peduncularis* showed significantly increased levels of Total-Albumin in comparison to disease control group. Administration of standard (Silymarin), the level of total-Albumin was found to be significant enhance and close to normal control animals. Methanol extract showed dose dependent increment of total-Albumin levels in blood plasma of animals. Methanol extract of both palnts were found more active than aqueous extract. Methanol extract showed maximum control than aqueous extract.

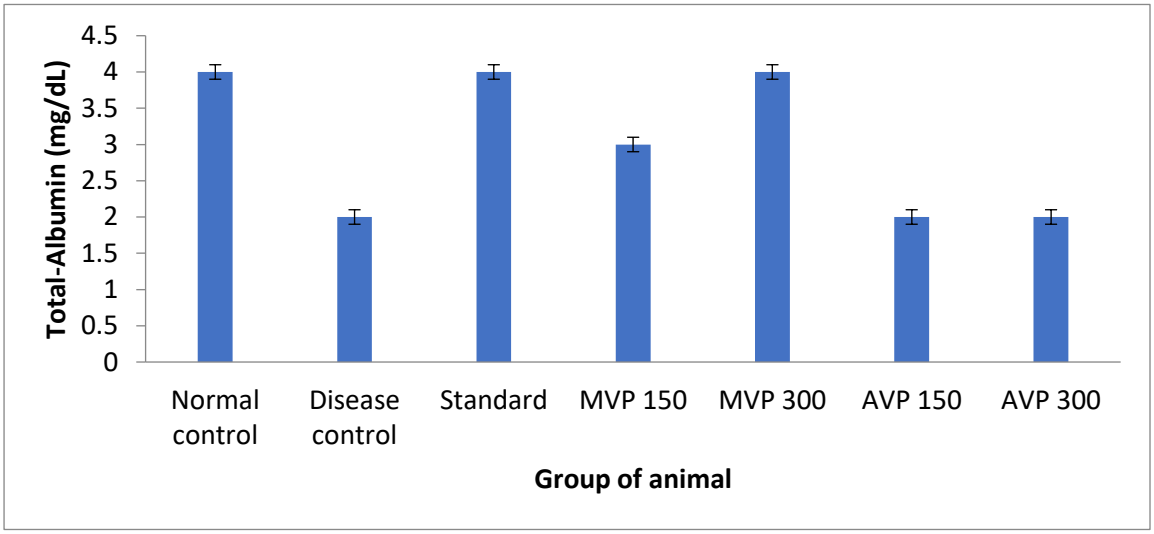


**Figure 6: Total-Albumin level of animals treated with *Vitex Peduncularis* leaves extract**

**Effect on absolute weight of Liver**

Hepatotoxicity can trigger the liver to try and compensate for the damage.

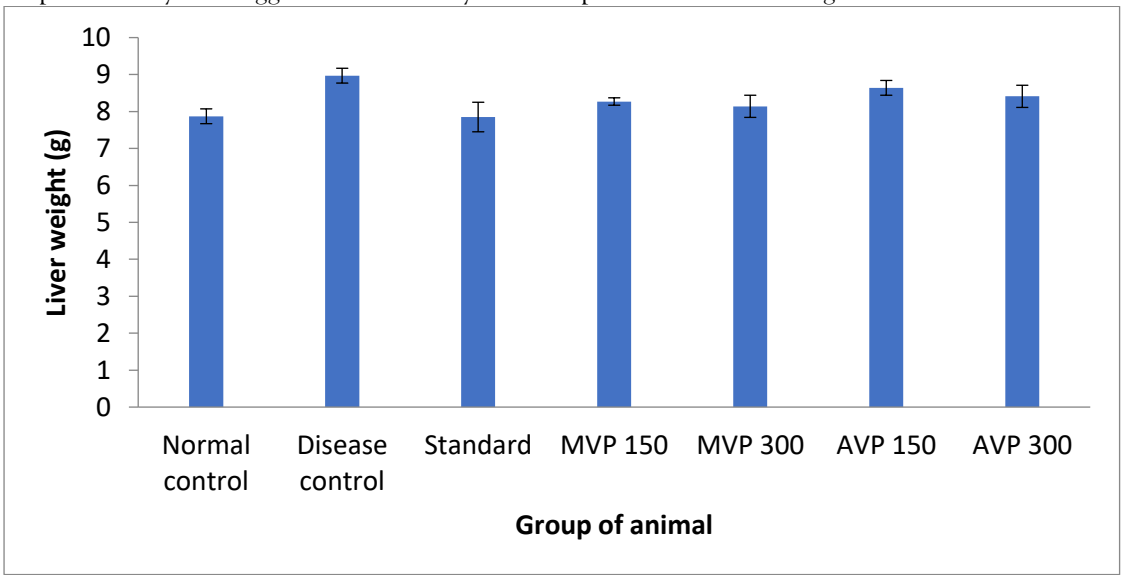


**Figure 7: Effect of *Vitex Peduncularis* leaves extract on absolute weight of liver**

This can lead to an increase in the size of liver cells (hypertrophy) or an increase in the number of liver cells (hyperplasia), both of which contribute to an overall increase in liver weight. The absolute weight of liver in disease group were found more than normal control group. Group treated with methanol extract of *Vitex Peduncularis* leaves were found to have improvement in liver weight significantly in comparison

to disease control group. Disease control group increased in liver weight comparatively to control group. Methanol extract was significantly (P<0.01) restored the liver weight of treated group.

**Effect on the MDA content in liver:**

In cases of hepatotoxicity levels of malondialdehyde (MDA), a marker of lipid peroxidation, tend to increase. This increase in MDA is often associated with oxidative stress and damage to liver cells. The severity of hepatotoxicity can correlate with the extent of MDA elevation. MDA as a marker of oxidative stress: MDA is a byproduct of lipid peroxidation, a process where free radicals damage cell membranes. Elevated MDA levels indicate increased oxidative stress in the liver. In cases of acetaminophen-induced liver injury, a significant increase in MDA has been observed.

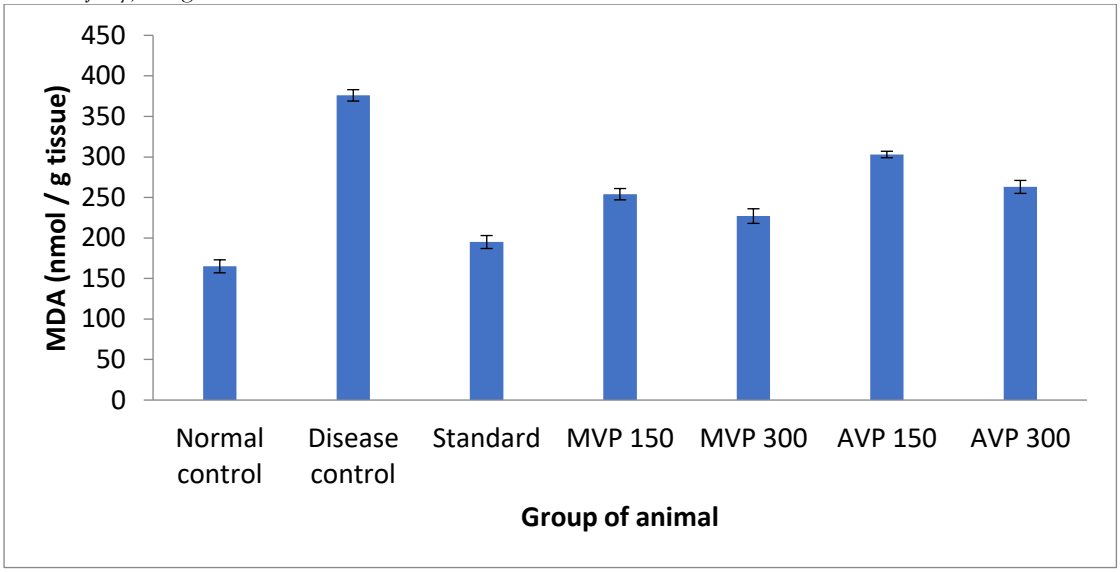


**Figure 8: Effect on MDA contents in liver of animals treated with *Vitex Peduncularis* leaves extract**

Neither the disease group or any other group given test drug nor standard drug had MDA levels comparable to that of control. All these groups had greater lipid peroxidation as compared to the control animals.

Methanol extract of the *Vitex Peduncularis* leaves were found more effective than aqueous extract in control of MDA. More recovery was shown by the group that received 300 mg/kg of *Vitex Peduncularis* leaves methanol extract. This is suggestive of the fact that supplementation of diet with any drug increases lipid peroxidation, and can be lowered by the methanol extract.

**Effect on SOD level in liver**

In hepatotoxicity, which is liver damage caused by harmful substances, superoxide dismutase (SOD) activity is often altered as part of the body's response to oxidative stress. SOD is a crucial antioxidant enzyme that neutralizes harmful superoxide radicals, protecting liver cells. Studies show that SOD levels can be used as a biomarker to assess the severity and prognosis of liver damage.

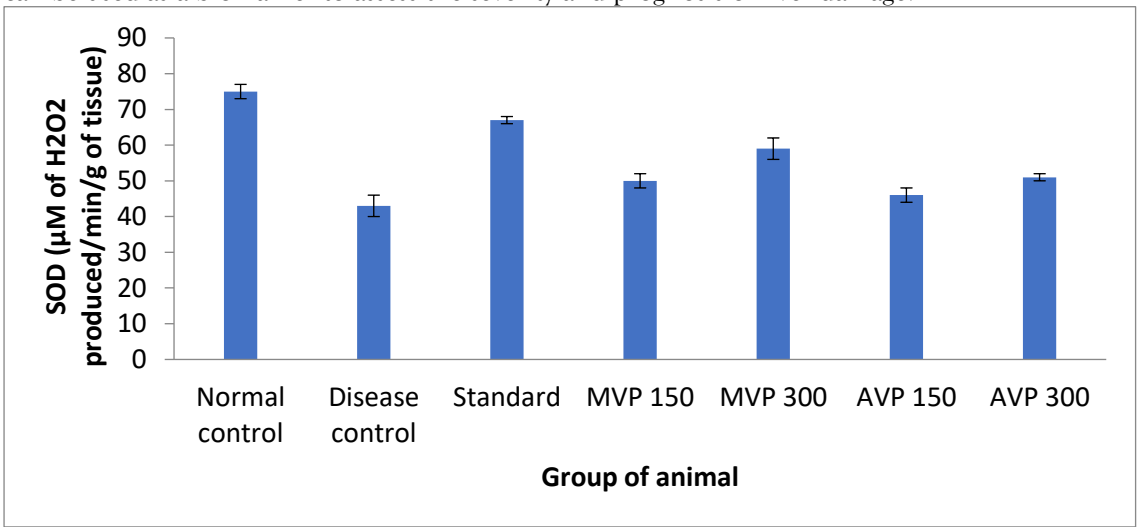


**Figure 9: Effect of *Vitex Peduncularis* leaves extract on SOD level in liver**

The result of superoxide dismutase (SOD) activity level in the liver of the animals of various experimental groups depicted. The SOD activity level in the normal control animals was 75.96±2.12 units, while in disease group it was found to be 43.98±4.67 units when compared to that of normal control group. In animals that were given methanol extracts of the *Vitex Peduncularis* were found to control SOD level significantly than aqueous extract. Methanol extract at 300 mg/kg were found more effective among other extract in control of SOD.

**Effect on catalase activity in liver**

Catalase converts harmful hydrogen peroxide into water and oxygen and protects the tissues from highly reactive hydroxyl radicals. The reduction in the activity of this enzyme may results in number of deleterious effects due to accumulation of highly toxic metabolites and hydrogen peroxide on paracetamol administration, which can induce oxidative stress in the cells. Co-administration of methanol extract of *Vitex Peduncularis* increases the activities of catalase in animals to prevent the accumulation of excessive free radicals and protects the liver from paracetamol intoxication.

In a dose dependent manner, various extracts of the *Vitex Peduncularis* leaves caused an increase in catalse activity in comparison to the disease control, to take the animals towards normalcy. The most effective recovery was met with in the animals fed with 300 mg/kg of methanol extracts of the *Vitex Peduncularis*. In animals fed with aqueous extracts, the catalase activity were also obtained but they found less effective than methanol extract.

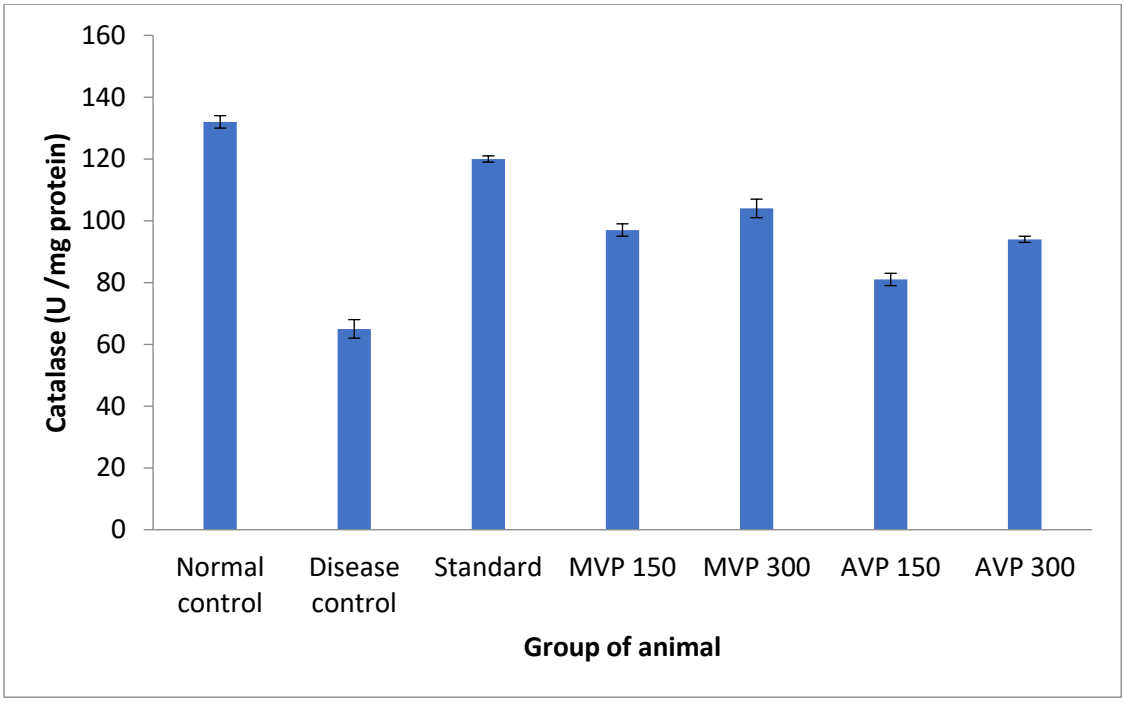


**Figure 10: Effect of *Vitex Peduncularis* leaves extract on catalase activity**

**Histopathology**

Hepatocellular necrosis can be defined as death of hepatic parenchyma which intiates an inflammatory reponse. Pyknosis is the terminus of cell death, where the nucleus shrinks in size and chromatin condenses to solid, structureless masses. Cytoplasmic vacuolation is a morphological phenomenon where giant vacuoles are formed in animal cells, leading to cell death. Vacuoles are formed in different cells by different mechanisms. Hepatoxicity leads to various pathological malfunctions. Perivascular leukocytic infilteration is accumulation of leukocytes in amount excess than of the normal around a vessel. Different chemical structure including medical drugs and industrial pollutants are known to induce irreversible cytoplasmic vacuolization.

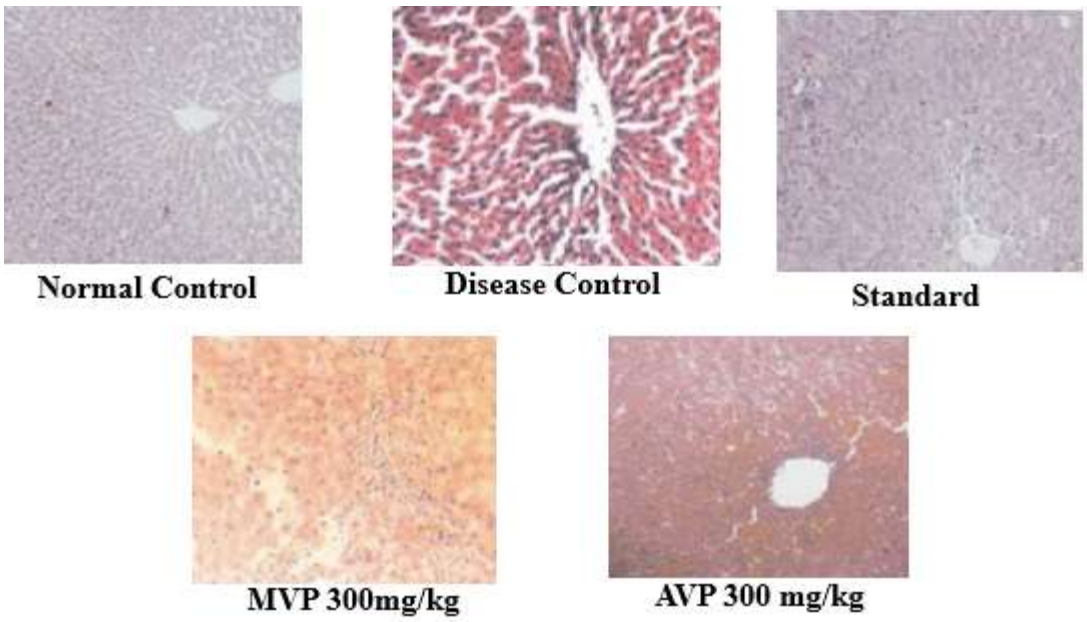


**Figure 11: Histopathology of Liver of the animals**
(MVP methanol extract of V. Peduncularis; AVP Aqueous extract of V. Peduncularis)

Normal control Group, histological sections revealed normal histology. The central vein and hepatocytes surrounding it were observed. The hepatocytes are polyhedral cells with one or rarely two spherical nuclei and contain abundant cytoplasm. The cytoplasm of such cells is granular and strongly eosinophilic. The nuclei of the hepatocytes are large with peripherally dispersed chromatin and prominent nucleoli. Hepatocytes are oriented in cords composed of a single row of cells separated from vascular sinusoids by endothelial cells. The wall of these sinusoids also contains phagocytic irregular cells with multiple processes known as Von Kupffer. Sinusoids and rounded nuclei with distinct one or two nucleoli were also seen. The sinusoids run radially, converging at the center of the hepatic lobule to form the central or centrolobular vein. The central vein has thin walls consisting only of endothelial cells supported by a sparse population of collagen fiber.

Disease control Group, animals showed minimal focal perivascular leukocytic infiltration, focal mild hepatocellular necrosis, hepatocytes with pyknotic nuclei, condensed cytoplasm and severe cytoplasmic vacuolation over a large area. Standard treated group did not reveal any lesion of pathological significance. Group received a dose of 300 mg/kg of aqueous extracts of of *Vitex Peduncularis* leaves showed multifocal mild cytoplasmic vacuolation

AST predominantly found in mitochondria of hepatocytes. ALT is more specific to liver, and thus is a better parameter for detecting liver injury. Serum ALP and bilirubin is also associated with liver cell damage. The ALT, AST and ALP activity and serum bilirubin level are largely used as most common biochemical markers to evaluate liver injury. Administration of paracetamol caused a significant elevation of enzymes level such as AST, ALT, ALP and bilirubin level has been attributed to the damage structural integrity of liver, because they are cytoplasmic in location and released into circulation after cellular damages indicating development of hepatotoxicity. The co administrations of extract have prevented the increased serum marker enzymes AST, ALT, ALP level and bilirubin level. This is in agreement with the commonly accepted view that serum levels of AST, ALT and ALP return to normal with the healing of hepatic parenchyma and the regeneration of hepatocytes. Reduction of serum albumin in paracetamol treated group may be due to formation of protein adduct. Toxic metabolites NAPQI leads to covalent modification of cellular target protein, cell death and organ damage.

Catalase converts harmful hydrogen peroxide into water and oxygen and protects the tissues from highly reactive hydroxyl radicals. The reduction in the activity of this enzyme may results in number of deleterious effect due to accumulation of highly toxic metabolites and hydrogen peroxide on paracetamol administration, which can induce oxidative stress in the cells

## CONCLUSION

Liver is an important organ and a central one for many of the metabolic functions of the body, decomposition of toxic and waste substances, and disposal of harmful substances from the body. Liver illnesses are still the serious problem of human health. Making active oxygen species is an unavoidable result in aerobic organisms, and their removal is done at a basic level and with regard to the useful physiological functions and their harmful effects. This sensitive balance is for retaining the intracellular redox state which has an important role in optimizing cell functions. Excessive accumulation of free radicals or the body's inability to remove them causes the relocation of redox equilibrium for creating oxidation states in the body

Paracetamol is a common analgesic and antipyretic drug. Several studies have demonstrated the induction of hepatocellular damage or necrosis by acetaminophen higher doses in experimental animals and humans. For screening of hepatoprotective agents, paracetamol-induced hepatotoxicity has been used as a reliable method. Paracetamol is metabolized primarily in the liver and eliminated by conjugation with sulfate and glucuronide, and then excreted by the kidney. Moreover, paracetamol hepatotoxicity has been attributed to the formation of toxic metabolites, when a part of paracetamol is activated by hepatic cytochrome P-450 to a highly reactive metabolite Nacetyl-p-benzoquinoneimine (NAPQI).

Co-administration of methanol extract of *Vitex Peduncularis* increases the activities of catalase in animals to prevent the accumulation of excessive free radicals and protects the liver from paracetamol intoxication. A massive decrease in lipid peroxidation in liver tissue of plant extract treated groups indicates that all studied plants possess antioxidative properties. From our results, it can be concluded that decrease levels of catalase, and increased serum marker enzymes and lipid peroxidation level in paracetamol treated animals was due to hepatocellular damage. Methanol extract of *Vitex Peduncularis* afforded protection from such paracetamol induced liver damage, and has shown the most pronounced hepatoprotective effect.

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