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HEPATOPROTECTIVE POTENTIALS OF AQUEOUS LEAF AND SEED EXTRACTS OF *ARTOCARPUS HETEROPHYLLUS* ON TESTOSTERONE PROPIONATE INDUCED PROSTATITIS IN WISTAR RATS.

[*1]Okolo, L. U., [1]Uwakwe, A.A., [1]Anacletus, F.C. and [2]Nwauche, K.T,
[1]Department of Biochemistry, University of Port Harcourt. Rivers State.
[2]Department of Biochemistry, Rivers State University, Port Harcourt.
*E-mail: okololuckyuche@gmail.com

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ABSTRACT

This study evaluated the hepatoprotective potentials of aqueous leaf and seed extracts of Artocarpus heterophyllus on testosterone propionate induced prostatitis in Wistar Rat. Male Wistar rats of 100-125g and 100 in number were obtained from the Department of Pharmacology, University of Port Harcourt animal house and was grouped into 10 of 10 rats each. The various groups were fed and administered with various concentrations (100mg/kg, 200mg/kg, 300mg/kg and 200mg/kg combined extract) of the leaves and seeds extracts of A. heterophyllus. The hepatoprotective potentials was studied by evaluating the liver function parameters on the male Wistar rats by day 21, 42 and 63 of the experiment using standard laboratory methods. The results obtained showed significantly ($p< 0.05$) increased ALP levels (401.57±0.85) on administration of testosterone propionate in group 2 (induced not treated group) day 21, as against the normal control group (294.57±0.06), while group 5 (Rats induced with TP (4 mg/kg) and administered 200 mg/kg of aqueous extract of A. heterophyllus leaves) revealed minimal level of ALP 293.47±0.006 by day 63. Minimum values for AST 23.00±0.51 was seen in group 8 day 21) with maximum activity 76.82±0.09 seen in group 1 day 21, ALT minimum level 7.67±0.33 was observed in group 4 day 21, while maximum levels 38.41±0.51 was seen in group 2 day 21, Albumin minimum level 17.87±0.09 was seen in group 2 day 63, with maximum level 31.13±0.18 observed in group 8 day 63, while minimum Total Protein 26.31±0.84 was shown in group 2 day 63 and maximum 64.63±0.49 in group 8 day 42. Obtained values from groups 5, 6, 9 and 10 were shown to be significantly different when compared with the negative control in group 2 but not significantly different with control group 1 and 3, hence depicting a more stabilized and hepatoprotective system in the plant extract treated groups compared to the negative control (group 2) at day 21. However, group 5 was shown to have higher hepatoprotective potentials by day 42 followed by group 10.

Keyword: *Arthocarpus heterophyllus*, Prostatitis, Hepatotoxicity, Testosterone propionate

INTRODUCTION

Herbs usage by locals have garnered wide acceptance even amidst ignorant usage and abused applications (Opotu *et al*., 2017). This comes as several plants have been shown to contain several bio active components, endowing them with lots of therapeutic potentials (Sheetal and Jamuna, 2009; Onuah *et al*., 2018; Opotu *et al*., 2017; Okolo *et al*., 2023). These therapeutic potentials in plants have been key to eradicating lots of toxicity effects, induced by some toxic compounds within our surrounding environment like

polluted food crops, drugs such as testosterone propionate (Anacletus et al., 2017; Okolo *et al*., 2023), chemicals, (Opotu *et al*., 2017), polluted Sea foods, vegetables and water (Ighariemu *et al*., 2023, Nyimone, *et al.*, 2023). Recently, research has beamed light on the therapeutic potentials and bio-active components of plants, thereby initiating their usage in ameliorating disease conditions with specification to safety dosages (Ibrahim and Fagbohun, 2012; Okolo *et al*., 2023); (Opotu *et al*., 2017).

Medicinal plants can greatly contribute to stemming the tide of this disease. However, because only a thin line of demarcation exists between a medicinal plant being therapeutic or protective and its being a poison at times, proper classification and screening is necessary. *Artocarpus heterophyllus* has been identified as one of such medicinal plant with high medicinal profile.

Artocarpus heterophyllus

Taxanomy

Kingdom:	Plantae
Order:	Rosales
Family:	Moraceae
Genus:	Artocarpus
Species:	A. heterophyllus

Binomial name: *Artocarpus heterophyllus* (Morton, 2016).

Artocarpus heterophyllus (*A. heterophyllus*) is of the family moraceae (Morton, 2016). It is widely cultivated globally, yielding large fruits. *A. heterophyllus* has a mild taste and meat-like texture that lends itself to being called a "vegetable meat"(Silver, 2016). Both ripe and unripe fruits of *A. heterophyllus* are consumed by locals. The leaves are alternate and spirally arranged. They are gummy and thick and are divided into a petiole and a leaves blade (Love and Paull, 2011).

Studies have shown that *A. heterophyllus* is rich in protein, calcium, iron, and Thiamine (Haq, 2006; Bhatia *et al.*, 2015; Kumar, *et al.*, 2018), several minerals and vitamins (Tiwari, and Vidyarthi, 2015), starch (Rahman *et al.*, 1999), amino acids like arginine, cystine, histidine, leucine, lysine, methionine, threonine, and tryptophan (Kumar, *et al.*, 2018), and various phytochemicals, (Onuah *et al*., 2018; Lin *et al.*, 2018). It's uses as an antioxidant and anti-inflammatory compound is suggestive for its application in this study which tend to ascertain the hepatoprotective potential of *A. heterophyllus* leaves and seeds in testosterone propionate induced prostatitis in Wistar Albino rats.

Testosterone have been shown to be a causative agent for enlarged prostate (Onyegeme-Okerenta *et al.*, 2022), which is now common amongst patients under this treatment. The adverse effect of this is increasing on daily basis, making it a health concern as cases of compromised liver is on the rise (Onyegeme-Okerenta *et al.*, 2022), hence informing the decision for this study.

MATERIALS AND METHODS

List of Apparatus and Equipment

UV-VIS Spectrophotometer (Single Beam) (LabTech. RE 1201007), Electronic weighing Balance (Mettler Toledo AB 204), General Laboratory Centrifuge (GLC) (Sorvall Instruments, GLC- 4, USA) Rotary Evaporator (R-1001-LN Zhengzhou Great wall Scientific), Spectrophotometer (TECH 2041).

All chemicals/reagents and analytical kits used for the analyses were of analytical grade. Samples were collected and prepared

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according to the procedures described in Okolo *et al.*, (2023)

Experimental Design

One hundred male Wistar rats (100-125g) from Animal House of Pharmacology Department, University of Port Harcourt, Nigeria was purchase acclimatised for one week and group with respect to close body weight into 10 groups as shown below. Methods of Obisike *et al*, (2019) was adopted for in duction of prostatitis in the Wistar rats.

GROUP	Treatment	
Group I	Normal control	Rats fed with normal feed and water
Group II	Negative control	Rats induced with TP (4 mg/kg) and untreated
Group III	Standard drug	(Dutasteride 4 mg/kg) Rats induced with TP (4 mg/kg) and treated with 4 mg/kg of dutasteride
Group IV	Induced 100 mg/kg leaves	Rats induced with TP (4 mg/kg) and administered 100 mg/kg of aqueous extract of *Arthocarpus heterophyllus* leaves.
Group V	Induced 200 mg/kg leaves	Rats induced with TP (4 mg/kg) and administered 200 mg/kg of aqueous extract of *Artocarpus heterophyllus* leaves.
Group VI	Induced 300 mg/kg leaves	Rats induced with TP (4 mg/kg) and administered 300 mg/kg of aqueous extract of *Artocarpus heterophyllus* leaves.
Group VII	Induced 100 mg/kg seeds	Rats induced with TP (4 mg/kg) and administered 100 mg/kg of aqueous extract of *Artocarpus heterophyllus* seeds.
Group VIII	Induced 200 mg/kg seeds	Rats induced with TP (4 mg/kg) and administered 200 mg/kg of aqueous extract of *Artocarpus heterophyllus* seeds
Group IX	Induced 300 mg/kg seeds	Rats induced with TP (4 mg/kg) and administered 300 mg/kg of aqueous extract of *Artocarpus heterophyllus* seeds.
Group X	Induced 200 mg/kg (combined extract)	Rats induced with TP (4 mg/kg) and administered 200 mg/kg of the combined (100 mg/kg aqueous leaves extract and 100 mg/kg aqueous seeds extracts of) *Artocarpus heterophyllus* leaves and seeds.

At days 21, 42, and 63 the Wistar rats were sacrificed following the methods described by Okolo *et al.*, (2023). Blood samples were collected and stored for liver function tests. The liver of the Wistar rats were also obtained for histopathology.

Determination of Alanine Aminotransferase Activity (Randox Method)

The plasma ALT activity was determined using Randox Test Kits (Randox Laboratories Ltd, Crumlin, England, UK) according to the method of Reitman and Frankel (1957). Two test tubes were set up labelled T1 (reagent blank) and T2 (test sample). T1 contained 0.10ml distilled water and 0.50ml Randox buffer solution, while T2 contained 0.10ml plasma sample and 0.50ml Randox buffer solution. The contents were mixed and incubated for 30min at 37oC. To each test tube was added 0.50ml of Randox 4 - dinitrophenylhydrazine solution and the contents were mixed and allowed to stand for 20mins at 25oC. Sodium hydroxide (5ml) solution was added to each of the tubes. The contents were then mixed, and after 5min, their absorbance was read at 546nm against blank in a spectrophotometer.

Determination of Aspartate Aminotransferase Activity (Randox Method)

The plasma AST activity was determined using Randox Test Kits (Randox Laboratories Ltd, Crumlin, England, UK) according to the method of Reitman and Frankel (1957). Two test tubes were set up labelled T1 (reagent blank) and T2 (test sample). T1 contained 0.10ml distilled water and 0.50ml Randox buffer solution, while T2 contained 0.10ml plasma sample and 0.50ml Randox buffer solution. The contents were mixed and incubated for 30min at 37oC. To each test tube was added 0.50ml of Randox 4-dinitrophenylhydrazine solution and the contents were mixed and allowed to stand for 20mins at 25oC. Then 5ml of sodium hydroxide solution was added to each of the tubes. The contents were mixed, and after 5min, their absorbance was read at 546nm against the reagent blank in a spectrophotometer.

Determination of Alkaline Phosphatase Activity (Randox Method)

Plasma ALP activity was determined using the end-point method according to the method of Reitman and Frankel (1957). To0.02ml of the plasma sample in a cuvette was added 1.0ml of Randox ALP reagent (at 30^{o}C). The content was mixed and the initial absorbance was taken, after which the readings were taken after 1, 2 and 3 min, at 405nm in a spectrophotometer.

Determination of Serum Total Protein (Randox Method)

The method of Reitman and Frankel (1957) was used. Three test tubes were assembled, T1 (blank), T2 (standard) and T3 (test sample). T1 contained three-point zero millilitre distilled water and five-point zero millilitre biuret reagent, T2 (standard) contained three-point zero millilitre standard protein solution and five-point zero millilitre biuret reagent. The contents were thoroughly mixed, incubated in a water bath (20 to 25˚C) for thirty minutes; absorbance was read at 560nm against the blank in a spectrophotometer.

Determination of Serum Albumin (Randox Method)

The method of Reitman and Frankel (1957) was used. Three test tubes were assembled, T1 (blank), T2 (standard) and T3 (test sample). The blank contained five-point zero millilitre bromocresol green reagent and zero point twenty millilitre distilled water, the standard contained five point zero millilitre bromocresol green reagent and zero point twenty millilitre standard protein solution. The test sample contained five-point zero millilitre bromocresol green reagent and zero-point

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twenty millilitre plasma sample and their contents were mixed and allowed to stand for ten minutes. The absorbance was read against the blank at 630nm in a spectrophotometer.

Statistical Analysis

The data obtained were analysed using SPSS Version 23 to determine the analysis of variance (ANOVA) at n=3 and at 95% degree of confidence. Analysed data were tabulated as mean ± standard error of mean.

RESULTS AND DISCUSSION

The results of the hepatoprotective potentials of aqueous leaves and seeds extracts of *Artocarpus heterophyllus* on testosterone propionate induced prostatitis on male Wistar albino rats is as shown in Tables 1 to 3. The result revealed a significantly ($p< 0.05$) increased ALP levels (401.57±0.85) on administration of testosterone propionate in group 2 (induced not treated group) at day 21, as against the normal control group (294.57±0.06), while group 5 (Rats induced with TP (4 mg/kg) and administered 200 mg/kg of aqueous extract of *Artocarpus heterophyllus* leaves) revealed minimal level of ALP 293.47±0.006 by day 63, while groups 3, 5, 6, 9 and 10 have values which are not significantly different from control group 1 (fed with feed and water only) depicting a more stabilized system compared to the negative control (group 2) at day 21. Minimum values for AST 23.00±0.51 was seen in group 8 day 21) with maximum activity 76.82±0.09 seen in group 1 day 21, ALT minimum level 7.67±0.33 was observed in group 4 day 21, while maximum levels 38.41±0.51 was seen in group 2 by day 21.

Table 1 Liver Markers After 21 DAYS

GROU	**ALP** (U/L)	**AST**(U/L)	**ALT** (U/L)	**Albumin**(g/	**Total Protein** (g/dl)
1	294.57±0.06^{a}	59.00±0.57^{a}	17.33±0.80^{a}	28.53± 0.33^{a}	49.20±0.36^{a}
2	401.57±0.85^{b}	76.82±0.09^{b}	38.00±0.54^{b}	19.06±0.63^{b}	28.74±0.66^{b}
3	296.37±0.43^{a}	57.00±0.16^{a}	19.00±0.58^{a}	27.33±0.23^{a}	50.43±0.29^{a}
4	327.30±0.41^{c}	46.00±0.55^{c}	7.67±0.33^{c}	25.73±0.88^{a}	59.07±0.32^{c}
5	293.73±0.64^{a}	59.00±0.58^{a}	17.00±0.54^{a}	28.43±0.26^{a}	48.33±0.20^{a}
6	294.10±0.42^{a}	36.00±0.08^{d}	17.67±0.31^{a}	28.47±0.55^{a}	49.63±0.33^{a}
7	329.47±0.79^{c}	40.00±0.38^{c}	20.00±0.56^{a}	29.83±0.12^{a}	47.90±0.95^{a}
8	359.20±0.47^{c}	23.00±0.51^{d}	12.33±0.38^{c}	22.10±0.06^{c}	54.83±0.08^{c}
9	296.97±0.39^{a}	56.00±0.24^{a}	16.67±0.31^{a}	30.90±0.32^{a}	47.00±0.58^{a}
10	293.90±0.60^{a}	58.33±0.32^{a}	17.67±0.62^{a}	30.50±0.29^{a}	50.20±0.20^{a}

Values are means±SEM. at n=3. Means in same column with same superscript alphabets are not significantly different at $p<0.05$, while means in same column with different superscript alphabets are significantly different at $p<0.05$. With the numbers denoting; **1** - Normal control- Rats fed with normal feed and water, **2** - Negative control - Rats induced with TP (4 mg/kg) and untreated, **3** - Standard drug (Dutasteride 4 mg/kg) Rats induced with TP (4 mg/kg) and treated with 4 mg/kg of dutasteride, **4** - Rats induced with TP (4 mg/kg) and administered 100 mg/kg of aqueous extract of Artocarpus heterophyllus leaves. **5** - Rats induced with TP (4 mg/kg) and administered 200 mg/kg of aqueous extract of Artocarpus heterophyllus leaves, **6** - Rats induced with TP(4 mg/kg) and

administered 300 mg/kg of aqueous extract of *Artocarpus heterophyllus* leaves, **7** - Rats induced with TP (4 mg/kg) and administered 100 mg/kg of aqueous extract of *Artocarpus heterophyllus* seeds, **8** - Rats induced with TP(4 mg/kg) and administered 200 mg/kg of aqueous extract of *Artocarpus heterophyllus* seeds, **9** - Rats induced with TP(4 mg/kg) and administered 300 mg/kg of aqueous extract of *Artocarpus heterophyllus* seeds, **10** - Rats induced with TP(4 mg/kg) and administered 200 mg/kg of the combined 100 mg/kg aqueous leaves and seeds extracts

Table 2 Liver Markers After 42 DAYS

GROUP	**ALP** (U/L)	**AST**(U/L)	**ALT** (U/L)	**Albumin**(g/dl)	**Total Protein**
1	293.57±0.06[a]	59.00±0.57 [a]	17.33±0.80 [a]	28.53± 0.33 [a]	49.20±0.36 [a]
2	411.57±0.85[b]	74.37±0.28 [b]	38.41±0.51[b]	18.47±0.29[b]	27.42±0.54[b]
3	296.37±0.43[a]	57.00±0.16[a]	19.00±0.58 [a]	27.33±0.23 [a]	50.43±0.29[a]
4	498.73±0.82 [c]	72.67±0.45 [b]	15.00±0.01[a]	24.13±0.47 [a]	64.17±0.29[c]
5	293.53±0.51 [a]	58.33±0.09 [a]	17.00±0.59[a]	28.17±0.60 [a]	49.40±0.36[a]
6	295.10±0.80 [a]	57.42±0.21[a]	18.00±0.28[a]	27.73±0.49 [a]	48.37±0.35[a]
7	263.50±0.48 [a]	69.00±0.55[c]	16.00±0.18[a]	26.53±0.55 [a]	51.53±0.41[a]
8	530.50±0.55 [d]	65.00±0.52 [c]	12.00±0.22[c]	19.40±0.03[b]	64.63±0.49[c]
9	293.60±0.32 [a]	60.33±0.88 [a]	19.00±0.14 [a]	28.17±0.12[a]	50.73±0.49 [a]
10	293.55±0.50 [a]	58.33±0.20[a]	16.33±0.31[a]	26.60±0.15[a]	48.87±0.58[a]

Values are Means±SEM. at n=3. Means in same column with same superscript alphabets are not significantly different at p<0.05, while means in same column with different superscript alphabets are significantly different at p<0.05. With the numbers denoting; **1** - Normal control- Rats fed with normal feed and water, **2** - Negative control - Rats induced with TP (4 mg/kg) and untreated, **3** - Standard drug (Dutasteride 4 mg/kg) Rats induced with TP (4 mg/kg) and treated with 4 mg/kg of dutasteride, **4** - Rats induced with TP (4 mg/kg) and administered 100 mg/kg of aqueous extract of Artocarpus heterophyllus leaves. **5** - Rats induced with TP (4 mg/kg) and administered 200 mg/kg of aqueous extract of Artocarpus heterophyllus leaves, **6** - Rats induced with TP(4 mg/kg) and administered 300 mg/kg of aqueous extract of *Artocarpus heterophyllus* leaves, **7** - Rats induced with TP (4 mg/kg) and administered 100 mg/kg of aqueous extract of *Artocarpus heterophyllus* seeds, **8** - Rats induced with TP(4 mg/kg) and administered 200 mg/kg of aqueous extract of *Artocarpus heterophyllus* seeds, **9** - Rats induced with TP(4 mg/kg) and administered 300 mg/kg of aqueous extract of *Artocarpus heterophyllus* seeds, **10** - Rats induced with TP(4 mg/kg) and administered 200 mg/kg of the combined 100 mg/kg aqueous leaves and seeds extracts

Table 3 Liver Markers after 63 DAYS

GROUP	**ALP** (U/L)	**AST**(U/L)	**ALT** (U/L)	**Albumin**(g/dl	**Total Protein**
1	293.52±0.06[a]	59.00±0.57[a]	17.33±0.80 [a]	28.53± 0.33[a]	48.20±0.36 [a]
2	400.57±0.85 [b]	74.67±0.88 [b]	38.20±0.51[b]	17.87±0.09[b]	26.31±0.84[b]
3	297.36±0.43[a]	57.00±0.16[a]	19.00±0.58 [a]	28.73±0.23[a]	47.43±0.29[a]

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4	391.03±0.89[c]	51.00±0.42[c]	22.00±0.25 [a]	27.03±0.19 [a]	49.13±0.33[a]
5	293.47±0.71[a]	59.00±0.78[a]	16.97±0.12[a]	27.97±0.26 [a]	48.73±0.41[a]
6	295.23±0.19[a]	59.07±0.09 [a]	18.30±0.27[a]	29.90±0.12[a]	48.53±0.29[a]
7	404.10±0.67[b]	66.00±0.43[d]	15.67±0.42[a]	29.43±0.54[a]	52.67±0.94[a]
8	379.37±0.87[d]	58.00±0.50 [a]	16.00±0.20[a]	31.13±0.18 [a]	46.93±0.07[a]
9	296.50±0.23[a]	60.67±0.33[a]	17.32±0.07[a]	29.87±0.45[a]	48.53±0.58[a]
10	293.77±0.06[a]	58.67±6.17[a]	18.02±0.58[a]	28.23±0.34 [a]	50.80±0.52[a]

Values are means±SEM. at n=3. Means in same column with same superscript alphabets are not significantly different at $p<0.05$, while means in same column with different superscript alphabets are significantly different at $p<0.05$. With the numbers denoting; **1** - Normal control- Rats fed with normal feed and water, **2** - Negative control - Rats induced with TP (4 mg/kg) and untreated, **3** - Standard drug (Dutasteride 4 mg/kg) Rats induced with TP (4 mg/kg) and treated with 4 mg/kg of dutasteride, **4** - Rats induced with TP (4 mg/kg) and administered 100 mg/kg of aqueous extract of Artocarpus heterophyllus leaves. **5** - Rats induced with TP (4 mg/kg) and administered 200 mg/kg of aqueous extract of Artocarpus heterophyllus leaves, **6** - Rats induced with TP(4 mg/kg) and administered 300 mg/kg of aqueous extract of *Artocarpus heterophyllus* leaves, **7** - Rats induced with TP (4 mg/kg) and administered 100 mg/kg of aqueous extract of *Artocarpus heterophyllus* seeds, **8** - Rats induced with TP(4 mg/kg) and administered 200 mg/kg of aqueous extract of *Artocarpus heterophyllus* seeds, **9** - Rats induced with TP(4 mg/kg) and administered 300 mg/kg of aqueous extract of *Artocarpus heterophyllus* seeds, **10** - Rats induced with TP(4 mg/kg) and administered 200 mg/kg of the combined 100 mg/kg aqueous leaves and seeds extracts

PHOTOMICROGRAPHS OF LIVER, MAG X400 H&E

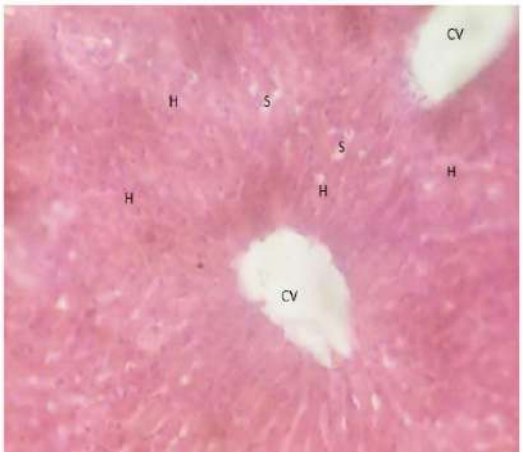

Plate 1 Group 1; Normal control (day 21); Rats fed with normal feed and water. Histologically normal liver; Patent central vein (CV) Intact

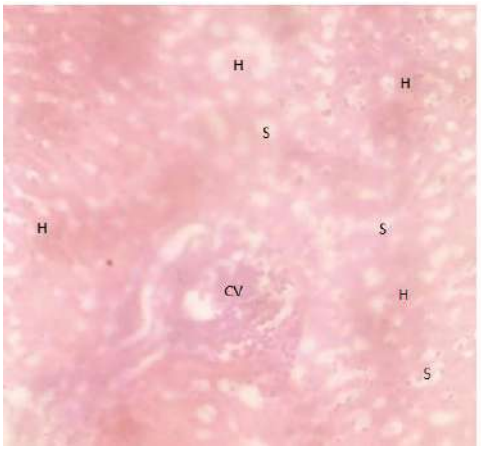

Plate 2 Group 2 (day 21); Negative control: Rats induced with TP (4 mg/kg) and untreated. Histologically distorted Liver; Hepatocytes, Sinusoids (S) containing

Hepatocytes (H), Sinusoids (S) containing Kupffer cells

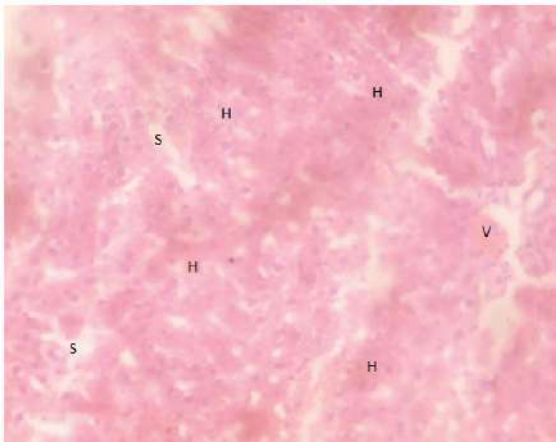

Plate 3 Group 3; (Day 21), Standard drug (Dutasteride 4 mg/kg): Rats induced with TP (4 mg/kg) and treated with 4 mg/kg of dutasteride

Histologically normal liver; patent portal vein (V), Intact Hepatocytes (H), Sinusoids (S) containing Kupffer cells.

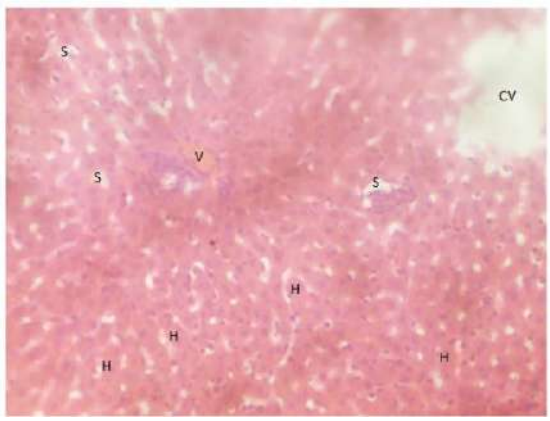

Plate 5, Group 5; (Day 21), (Induced 200 mg/kg leaves): Rats induced with TP (4 mg/kg) and administered 200 mg/kg of aqueous extract of Artocarpus heterophyllus leaves. Histologically normal liver showing; portal vein (V) Intact Hepatocytes (H), Sinusoids (S) containing, Kupffer cells

Kupffer cells. Central vein (CV) filled with inflammatory cells

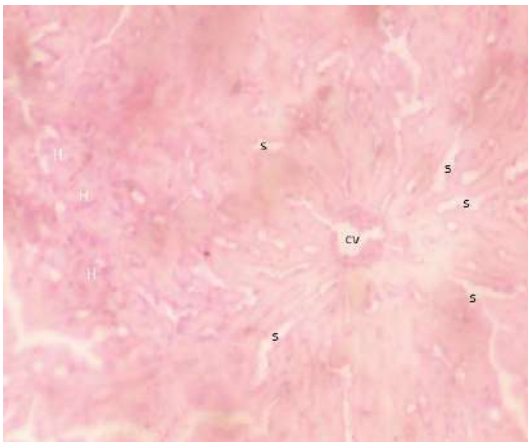

Plate 4, Group 4; (Day 21), (Induced 100 mg/kg leaves): Rats induced with TP (4 mg/kg) and administered 100 mg/kg of aqueous extract of *Artocarpus heterophyllus* leaves. Histologically normal liver; Congested central vein (CV), Intact Hepatocytes (H), Sinusoids (S)

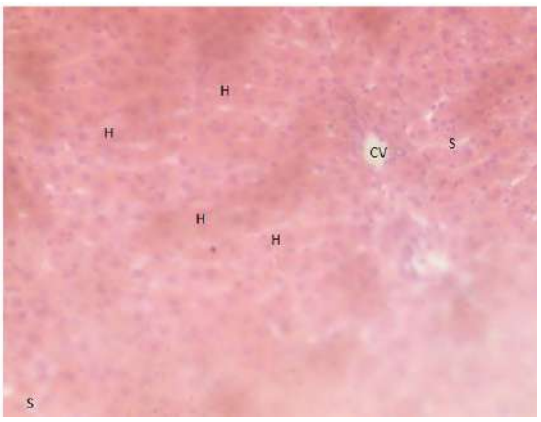

Plate 6, Group 6; (Day 21), (Induced 300 mg/kg leaves): Rats induced with TP (4 mg/kg) and administered 300 mg/kg of aqueous extract of Artocarpus heterophyllus leaves. Histologically normal liver showing; Patent central vein (V), Intact Hepatocytes (H), Sinusoids (S) containing Kupffer cells

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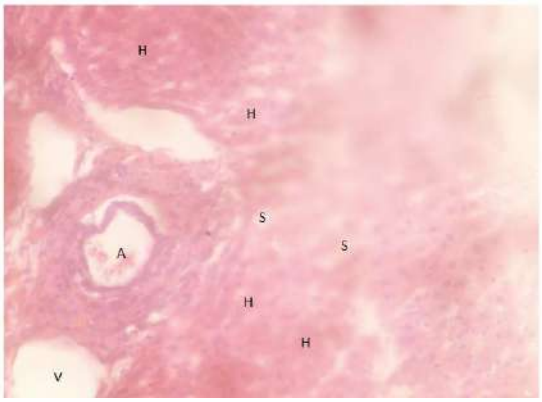

Plate 7, Group 7; (Day 21), (Induced 100 mg/kg seeds): Rats induced with TP (4 mg/kg) and administered 100 mg/kg of aqueous extract of Artocarpus heterophyllus seeds. Histologically normal liver; Patent vein (V), Hepatic artery (A), Intact Hepatocytes (H), Sinusoids (S)

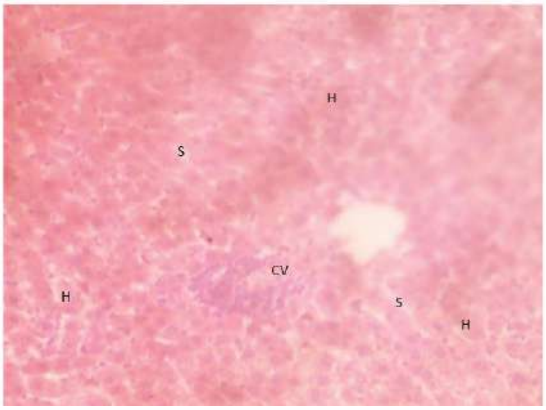

Plate 8, Group 8; (Day 21), (Induced 200 mg/kg seeds) Rats induced with TP (4 mg/kg) and administered 200 mg/kg of aqueous extract of Artocarpus heterophyllus seeds. Histologically normal liver; Intact Hepatocytes (H) Sinusoids (S) containing Kupffer cells. Congested central vein (CV)

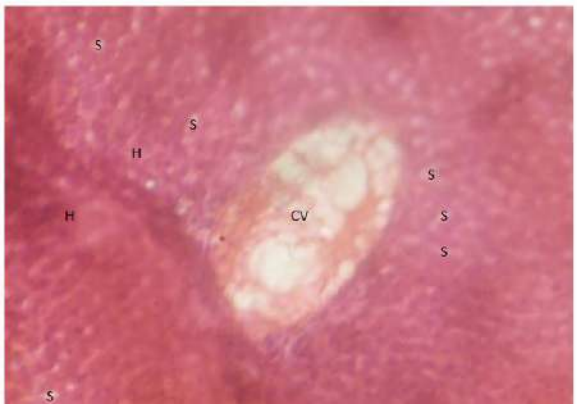

Plate 9, Group 9; (Day 21), (Induced 300 mg/kg seeds): Rats induced with TP (4 mg/kg) and administered 300 mg/kg of aqueous extract of Artocarpus heterophyllus seeds. Patent central vein (CV), Intact Hepatocytes (H). Sinusoids (S).

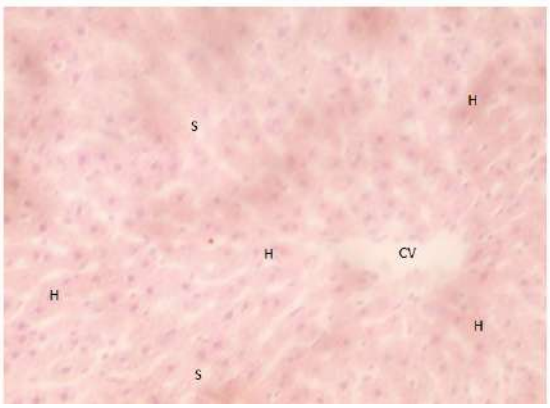

Plate 10, Group 10; (Day 21): (Induced 200 mg/kg; combined extract): Rats induced with TP (4 mg/kg) and administered 200 mg/kg of the combined 100 mg/kg aqueous leaves and seeds extracts Histologically normal liver; Patent central vein (CV). Cords of normal Hepatocytes (H) away from CV. Sinusoids (S) containing Kupffer cells.

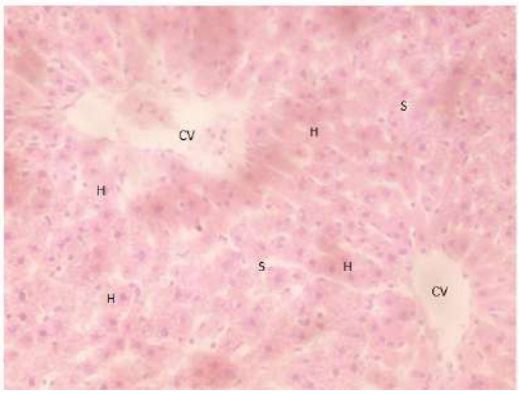

Plate 11 Normal control (day 42); Rats fed with normal feed and water. Histologically normal liver; Patent central vein (V), Intact Hepatocytes (H), Sinusoids (S)

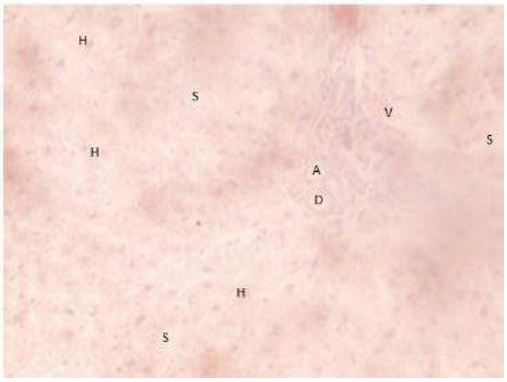

Plate 12 Group 2 (day 42); Negative control: Rats induced with TP (4 mg/kg) and untreated. Mildly distorted liver; Hepatocytes with tatty changes; micro vesicular steatosis (ST), Congested Central Vein (CV), Sinusoids (S)

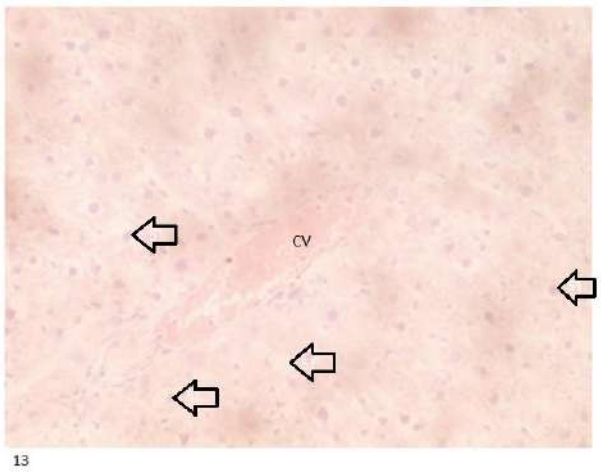

Plate 13, Group 3; (Day 42), Standard drug (Dutasteride 4 mg/kg): Rats induced with TP (4 mg/kg) and treated with 4 mg/kg of dutasteride, histologically distorted liver; Hepatocytes (H), Sinusoids (S), Congested Portal Vein (V), Hepatic Artery (A) & Bile Duct D.

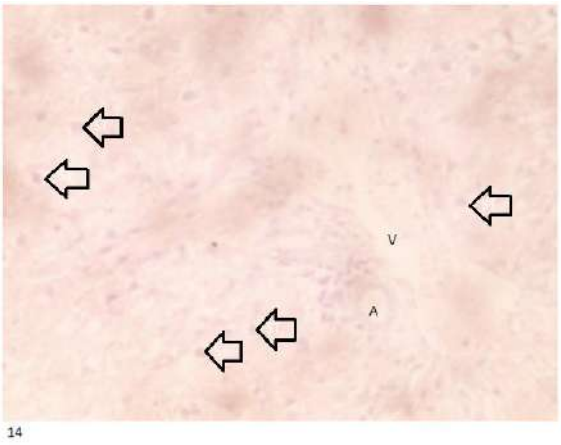

Plate 14, Group 4; (Day 42), (Induced 100 mg/kg leaves): Rats induced with TP (4 mg/kg) and administered 100 mg/kg of aqueous extract of Artocarpus heterophyllus leaves. Mildly distorted liver; Micro vesicular steatosis (ST) Congested Portal Vein (V), Hepatic Artery (A) Sinusoids (S)

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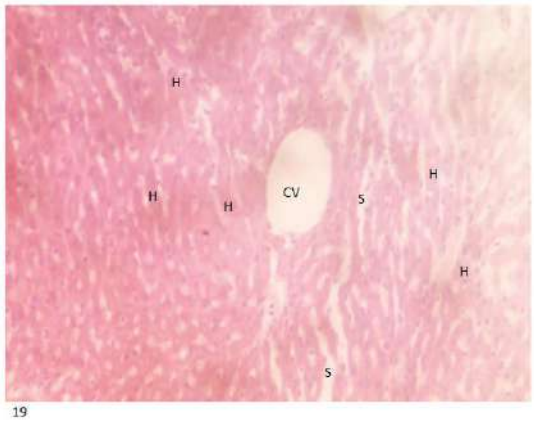

Plate 15, Group 5; (Day 42), (Induced 200 mg/kg leaves): Rats induced with TP (4 mg/kg) and administered 200 mg/kg of aqueous extract of Artocarpus heterophyllus leaves. Histologically normal liver; Patent central vein (CV), Intact Hepatocytes (H), Sinusoids (S)

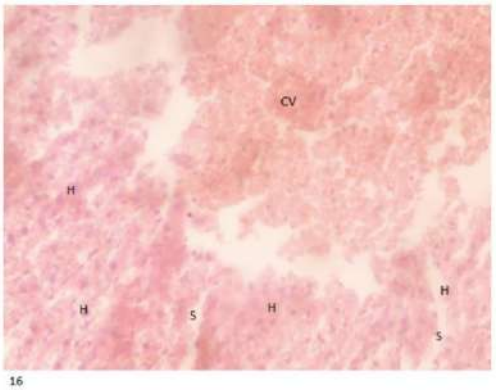

Plate 16, Group 6; (Day 42), (Induced 300 mg/kg leaves): Rats induced with TP (4 mg/kg) and administered 300 mg/kg of aqueous extract of Artocarpus heterophyllus leaves. Histologically normal liver; Intact Hepatocytes (H), Sinusoids (S), Congested central vein (CV)

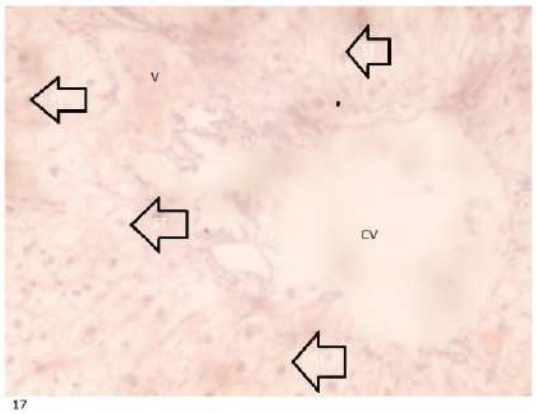

Plate 17, Group 7; (Day 42), (Induced 100 mg/kg seeds): Rats induced with TP (4 mg/kg) and administered 100 mg/kg of aqueous extract of Artocarpus heterophyllus seeds. Histologically distorted liver (severely damaged) Hepatocytes with different stages of steatosis (ST), Patent central vein (CV), Congested portal vein (V)

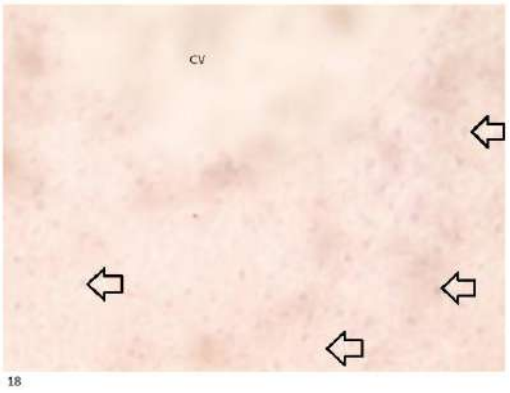

Plate 18, Group 8; (Day 48), (Induced 200 mg/kg seeds) Rats induced with TP (4 mg/kg) and administered 200 mg/kg of aqueous extract of Artocarpus heterophyllus seeds. Histologically distorted liver; Hepatocytic steatosis (ST), Patent central vein (C)

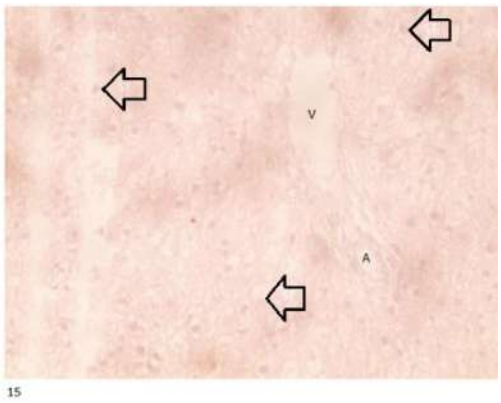

Plate 19, Group 9; (Day 42), (Induced 300 mg/kg seeds): Rats induced with TP (4 mg/kg) and administered 300 mg/kg of aqueous extract of Artocarpus heterophyllus seeds. Histologically distorted liver: Hepatocytes with different stages of Hepatocytic steatosis (ST), Patent portal vein (V), Hepatic artery (A).

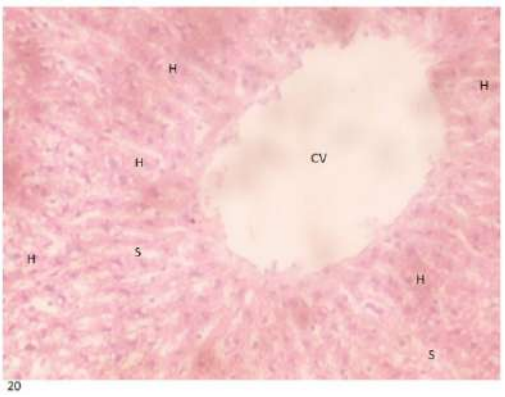

Plate 20, Group 10; (Day 42): (Induced 200 mg/kg; combined extract): Rats induced with TP (4 mg/kg) and administered 200 mg/kg of the combined 100 mg/kg aqueous leaves and seeds extracts, histologically normal liver; Patent central vein (CV), Intact Hepatocytes (H), Sinusoids (S) containing Kupffer cells.

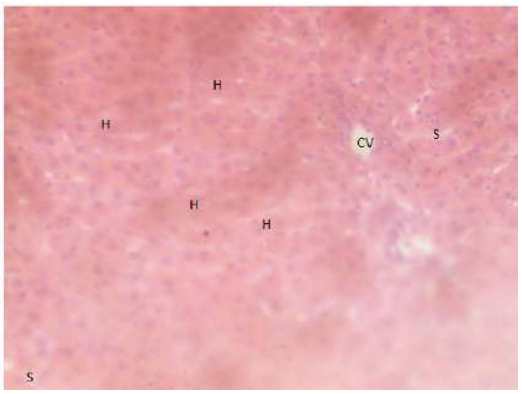

Plate 21, Group 1; (Day 63): Plate 21 Normal control (day 63); Rats fed with normal feed and water. Histologically normal liver; Patent central vein (CV), Intact Hepatocytes (H), Sinusoids (S) containing Kupffer cells

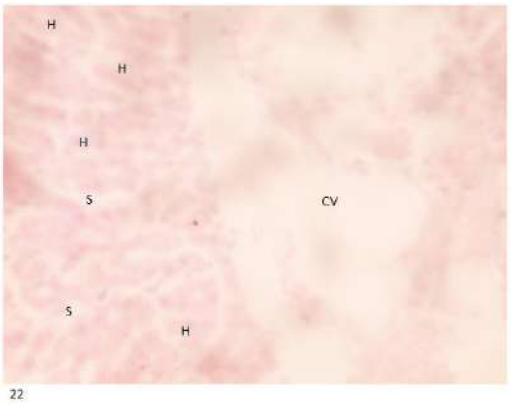

Plate 22 Group 2 (day 63); Negative control: Rats induced with TP (4 mg/kg) and untreated, histologically distorted liver; Hepatocytes (H), Sinusoids (S), congested central vein (CV).

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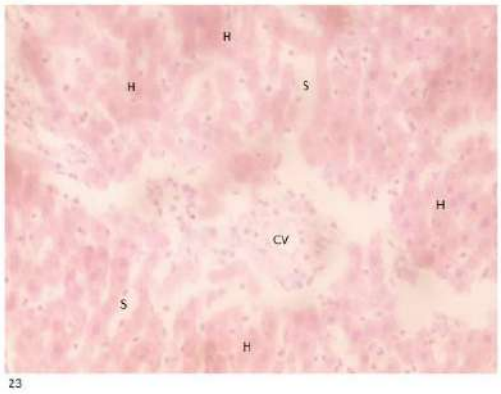

Plate 23, Group 3; (Day 63), Standard drug (Dutasteride 4 mg/kg): Rats induced with TP (4 mg/kg) and treated with 4 mg/kg of dutasteride. Histologically normal liver; Intact Hepatocytes (H), Sinusoids (S) containing Kupffer cells. Patent central vein (CV).

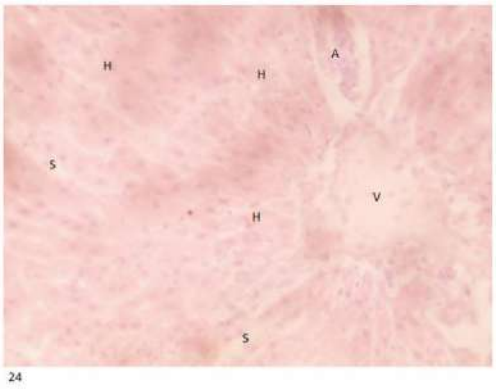

Plate 24, Group 4; (Day 63), (Induced 100 mg/kg leaves): Rats induced with TP (4 mg/kg) and administered 100 mg/kg of aqueous extract of Artocarpus heterophyllus leaves. Histologically normal liver; Congested portal vein (V), Hepatic artery (A), Intact Hepatocytes (H)Sinusoids (S).

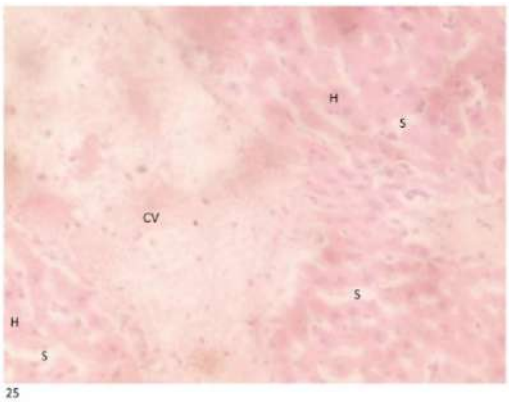

Plate 25, Group 5; (Day 63), (Induced 200 mg/kg leaves): Rats induced with TP (4 mg/kg) and administered 200 mg/kg of aqueous extract of Artocarpus heterophyllus leaves. Histologically normal liver; Congested central vein (CV), Intact Hepatocytes (H), Sinusoids (S). containing Kupffer cells.

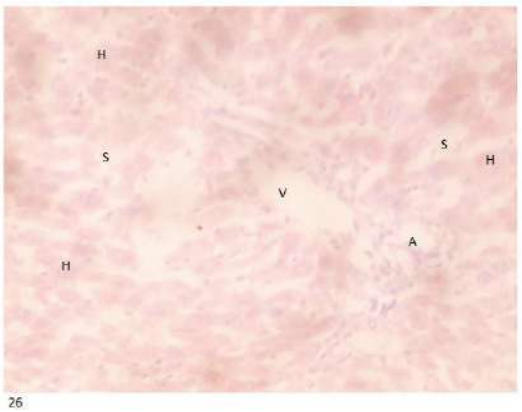

Plate 26, Group 6; (Day 63), (Induced 300 mg/kg leaves): Rats induced with TP (4 mg/kg) and administered 300 mg/kg of aqueous extract of Artocarpus heterophyllus leaves. Histologically normal liver; Patent portal vein (V), Hepatic artery (A), Intact Hepatocytes (H), Sinusoids (S).

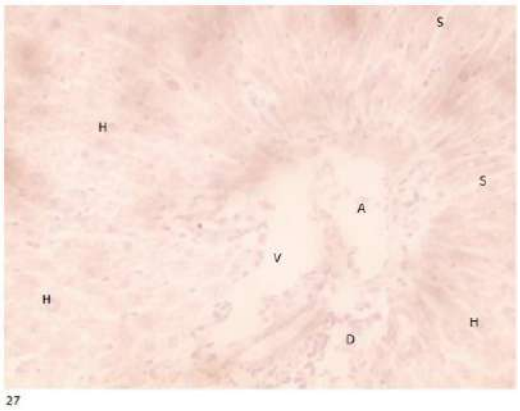

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Plate 27, Group 7; (Day 63), (Induced 100 mg/kg seeds): Rats induced with TP (4 mg/kg) and administered 100 mg/kg of aqueous extract of Artocarpus heterophyllus seeds. Histologically normal liver; Intact Hepatocytes (H), Sinusoids (S). Patent portal vein (V), Hepatic artery (A) {& bile duct (D)

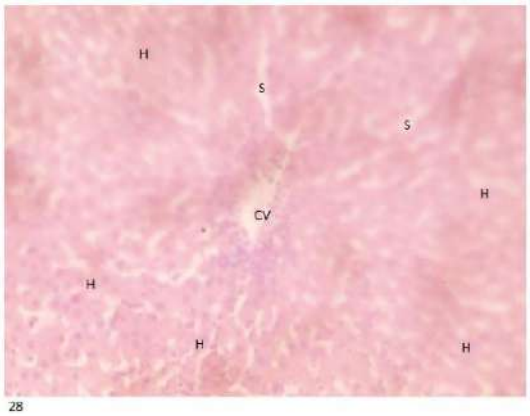

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Plate 28, Group 8; (Day 63), (Induced 200 mg/kg seeds) Rats induced with TP (4 mg/kg) and administered 200 mg/kg of aqueous extract of Artocarpus heterophyllus seeds. Histologically normal liver; Intact Hepatocytes (H), Sinusoids (S) containing Kupffer cells, Patent portal vein (V).

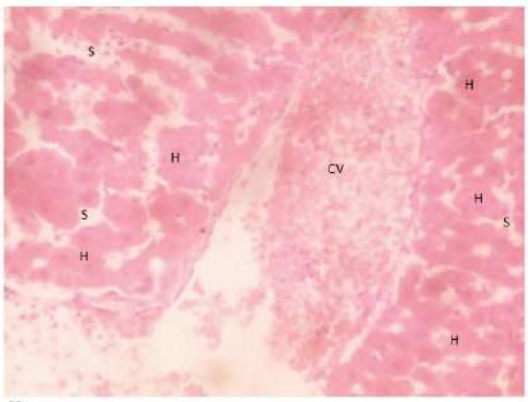

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Plate 29, Group 9; (Day 63), (Induced 300 mg/kg seeds): Rats induced with TP (4 mg/kg) and administered 300 mg/kg of aqueous extract of Artocarpus heterophyllus seeds. Histologically normal liver; Congested central vein (CV), Intact Hepatocytes (H), Sinusoids (S).

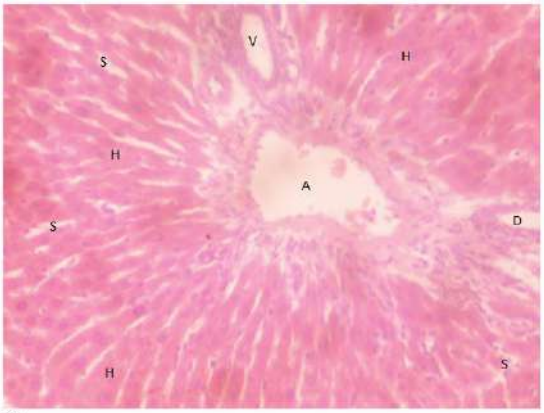

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Plate 30, Group 10; (Day 63): (Induced 200 mg/kg; combined extract): Rats induced with TP (4 mg/kg) and administered 200 mg/kg of the combined 100 mg/kg aqueous leaves and seeds extracts. Histologically normal liver; Patent Hepatic artery (A), portal vein (V), Intact Hepatocytes (H), Sinusoids (S)

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Albumin minimum level 17.87±0.09 was seen in group 2 day 63, with maximum level 31.13±0.18 observed in group 8 day 63 while minimum Total Protein 26.31±0.84 was shown in group 2 day 63 and maximum 64.63±0.49 in group 8 day 42. Obtained values from groups 5,6 ,9 and 10 were shown to be significantly different when compared with the control in group 2 but not significantly different with control group 1 and 3.

Testosterone propionate induced prostatitis in male Wistar rats as shown in group 2, was shown to have caused significant increase in the levels of AST, ALT and ALP. This is an indication of hepatocellular damage. Also, decrease in total protein and albumin observed in the testosterone propionate treated group depicts liver dysfunction. Elevated levels of liver function markers are often found in blood circulation when the integrity of liver is compromised (Green and Flamm, 2002., Robert *et al.*,2009). These findings corroborate with reports by (Robert *et al.*,2009) on studies conducted to determine the effects of treatment of sativum extracts on paracetamol induced hepatotoxicity in Albino rats. Plants like *Annona muricata* have also been shown to have a hepatoprotective effect on the testosterone induced prostatitis (Onyegeme-Okerenta *et al.*, 2022). Chukwu *et al.*, (2020) also reported hepatoprotective potentials of combined ethanol extract of *Anthocleista vogelii* and *Alstonia boonei* Stem Barks in testosterone propionate induced Benign Prostatic Hyperplasia in Rats. Co administration with different doses 100, 200 and 300 mg/kg of aqueous leaves and seeds extracts of Jackfruit showed significant reversal in the levels of these enzymes compared to the negative control group 2 which is an indication of the hepatoprotective activity of these plant extracts. This is a marked indication of normal hepatocytes, improvement upon functional, secretory and synthetic ability of the hepatocytes to ameliorate testosterone propionate induced hepatotoxicity. The findings from the liver marker assay was further authenticated by the histopathology results from the sampled Wistar rats, which showed patent hepatic artery, portal vein, intact hepatocytes, sinusoids and central vein in groups 5,6 and 10.

CONCLUSION

From the hepatotoxicity study it was observed that *Artocarpus heterophyllus* has ameliorative effects on hepatotoxicity seen in testosterone propionate induced prostatitis on male Wistar albino rats. This was observed on evaluation of the liver marker enzymes and liver histopathology of the experimental animals which shows that co administration with different doses 100, 200 and 300 mg/kg of aqueous leaves and seeds extracts of Jack fruit showed significant reduction in the levels of liver marker enzymes compared to the negative control group 2 which is an indication of the hepatoprotective activity of these plant extracts. This is a marked indication of normal hepatocytes, improvement upon functional, secretory and synthetic ability of the hepatocytes to ameliorate testosterone propionate induced hepatotoxicity.

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