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Pharmacology of *Spondias mombin* in liver cancer treatment and toxicity evaluation

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Abstract

Cancer is among the major causes of death in the world. *Spondias mombin* is a natural product being accepted as medication for many diseases. This research aimed at evaluating the toxicity potential and pharmacology properties of *Spondias mombin* leaves in liver cancer treatment. *Spondias mombin* leaves were shade dried at room temperature and size reduced to powder and extracted using cold maceration. Phytochemical screening of the plant extract was conducted. Six weeks of healthy mice; weighing 22-25g were used. For acute toxicity studies, ten mice were grouped into a normal control group and another group received 2000mg/kg of the extract. The animals were observed closely for 14 days. Twenty-four mice were divided into 4 groups. One group served as control and received only saline at 10mls/kg and the other groups received one percent diethylnitrosamine (DEN) given via peritoneal injection to the mice weekly at a dose of 35mg/kg for six weeks. The remaining three groups received 250 mg/kg, 500 mg, and doxorubicin 2 mg/kg after four weeks of induction. The treatment commenced with the extract while still giving the DEN for cancer induction. The phytochemical analysis shows the presence of alkaloids, cardiac glycosides, saponins, tannins, phenolic compounds, steroids, flavonoids, and terpenoids, and the absence of carbohydrates anthraquinones. Animals exposed to the extract and observed for 14 days exhibited no obvious sign of toxicity with zero mortality during the period of observation. There is a slight weight change among the control group between 20.8±3.56 to 25.63 ±2.60.The creatinine, CL, and HCO3 of the control significantly ($P<0.005$) differed from the study groups. There was a slight increase in weight after the first dose, though a steady decrease was noticed following the second, third, and fourth doses of DEN in the mice. ALT and AST were higher in the extract-treated groups compared to both Dox-treated and saline-treated groups. The extract was shown to have no obvious physical sign of toxicity and it doesn't cause mortality in all the tested animals. Ethanol extract of the plant reversed the loss in weight, deterioration in liver enzymes, and protein production to an extent similar to that of standard anti-cancer agents.

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1.0 Introduction

Cancer is among the major cause of death in both developing and developed countries of the world and the burden associated with its management is predicted to grow even higher due to the growth and growing of the elderly population (Qianru *et al*., 2020; Llovet *et al*., 2021; Harriet *et al*., 2022). Lifestyle changes and or adoption of new lifestyles were acknowledged to have expanded the risk of developing

cancers, especially among developing countries. The incidence of liver cancer like other cancers is attributed to factors such as an increase in smoking, poor diet, physical inactivity, and alcohol consumption among many others. The ranking of cancer in men is liver, colon, and lung cancers while breast and cervical cancers are leading in women (Harriet *et al.,* 2022). Hepatitis B and C are very much implicated in the development of liver cirrhosis that culminates into liver cancer in most patients over some time (Okeke *et al*., 2020). Epidemiological surveys recognized hepatitis virus infections to be the strongest factor associated with HCC, studies further have proven that HBV-infected sufferers have up to a 20-fold increased chance of HCC development compared to non-infected humans (Yang *et al.,* 2019). Male, older, smokers, high alcohol intake, and drug abusers especially the needle users are more prone than the rest of the population (José, 2022). Cases of liver diseases and cancer continue to rise, reported to have risen from 746,000 in 2012 to 841,080 in 2018, accounting for 5% of all cancers in the world (Okeke *et al.,* 2019). Co-exposure to the Hepatitis B virus and dietary intake of aflatoxin coexist in most parts of Africa, especially in areas with the heaviest burden of cancer where younger patients are commonly seen with HCC (Lemoine, 2017).

Iron overload either due to hereditary issues or as a result of dietary intake seen mostly in many African countries notably Kenya is a confirmed threat and a cause of HCC, independent of any underlying liver disease. Though, other organs are affected by this iron overload but the liver is the organ most affected with the aid of iron overload (Keisuke *et al.,* 2022).
A multistep process encompassing a combination of oxidative stress, inflammation, some epigenetic changes, fatty changes, fibrosis, and irreversible liver cirrhosis are the prerequisites that sway the development of HCC (Farazi *et al.,* 2006; Hall *et al.,* 2016; Llovet *et al.,* 2021).

A pathological type of liver cancer called hepatocellular carcinoma (HCC) is the most common form of liver cancer seen, accounting for about 75% of all cases. Other types that seldom occur are cholangiocarcinomas, angiosarcomas, and hepatoblastomas in children. (Ashwin *et al.,* 2006; Llovetet *et al.,* 2021). Researchers use several models to mimic liver cancer called the liver cancer models to learn about both the disease and or the impact of treatment among which are the chemical induction and genetic modifications (Zachary *et al*., 2018; Alexandru *et al.,* 2021).The carcinogenic chemical diethylnitrosamine (DEN) is amongst the most fundamental agents in use (Arboatti *et al.,* 2018; Zachary *et al*., 2018). The chemical DEN exists n cured and fried meals, tobacco smoke, cheddar cheese, water, occupational settings, cosmetics, and agricultural chemical substances among others (Arboatti *et al.,* 2018).
Surgery and the use of anti-cancer agents either in isolation or by combination are among the methods used in the treatment of liver cancer (Farmer *et al.,* 1994; Liu *et al.,* 2015; Singh *et al.,* 2023). The choice of any method depends on the type and stages of the liver cancer. Anticancer drugs either kill cancer cells or modify their growth, they can also be treated by the use of "Thermal ablation". The overall cost of treatment varies based on the treatment type, in general, the cost is high and usually out of reach for the average population. Five hundred thousand to one million and five hundred thousand (500,000-1,500,000) per session is the amount required for liver cancer management especially at advanced in the United States and UK among others (Kaplan *et al*., 2018; Cullen *et al*., 2023). The majority of these agents are known to cause several side effects some of which are unbearable to the patient others are the cause of another form of cancers as well.

Despite the advancements in cancer therapy, liver cancer remains a significant health burden, with limited treatment options and considerable toxicity associated with current therapies. The use of herbal medications as complementary or alternative medicine is getting more acceptability in the treatment of many chronic diseases including cancers (Tavakoli *et al*., 2012; Ali *et al*., 2023), *Spondias mombin* also known as yellow mombin or hog plum in English, tsardar-misra in Hausa (Northern region), iyeye\yeye in Yoruba (Southern western region) and ichikara in Igbo (Southern eastern region) is one such natural product being accepted as medication in many diseases. It's a species of tree and flowering plant in the family anacardiaceae. It is native to be tropical America including West India. In Africa, it is commonly found in the forest and savanna region of Nigeria and it's a medium size plant but occasionally a large tree (Ogunro *et al.,* 2023).

The leaves, seeds, stems and roots of the plant were reported to be medically useful (Sameh *et al.,* 2018; Ogunro *et al.,* 2023). The plant is traditionally used for a variety of ailments, the fruit has been used as a diuretic and febrifuge (Samehet *et al.,* 2018). The bark is astringent and used as an emetic for diarrhea, dysentery, hemorrhoid, gonorrhea, and leukorrheal. (Olalekan *et al.,* 2023). The flower and leaves are used to make tea for stomachache biliousness, urethritis, cystitis, and inflammation. It's also known to reduce anxiety, stop convulsions, calm and sedate, relieve

pain and suppress cough, aid digestion and stimulate the uterus (Uchendu *et al.*, 2008; Osuntokun, 2019; Olalekan *et al.*, 2023) The antimicrobial, antibacterial, antifungal, and the antiviral residences of *Spondias mombin* have been reported (Abo *et al.*, 1999; Olukemi Aromolaran *et al.*, 2014). This research aimed at evaluating the toxicity potential and pharmacology properties of *Spondias mombin* in liver cancer treatment.

2. 0 Materials and Methods

2.1 Study Area

The study was carried out at Bauchi State University Gadau, Nigeria.

2.2 Sample collection and preparation

Spondias mombin mature leaves were obtained from Bauchi State University Gadau in July 2023 and authenticated at the Department of Biological sciences with voucher number UBH-S345. The plant was air dried at room temperature and pounded into powdery structure. The powdered sample was extracted through cold maceration using 70% ethanol as the extracting solvent for 72 hours. The extract was filtered and concentrated at a temperature of 50^0C using a water bath.

2.3 Experimental Animals

Six weeks healthy mice; weighing twenty two to twenty five gram (20-25g) were used for this study, the mice were acquired from the animal house of the Department of Pharmacology, Faculty of Basic Medical Sciences, Bauchi State University Gadau. Animal ware kept for 5 days to get acclimatize before commencement of the study. They were caged in rubber cages of 6 mice per cage, the bedding were regularly change, water and food were constantly provided. A cycle of 20-23°C temperature, 50%-60% relative humidity with 12:12 h light/dark cycle was maintained throughout the study period. The experimental protocols were approved by Faculty of Basic Medical Sciences' Research and Ethics Committee (BASUG/FBMS/REC/VOL.07/093) Bauchi State University Gadau.

2.4 Phytochemical Screening

A preliminary analysis of the phytochemicals constituents of the plant extract was conducted using a method described by Pranshant *et al.* (2011).

2.5 Toxicity Study

Ten mice were randomly selected and divided into 2 groups containing 5 animals each. One group served as control and received only saline at 10mls/kg and the other group received 2000mg/kg of the ethanol extract of *Spondias mombin*, four hours of fasting were instituted before the dosing. Group 1 animals were administered with normal saline orally while Group 2 animals were administered a single dose of 2000mg/kg of ethanol extract. They were observed for behavioral changes, signs of toxicity, and mortality for the first 4 hours and thereafter daily over 14 days.

2.6 Induction of Cancer

Cancer was induced using one percent diethylnitrosamine (DEN) given via peritoneal injection to the mice weekly at a dose 35mg/kg for six weeks. The mice were divided into four group after four weeks of induction and treatment commenced with the extract while still given the DEN for cancer induction.

2.7 Experimental Design

Group 1 animals (6 mice) as a control group were treated with normal saline (10 ml/kg) intraperitoneally after the fourth week of DEN induction. Groups2, 3, and 4 containing animals (6 mice each) were treated with ethanol extract of *Spondias mombin* at a dose of 250mg/kg, 500 mg/kg, and doxorubicin (2 mg/kg) intraperitoneally.

2.8 Sample collection

At the end of the two week anti-cancer treatment animals were fasted overnight and then anaesthetized using chloroform before sacrifice. Blood was collected by cardiac puncture for biochemical analysis. The liver was excised using sterilized dissecting kits and surgical blades and a process for histological studies.

2.9 Statistical Analysis

Statistical analysis were carried out using Mean ± standard deviation (STD) and analyzed with standard statistical software package for social science (SPSS) software using one-way Analysis of Variance (one-way ANOVA) and Dunnetts *posthoc* test deployed were differences between multiple and two means respectively. Differences are considered at $P < 0.05$. Bar charts were drawn using Excel 2013 software.

3.0 Results and Discussion

The crude and the ethanol fraction of *Spondias mombin* leaves were obtained using cold maceration technique and resulting phytochemicals analysis shows the presences of alkaloids, cardiac glycosides, saponins, tannins, phenolic compounds, steroids, flavonoid, terpenoids and absences of carbohydrates anthraquinones in the ethanol extract, the same constituents were seen in the crude extract as shown in table 1.

Table 1: Preliminary phytochemical screening of different fractions of crude extract of *Spondias mombin* leaves

S/No	Phyto constituents	Test	Crude	Hexane	ChCl3	Ethanol	Aqueous
1	Alkaloids	Dragendorff test	+	-	-	+	+
2	Cardiac Glycosides	Keller-Kiliani test	+	+	+	+	+
3	Saponins	Frothing test	+	-	-	+	+
4	Phenolic compounds	Lead acetate test	+	-	+	+	+
5	Tannins	Ferric Chloride test	+	-	-	+	+
6	Steroids	Salkowiski test	+	+	+	+	+
7	Carbohydrates	Molisch test	+	-	+	+	+
8	Flavonoids	Shinoda test	+	-	+	+	+
9	Terpeniods	Liebermann Burchardtest	+	+	+	+	+
10	Anthraquinones	Bontragers test	-	-	-	-	-

KEYS: + PRESENT – ABSENT

Table 2 shows the body weight changes for mice in the acute toxicity study where the weight increases after administration of the ethanol fraction of *Spondias mombin* from day 1 to day 14. An acute oral toxicity test was performed on both male and female Balb C mice following Organization for Economic Cooperation and Development (OECD) test guideline 423 (OECD, 2001). A slight weight change among the experimental animals between 20.8±3.56 to 25.63±2.60 was seen and the increase was shown to be statistically ($P < 0.05$) significant at day 14.

Table 2: Body weight changes for acute toxicity animals after single dose of 2000mg/kg ethanol fraction of *Spondias mombin* leaves extract

GROUPS	Day 0	Day 3	Day 7	Day14 days
Ethanol fraction 2000mg/kg	20.8±3.56	20.7±2.2	22±3.65	25.63±2.60*
Control group	25.7±4.19	23.25±3.77	25.5±3.87	26.63±3.93*

Values are expressed as mean ± STD of n=6. Values with the same superscript are statistically significant, Dependent t-test

Table 3 showing observed morbidity and mortality data of mice in acute toxicity study after a single fixed dose test of 2,000 mg/kg given to the mice and 10 ml/kg of normal saline given to the control group mice. No mice showed any physical any sign of clinical toxicity, none died and no obvious gross pathology seen in the major organs on necropsy.

The finding from a single dose exposure of this extract in the acute toxicity study indicated that the ethanol extract of *Spondias mombin* is safe up to a limit dose of 2000 mg/kg, thus the LD50 is greater than 2000 mg/kg. The obvious sign of toxicity like convulsion, bleeding, lethargy, vomiting and general distress were equally checked and none of which was recorded over the 14day study period.

Table 3: Morbidity and mortality data of experimental rats exposed to ethanol extract of *S. mombin* leaves

Groups	Toxicity sign t/n	Mortality d/a	Gross pathology l/nl
10ml/kg N/Saline	0/6	0/6	0/6

2000mg/kg Ethanol extract of *S.mombin* leaves	0/6	0/6	0/6

t/n = toxic/normal, d/a= dead/alive, l/nl = lesion/ no lesion.

The table shows changes in liver enzymes following a single dose exposure of the ethanol extract as compared to those that received only normal saline. ALT, AST, ALP, TP and AL were all measure in both groups.

The ALT and AST of the group were found to be elevated more on the control group, however the ratio of ALT/AST is higher on the ethanol exposed group compared to saline group 2.56 and 3.61 respectively. The body total protein is slightly higher in the treatment group with low albumin constituents, while the albumin constituent of the treatment group showed higher value despite the lower concentration of the total protein**.**

Table 4: Liver enzymes analysis after single dose exposure of ethanol extract of *S. mombin* leaves

Group	ALT (IU/L)	AST(IU/L)	ALT/AST	ALP (IU/L)	TP(G/DL)	ALB (G/DL)
N/SALINE	56.5±5.44	144.5±7.8	2.56	29.4±5.13	11.55±2.45	2.2±0.11
ETH	39.5±3.43	142.5±8.03	3.61	24.8±4.34	10.3±1.69	2.6±0.14

Values are expressed as mean ± STD of n=6

Plasma Urea, electrolyte and creatinine predicting the kidney function test of mice treated with ethanol extract as compared to those given normal saline was shown on the table 3.5. The creatinine, CL and HCO3 of the control and study group were significantly different statistically with P<0.005 as tested by T-test. Noticed on the kidney function test of mice after exposure to the single dose of the ethanol extract compared to the control group are slight increases in the level of Na, Urea, creatinine, and CL. The HCO3 was slightly decreased compared to that of the control group.

Table 5: Urea, Electrolyte and Creatinine of mice exposed to ethanol extract of *S. mombin* leaves

Group	UREA (MG/DL)	NA (MOL/L)	K (MOL/L)	CREATININE (MEQ/L)	CL (MG/DL)	HCO3 (MG/DL)
N/Saline	97.5±24.75	431.25±26.52	20.5±6.58	0.9±0.10*	32±4.24*	122.5±24.74*
ETH	100±7.10	437.8±74.60	21.75±4.03	1.15±0.10*	47±8.49*	101±7.10*

Values are expressed as mean ± STD of n=6 and were analyze using one-way ANOVA. Values with same superscript are significantly different with the control group, NA: sodium ion, K: potassium ion, CL: chloride ion, ETH: Ethanol extract

The chart shows slight increase in weight of mice despite the injection of DEN within the week of experiment. The weights continue to slightly decrease steadily over the next three weeks. The differences in the weight were statistically insignificant as compared using one-way ANOVA between the weeks of study. The mice exhibited slight increase in weight after the first dose, however there was continues steady decrease in weight noticed following the second, third and fourth dose of DEN in the mice.

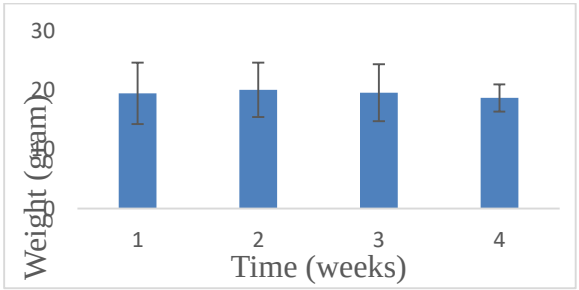

Figure 1: Weekly changes in weight of mice induce liver cancer with DEN after treatment with ethanol extract of *S. mombin* leaves.

The table is depicting weight changes in mice induced liver cancer with DEN before and after commencement of treatment with the ethanol extract different doses compared to DOX and negative control. Body weight at week 4 is the initial weight at the commencement of treatment, while the final body weight (week 6) signifies the body weight after 2 weeks of treatment. The Normal saline group have 15.00 ± 1.40 g, and 14.00 ± 1.70 g, DOX 18.30 ± 2.60 g and 20.00 ± 2.80 g, Ethanol 250 mg/kg 15.80 ± 2.20 g and 16.70 ± 20 g while Ethanol 500mg/kg is 26.30±1.90 g and 24.80±1.90 g respectively for the 4th and 6th week. There is an increase in weight of the experimental mice in the positive control group and the lower dose ethanol extract between the fourth and sixth week of treatment. The negative control group and the high dose ethanol group showed decrease on the weight.

Table 6: Effect of *Spondias mombin* leaves extract on the body weight of DEN cancer induced mice

GROUP	*TREATMENT*	*WEIGHT(week 4)*	*WEIGHT (week 6)*
1	DEN+N/SALINE	15± 1.4	14.5± 1.7
2	DEN+DOX 2mg/kg	18.3 ±2.6	20±2.8
3	DEN+ETH 250mg/kg	15.8 ±2.2	16.7 ± 2.1
4	DEN+ETH 500mg/kg	26.3 ± 1.9	24.8 ± 1.9

Values are expressed as mean ± STD of n=6 and were analyze using one-way ANOVA. Values with same superscript are significantly different with the control group.

Biochemical analysis of Liver enzymes showing the level of AST, AST, ALP, TP and ALB was shown in the table. The total protein of the negative control 2.9±0.56 to be lower than the remaining three treatment groups3.7±0.57, 3.55±1.90 and 4.35±0.77. The level of albumin 2.85±0.49 also followed the same pattern as the total protein showing high level in the normal saline group compared to all treatment groups 0.85±0.07, 0.90±0.70 and 0.95±0.07. The difference between the saline controls group were found to statistically significant compared to the treatment groups in both parameters as tested by T-test with $p<0.005$.

The ALP, TP and Albumin of Normal saline group were found to be higher than those obtained from all the three treatment groups. However, the main liver enzymes notably the ALT and AST were higher in the extract treated groups compared to both Dox treated and saline treated groups.

Table 7: Biochemical analysis of liver enzymes in mice induced with DEN after Treatment with ethanol extract of *S. mombin* leaves

Group	**ALT (IU/L)**	**AST(IU/L)**	**ALP(IU/L)**	**TP(G/DL)**	**ALB(G/DL)**
N/SALINE	5.5±2.12	4.5±2.12	18.3±3.95	2.9±0.56	2.85±0.49
ETH 250	10.5±2.12	31±29.7	11.1±0.57	3.7±0.57	0.85±0.07
ETH 500	7±8.49	39±52.36	9.3±0.56	3.55±1.90	0.90±0.70
DOX	8±5.66	9.5±9.19	11.15±2.05	4.35±0.77	0.95±0.07

Values are expressed as mean ± STD of n=6 and were analyze using one-way ANOVA. Values with same superscript are significantly different with the control group.

4.0 Discussion

Liver cancer like most other cancers is a progressive disease and difficult to treat unless diagnose dearly, prevention is rather easier and more cost-effective, vaccine against Hepatitis B and avoidance of excessive alcohol consumption may serve as good preventive measures. Promising practices like an increase in surveillance, public awareness, and adequate knowledge of infection status especially of hepatitis, improved hepatitis treatment services will likely reverse the liver cancer trends of the world (Chang *et al.*, 2011; Momin *et al*., 2018). The treatment of liver cancer is rather a multidisciplinary approach including drugs, surgery and psychotherapy either in combination or alone (Salgia *et al*., 2021). In recent years several clinical trials that target the progression process of liver cancer have being tested, notably the signaling pathways involved in the control of this process but the efficacy of those agents tested revealed no relevant improvement in the prognostic and or survival of patients with HCC, thus the need for the identification of novel therapeutic agents for the management of HCC (Anwanwan *et al.*, 2019; Duspara *et al.*, 2021).

Several plants were shown to have valuable anticancer activity against different types of cancer, they are generally accepted by society based on availability, effectiveness, and safety profile. *Spondias mombins* is a plant with such projection against many diseases, thus it is used in this study. An ethanol fraction of leaf extracts of *Spondias mombins* contains the following phytochemical constituents namely terpenoids, steroids, phenolic compounds, tannins, cardiac glycosides, and carbohydrates (table 3.1). An analysis of the same plant demonstrated the presence of similar important constituents by Njoku and Akumefula, (2007). Similarly, tannins, carbohydrate, flavonoid, glycoside, alkaloid, steroid and terpenoid compounds were seen in another extraction of the same plant in Abia State University (Nwaogwugwu, 2018).

Most of these phytochemicals exhibit beneficial pharmacological and biochemical actions in animals. An anti-nutritional factor via reduction in the uptake of cholesterol and glucose at the gut through intra-luminal physicochemical interaction with saponins is one of such pharmacological activity of phytochemicals making relevant as antidiabetic agents (Marrelli *et al.*, 2016). Alkaloids repel predators and parasites in plants and it has effects on glucagon, thyroid stimulating hormone and inhibit certain mammalian enzymic activities (Divekar *et al.*, 2022). A tremendous anti-oxidant and anti-inflammatory or antibacterial activities are seen with flavonoids (Al-Khayri *et al.*, 2022)

An acute oral toxicity test was performed on both male and female baldC mice following Organization for Economic Cooperation and Development (OECD) test guideline 423 (OECD, 2001). Animals exposed to the extract and observed for 14 days exhibited no obvious sign of toxicity and none of the mice died during the period of observation (Table 3.2). Thus, the ethanol extract of *Spondias mombin* extract is said to have a lethal dose above 2000mg/kg as seen a study conducted by Feoluwa *et al.* (2014).

The effect of the extract on the weight of the mice revealed a slight weight changes among the control group animals between 20.8±3.56 to 25.63±2.60 as recorded on day 0, 3, 7 and 14. The changed was shown to be statistically significant at day 14. The observed body weight changes of the experimental animals notice to be slightly lower than observed in the control group, though not significant statistically ($p > 0.05$). The plasma Urea, electrolyte and creatinine are clinically used to access the kidney functions, its damage and also to monitor diseases progress (Gowda *et al.*, 2010; Fuchs *et al.*, 2011). Here, the three were accessed to predict the possible level of renal damage due to exposure to high-dose ethanol extract of the plant as compared to normal saline intake by the mice. The creat, CL, and HCO_3 of the control and study group were significantly different statistically with $P<0.005$ as tested by T-test. There is a slight decrease in the level of HCO_3 in mice of the study group compared to the control group showing evidence of acidosis either due direct effect of the extract on mice or secondary to dehydration.

The highest weight gain at the second weeks of induction with DEN is 20.1 ± 4.6. A decrease in weight were discovered in week 3 and 4 respectively which is an indication of possible liver cancer induced

by DEN on the animals. Disease like cancer, diabetics, arthritis and chronic infections are generally associated weight changes characterized by a distinct patterns up to 10% loss 0f body weight within a year have likely is seen in these ailment (Vierboom, 2018).

The initial body weight signifies the body weight in the first week of treatment, while the final body weight signifies the body weight in the second week of treatment. The initial body weight of Group 1 was 15±1.4, upon the treatment with N/saline there was a decrease to a body weight of 14±1.7. In group 2 there was also an observable change in weight from 18.3±2.6 to 20±2.8. In group 3 treated with ethanol extract 250mg/kg after DEN induction, the weight of the mice showed a significant increase from 15.8±2.2 to 16.7 ±2.1 administration of ethanol extract 500mg/kg shows rather a significant decrease in the body weight from 26.3±1.9 to 24.8±1.9.Loss of weight is a major indicator of chronic diseases seen in cancers, infections, and famine. The loss in body weight is usually as a result of loss in body fats due to continuous mobilization by the liver to produce the needed energy in the form of glucose for the body (El-Zayat *et al.*, 2019). The inability of the liver to metabolize chemical as well as food during chronic diseases like the cancer will equally add to the lost in body weight and a vicious cycle of continues damage of body tissues by chemicals the body is exposed to.

Changes in the level of liver enzyme in the blood can indicate liver damage or diseases in mice induced and treated with Normal saline, doxorubicin, and ethanol extract. The two transferases and plasma protein were biochemically analyzed as shown in table3.7, the total protein of the negative control 2.9±0.56 found to be lower than the remaining three treatment groups3.7±0.57, 3.55±1.90 and 4.35±0.77. This is the usual presentation in pathological conditions of liver damage especially in chronic cases due to decreased production of basic plasma protein, also seen in renal diseases where proteins are excreted in urine because of glomerular damage (Hällfin and Laurell, 1972; Rogos *et al.*, 1978; Tufoni *et al.*, 2020) The level of albumin 2.85±0.49 also followed the same pattern as the total protein showing high level in the normal saline group compared to all treatment groups 0.85±0.07, 0.90±0.70 and 0.95±0.07. The ALP, TP and Albumin of Normal saline group were found to be higher than those obtained from all the three treatment groups. However, the main liver enzymes notably the ALT and AST were higher in the extract treated groups compared to both Dox treated and saline treated groups. Thus the two chosen doses of the extract shows improvement of both liver enzymes and the protein especially the albumin level almost similar to doxorubicin in mice when compared to negative control.

5.0 Conclusion

Spondias mombins is a plant very reach in important phytochemical constituents and the ethanol extract revealed the presence of some of those pharmacological constituents. The extract was shown to have no obvious physical sign of toxicity and it doesn't cause mortality in all the tested animals. The likely anticancer potential of the extract is similar to that seen in doxorubicin at the tested doses. Ethanol extract of the plant reversed loss in weight, deterioration in liver enzymes, and protein production to an extent similar to that of standard anti-cancer agents.

Declarations

Competing interests

The authors declare that they have no competing interests.

Ethics approval and consent to participate

Ethical approval was obtained from Faculty of Basic Medical Sciences' Research and Ethics Committee (FBMSREC) Bauchi State University Gadau (Approval Number: BASUG/FBMS/REC/VOL.07/093).

Authors' contributions

JGE performed the experiments, data gathering, and initial draft of the write-up. KAN and MAM were involved in the result analysis, editing of the drafted manuscript while AUK did an intellectual revision and gave approval for the final manuscript. All authors read and approved the final manuscript.

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Consent for publication
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