# Research Journal of Medicinal Plant

ISSN 1819-3455

Academic Journals Inc.

www.academicjournals.com

OPEN ACCESS Research Journal of Medicinal Plants

ISSN 1819-3455
DOI: 10.3923/rjmp.2017.148.159

# Research Article
# Effects of Aqueous Extracts of Palm Fruits (*Elaeis guineensis*) on Liver Function Indices of Male Wistar Albino Rats

[1]Uroko Robert Ikechukwu, [1]Egba Simeon Ikechukwu, [1]Achi Ngozi Kalu, [1]Uchenna Oluomachi Nancy, [1]Agbafor Amarachi, [2]Ngwu Ogochukwu Rita, [3]Nweje-Anyalowu Paul Chukwuemaka and [1]Ogbonna Chisom Esther

[1]Department of Biochemistry, College of Natural Sciences, Michael Okpara University of Agriculture, Umudike, Abia State, Nigeria
[2]Department of Biochemistry, Faculty of Natural Sciences, Caritas University, Amorji Nike, Enugu State, Nigeria
[3]Department of Biochemistry, Faculty of Science, Clifford University, Owerrinta, Abia State, Nigeria

## Abstract

**Background and Objective:** There is increase in the rate of consumption of aqueous extracts of ripe palm fruits (*Elaeis guineensis*) by humans in their daily diets but there is little or no toxicological data to support the safety of their consumption. This study investigated the effects of aqueous extracts of palm fruits on liver function indices of male Wistar albino rats with the view of understanding the hepatotoxic potentials of the extracts. **Materials and Methods:** Acute toxicity study was carried out with 18 male Wistar albino mice. Liver function indices were evaluated using 45 male Wistar albino rats and by following standard analytical protocols. The rats were divided into 5 groups with group 1 having 5 rats only and group 2-5 had 10 rats each. Group 1 rats were the normal control that received 2 mL $kg^{-1}$ b.wt., of normal saline. Five rats each from group 2-5 received 100, 200, 400 and 600 mg $kg^{-1}$ b.wt., of the fresh and fermented aqueous extracts of palm fruits, respectively for 28 days. Data was analyzed by one way ANOVA using SPSS. **Results:** The aqueous extracts were relatively safe as no death or adverse reactions were observed in the mice in 24 h after administration. There were significant ($p<0.05$) dose-dependent increase in all the liver marker enzymes assayed in all the groups administered the aqueous extracts when compared with the normal control. Total protein concentrations of groups 2 and 3 that received low doses of the fresh aqueous extract of palm fruit decreased significantly ($p>0.05$) when compared to the normal control. However, groups 4 and 5 that received higher doses of the fresh extract showed significant ($p<0.05$) increase in total protein and bilirubin concentrations when compared to the normal control. A significant ($p<0.05$) decrease in albumin concentrations was observed when the extracts were administered to the rats in higher doses, respectively when compared to the normal control. **Conclusion:** The findings suggest that the fresh and fermented aqueous extracts of palm fruit have little or no toxic effects on liver integrity and functions at very low concentration, however, it could cause significant chronic toxic effects on liver integrity and functions at higher concentrations.

Key words: Palm fruits, liver marker enzymes, liver integrity, protein, albumin

Citation: Uroko Robert Ikechukwu, Egba Simeon Ikechukwu, Achi Ngozi Kalu, Uchenna Oluomachi Nancy, Agbafor Amarachi, Ngwu Ogochukwu Rita, Nweje-Anyalowu Paul Chukwuemaka and Ogbonna Chisom Esther, 2017. Effects of aqueous extracts of palm fruits (*Elaeis guineensis*) on liver function indices of male Wistar albino rats.. Res. J. Med. Plants, 11: 148-159.

Corresponding Author: Uroko Robert Ikechukwu, Department of Biochemistry, College of Natural Sciences, Michael Okpara University of Agriculture, Umudike, Abia-State, Nigeria Tel: +2348065914471



Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

## INTRODUCTION

The aqueous extract of palm fruit is the major by-product of palm oil production[1]. Although, it is usually removed as wastewater during palm oil production and many people value it as essential component of normal food mainly in the Southeastern region of Nigeria, where it is consumed as whole palm fruit extract in a local dish (ofe-akwu). Palm oil is an edible vegetable oil derived from the fleshy mesocarp of the oil palm fruit, which is considered as one of the most healthful oils full of vitamin E and other antioxidants as well[2]. Palm oil is naturally reddish in color because of its high beta-carotene content which is also found in the aqueous fractions[3].

The composition of the aqueous extract of palm oil are mainly water, oil, solids (suspended and dissolved) and sand. It also consists of cell wall organelles, a variety of carbohydrates ranging from cellulose to simple sugars, a range of nitrogen-pus compounds from proteins to amino acids, free organic acids and an assembly of minor organic and mineral constituents[4]. Micronutrient content in aqueous extract of palm fruits (i.e., palm oil mil effluents) are nitrogen, phosphorus, potassium, magnesium and calcium that are all vital nutrient elements. Aqueous extract of palm oil, is a thick, brownish colloidal mixture of water, oil and fine suspended solids[5,6]. Fresh aqueous extract of palm fruit is non-toxic as no chemicals are added during the extraction process of palm oil, however, its metabolites may be toxic[3]. The aqueous extract of palm oil is economically important, because of its potential harmful effects attributed to its composition of phenols and other organic compounds that could be responsible for its phytotoxicity and antibacterial activity[7].

In Umuaka, Njaba the aqueous extracts of palm fruits are used to reproduce palm oil for commercial consumption without any treatment while in other parts of the country like Enugu, the aqueous extracts are filtered to remove sludge before they are reused for palm oil production. However, if these aqueous extracts contain toxic constituents or metabolites, they could cause long time health effects to the consumers, if not immediate health effects. Umuaka, Njaba in Imo State, Nigeria has been noted as one of the several areas where rural small-scale palm oil milling occurs. Due to increase in the prevalence of diseases and metabolic malfunctions such as liver disorders and ailments, the study was expected to capture effects of aqueous extract of palm fruit on liver marker enzymes and liver functions. Since humans consume this aqueous extract of palm fruit as "ofe-akwu" the contribution of this study will help to explain the health consequences of its consumption or its reuse in the production of palm oil while creating awareness on the importance of maintaining safe limit. This study was aimed at investigating the toxic effect of fresh and fermented aqueous extract of palm fruit on liver marker enzymes and on the concentration of some other selected liver function parameters.

## MATERIALS AND METHODS

The study was carried out between March, 24 and August, 25, 2016 at the Department of Biochemistry, College of Natural Sciences, Michael Okpara University of Agriculture, Umudike, Abia State, Nigeria.

**Preparation of aqueous extract of palm fruit:** A known volume, 20 L of freshly prepared aqueous extract of palm fruit was obtained from Obeakpu palm oil milling site in Njaba, Imo State. It was filtered with a mesh cloth, followed by Whatman No. 1 filter paper. The filtrate was divided into equal volumes, one portion was stored in a refrigerator and the other portion was not kept in a refrigerator and allowed to ferment for 21 days. This was carried out to mimic the situations where people consume the fresh aqueous fraction in the form of "ofe-akwu" and the second situation where it is used as water substitute to produce palm oil irrespective of its age. The two extracts were concentrated to dryness in a water bath at 60°C and were used for the study.

**Collection of animals for the study:** The animals were obtained from the animal house of the Department of Zoology, University of Nigeria, Nsukka. The animals were acclimatized at the animal house of the Department of Biochemistry, College of Natural Sciences, Michael Okpara University of Agriculture, Umudike for 7 days under 12 h dark and light cycle with free access to standard animal feed and water.

**Experimental design:** A total of 45 male Wistar albino rats and 18 male albino mice were used for this study. The mice were divided into 2 major groups of 9 mice each. Each of the 2 groups were then divided into 3 groups of 3 mice each and used for the phase 1 and phase 2 of the acute toxicity study, respectively. The rats were divided into 5 groups with group 1 having 5 rats and served as the normal control. The remaining 4 groups had 10 rats each with 5 rats in each group receiving fresh and fermented aqueous extracts, respectively for 28 days after which the rats were sacrificed on the 29th day and blood samples collected for biochemical analysis.

**Group 1:** Normal saline was administered orally daily for 28 days

**Group 2:** Five rats each received 100 mg $kg^{-1}$ b.wt., of fresh and fermented aqueous extracts 28 days, respectively

**Group 3:** Five rats each received 200 mg $kg^{-1}$ b.wt., of fresh and fermented aqueous extracts for 28 days, respectively

**Group 4:** Five rats each received 400 mg $kg^{-1}$ b.wt., of fresh and fermented aqueous extracts for 28 days, respectively

**Group 5:** Five rats each received 600 mg $kg^{-1}$ b.wt., of fresh and fermented aqueous extract for 28 days, respectively

**Acute toxicity study and lethality test:** The acute toxicity study of the fresh and fermented aqueous extract of palm fruit were carried out according to the method described by Lorke[8].

**Determination of alanine aminotransferase (ALT):** The alanine aminotransferase activity was assayed according to the method described by Wroblewski and LaDue[9].

**Determination of aspartate aminotransferase (AST):** This assay was carried out according to the method described by the International Federation of Clinical Chemistry[10].

**Determination of alkaline phosphatase (ALP):** Determination of ALP was carried out according to the method described by the International Federation of Clinical Chemistry (IFCC)[10].

**Determination of albumin concentration (ALB):** Albumin concentration was assayed according to the method described by Rodkey using the Randox laboratory kit[11].

**Determination of total protein concentration (TP):** Total protein concentration was determined according to the method described by Weichselbaum[12].

**Determination of total bilirubin and conjugated bilirubin concentration:** The concentration of total bilirubin was determined according to the method of Jendrassik and Grof as contained in Randox assay kits[13].

**Tissue preparation for histological analysis:** The surviving experimental animals were humanely sacrificed at the end of the study. Gross lesions were recorded as observed during the postmortem examination. Sections of the liver were collected for histopathological examination. The collected samples were fixed in 10% phosphate buffered formalin for a minimum of 48 h. The tissues were subsequently trimmed, dehydrated in 4 grades of alcohol (70, 80, 90% and absolute alcohol), cleared in 3 grades of xylene and embedded in molten wax. On solidifying, the blocks were sectioned, 5 µm thick with a rotary microtome, floated in water bathe and incubated at 60°C for 30 min. The 5 µm thick sectioned tissues were subsequently cleared in 3 grades of xylene and rehydrated in 3 grades of alcohol (90, 80 and 70%). The sections were then stained with Hematoxylin for 15 min. Blueing was done with ammonium chloride. Differentiation was done with 1% acid alcohol before counterstaining with Eosin. Permanent mounts were made on degreased glass slides using a mountant, DPX.

**Slide examination:** The prepared slides were examined with a Motic™ compound light microscope using 4, 10 and 40x objective lenses. The photomicrographs were taken using a Motic™ 9.0 megapixels microscope camera at 100 and 400x magnifications.

**Statistical analysis:** The results obtained were analyzed using the Statistical Products and Service Solutions (IBM Statistics SPSS 20) and the results were presented as mean±standard deviation. Significant differences of the result were established by one-way analysis of variance (ANOVA) and the acceptable level of significance was $p<0.05$ (95% confidence level)[14].

## RESULTS

**Percentage yield:** After filtration and concentration of 10 L, each of fresh and fermented aqueous extract of palm fruits, percentage yields of 22.4 and 23.9%, respectively were obtained.

No death was recorded in the mice after 24 h administration of graded doses of the fresh and fermented aqueous extract of palm fruit, even when very high dose of 5000 mg $kg^{-1}$ b.wt., was administered as shown in Table 1.

Table 1: Acute toxicity study of the fresh and fermented aqueous extracts of palm fruit

| Treatment groups | Dosage (mg $kg^{-1}$ b. wt.) | Mortality |
|---|---|---|
| **Phase I** | | |
| Group 1 | 10 | 0/3 |
| Group 2 | 100 | 0/3 |
| Group 3 | 500 | 0/3 |
| **Phase II** | | |
| Group 4 | 1000 | 0/3 |
| Group 5 | 2900 | 0/3 |
| Group 6 | 5000 | 0/3 |

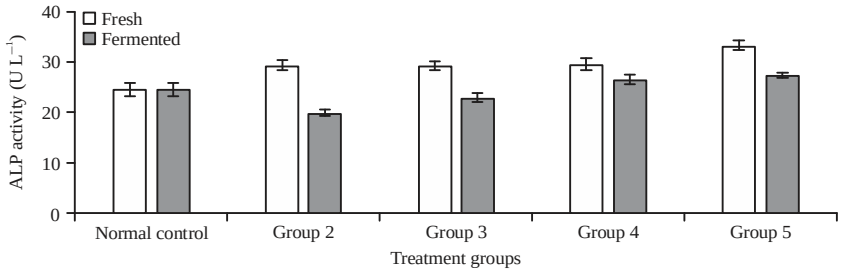


Fig. 1: Alkaline phosphatase (ALP) activity of male Wistar albino rats administered fresh and fermented aqueous extracts of palm fruits, bars are Mean±Standard deviation (n = 5)

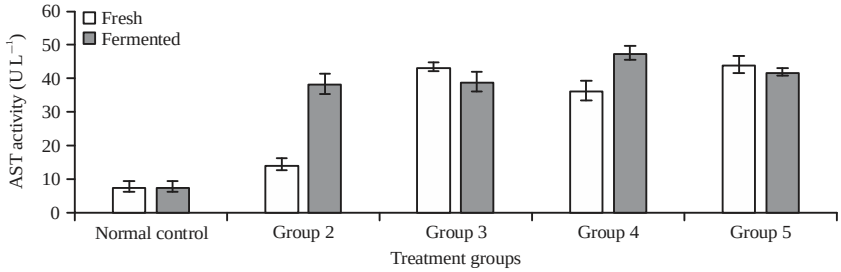


Fig. 2: Aspartate transaminase (AST) activity of male Wistar albino rats administered fresh and fermented aqueous extracts of palm fruit, bars are Mean±Standard deviation (n = 5)

All the groups administered graded doses of the fresh aqueous extract of palm fruit had significant ($p<0.05$) increase in ALP activity when compared with the normal control as shown in Fig. 1. However, rats in group 2 and 3 administered 100 and 200 mg kg$^{-1}$ b.wt., of the fermented aqueous extract of palm fruit, respectively showed no significant decrease in ALP activity with respect to the normal control. However, groups 4 and 5 that received 400 and 600 mg kg$^{-1}$ b.wt., of the same fermented aqueous extract of palm fruit showed significant ($p<0.05$) increase in ALP activity when compared with the normal control. When the groups administered graded doses of the fresh aqueous extract of palm fruit were compared with their respective groups which received equivalent doses of the fermented aqueous extract of palm fruit, it was observed that those that received fermented extract had significant ($p<0.05$) decrease in ALP activity relative to their respective groups that received fresh extract.

Group 2 rats administered 100 mg kg$^{-1}$ b.wt., of the fresh aqueous extract of palm fruit had no significant increase in AST activity when compared to the normal control as shown in Fig. 2. Unlike group 2 rats, all other groups (3, 4 and 5) that received graded doses of the fresh extract had significant ($p<0.05$) increase in AST activities when compared with the normal control. The evidence in Fig. 2 also show that all the groups administered graded doses of fermented aqueous extract of palm fruit had significant ($p<0.05$) increase in AST activity in a dose dependent manner except when the highest dose of 600 mg kg$^{-1}$ b.wt. of the fermented extract was administered when compared to the normal control group. Group 2 that received the fermented extract showed significant ($p<0.05$) increase in AST activity when compared with group 2 that received equivalent dose of fresh extract. However, groups 3 and 5 administered the fermented extract showed no significant decrease in AST activity when compared to groups 3 and 5 that received equal dose of the fresh extract. Group 4 rats, that received the fermented extract had no significant increase in AST activity with respect to AST activity of group 4 that received equal doses of the fresh extract.

Significant ($p<0.05$) increase in alanine aminotransferase (ALT) activity of all the groups administered fresh and fermented aqueous extract of palm fruit when compared to the normal control group was observed as shown in Fig. 3. However, comparisons between groups show that groups 3, 4 and 5 administered 200, 400 and 600 mg kg$^{-1}$ b.wt., respectively showed significant ($p<0.05$) increase in ALT activity while group 2 that received the 100 mg kg$^{-1}$ of the fermented extract showed significant ($p<0.05$) decrease when they were compared to the groups that received equivalent doses of the fresh extract.

Groups 2 and 3 administered fresh extract had no significant increase in total protein when compared with the normal control as shown in Fig. 4. However, groups 4 and 5 which received the fresh aqueous extract and groups 2 and

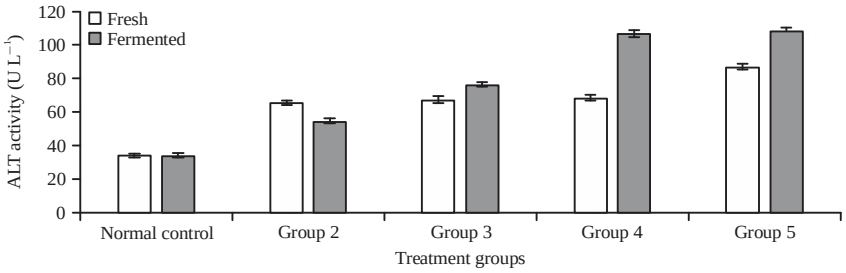


Fig. 3: Alanine transaminase (ALT) activity of male Wistar albino rats administered fresh and fermented aqueous extracts of palm fruits, bars are Mean±Standard deviation (n = 5)

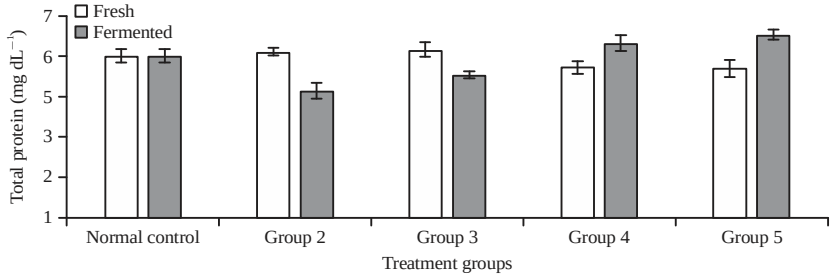


Fig. 4: Total protein concentration (TP) of male Wistar albino rats administered fresh and fermented aqueous extracts of palm fruits, bars are Mean±Standard deviation (n = 5)

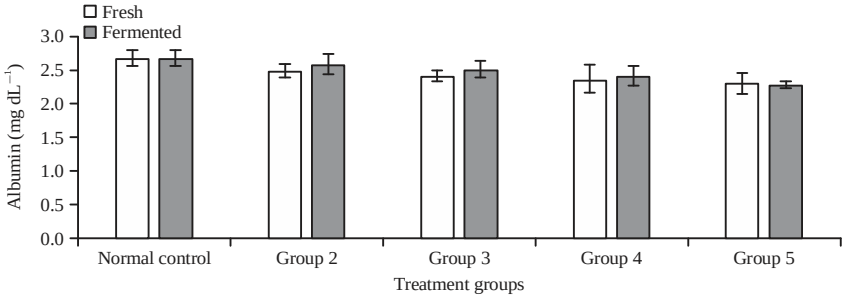


Fig. 5: Albumin (ALB) concentration of male Wistar albino rats administered fresh and fermented aqueous extracts of palm fruits, bars are Mean±Standard deviation (n = 5)

3 which received the fermented extract showed significant ($p<0.05$) decrease in total protein concentration when compared to the normal control while groups 4 and 5 administered fermented extract had significant ($p<0.05$) increase in total protein concentration when compared to the normal control. However, comparison between the groups indicated that groups 2 and 3 which received the 100 and 200 mg kg$^{-1}$ b.wt., of the fermented extract had significant ($p<0.05$) decrease when compared to the control. Contrarily to the groups 2 and 3, groups 4 and 5 which received 400 and 600 mg kg$^{-1}$ b.wt., of the same extract had significant ($p<0.05$) increase in total protein concentration when compared with respective groups that received fresh extract of palm fruit.

Group 2 which received the fresh extract and group 3 which received the fermented extract showed no significant decrease in albumin concentration with respect to the normal control as shown in Fig. 5. Groups 3 and 4 rats administered fresh extract and groups 4 and 5, which received the fermented, extract showed significant ($p<0.05$) decrease in albumin concentrations when compared to the normal control. However, group 5 which was administered the fresh extract showed significant ($p<0.05$) increase in albumin concentration while group 2 which received the fermented extract showed no significant increase in albumin concentration when compared to the normal control. Comparisons between the administered groups indicated

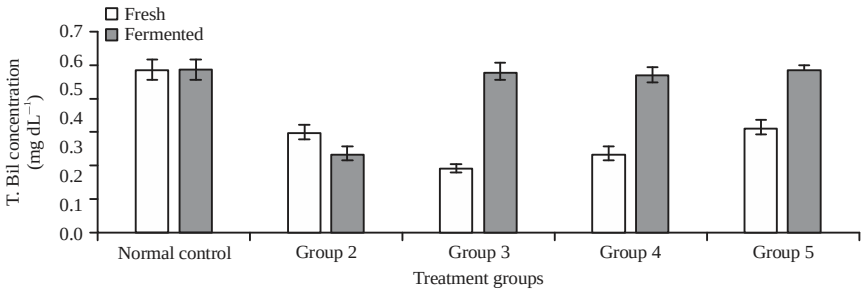


Fig. 6: Total bilirubin (T. Bil) concentration of male Wistar albino rats administered fresh and fermented aqueous extracts of palm fruit, bars are Mean±Standard deviation (n = 5)

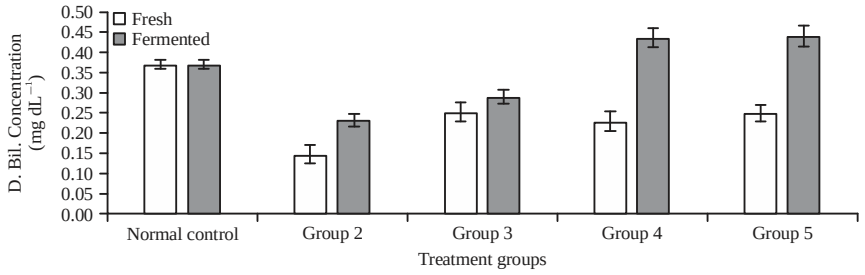


Fig. 7: Direct bilirubin (D.Bil) concentration of male Wistar albino rats administered fresh and fermented aqueous extracts of palm fruit, bars are Mean±Standard deviation (n = 5)

that groups 3 and 4 which received the fermented extract of palm fruits showed no significant increase in albumin concentration, respectively. On the other hand, groups 2 and 5 administered the fermented extract showed significant ($p<0.05$) increase and decrease in albumin concentration when compared with their respective groups administered the fresh extract at equivalent doses.

There was a significant ($p<0.05$) decrease in the concentration of total bilirubin concentrations of the rats in groups 2, 3, 4 and 5 which received the fresh extract and group 2 which received the fermented aqueous extracts of palm fruit, respectively when compared to the normal control as shown in Fig. 6. However, groups 3, 4 and 5 administered graded doses of the fermented extract showed no significant decrease in total bilirubin concentrations when compared to the normal control. It was observed that groups 3, 4 and 5 rats that received graded doses of fermented extract of palm fruit, showed a significant ($p<0.05$) increase in total bilirubin concentration when compared to the group administered with an equivalent dose of the fresh extract. However, group 2 rats administered 100 mg $kg^{-1}$ b.wt., of fermented extract showed no significant decrease in total bilirubin concentration when compared to the group administered an equivalent dose of the fresh extract.

Groups 2, 3, 4 and 5 administered graded doses of fresh extract of palm fruit and group 2 and 3 administered with the fermented extract showed significant ($p<0.05$) decrease in direct bilirubin concentrations when compared to the normal control as shown in Fig. 7. The direct bilirubin concentrations in groups 4 and 5 rats administered graded doses of the fermented aqueous extract of palm fruit significantly ($p<0.05$) increased when compared to the normal. It was further observed that except group 3 which showed no significant increase in direct bilirubin concentration, groups 2, 4 and 5 which received graded doses of the fermented extract showed significant increase in direct bilirubin concentration when compared with their respective groups administered equivalent doses of the fresh aqueous extract of palm fruit.

**GROUP (1) (Normal control):** Sections of the liver collected from the animals in this group showed the normal hepatic histo-architecture. The sections showed normal hepatic lobules composed of normal hepatocytes arranged in cords (hepatic chords) separated by sinusoidal spaces. The hepatic cords are arranged in a radiating manner around the central veins (V), radiating towards the portal areas which contained normal structures of the portal area (hepatic artery, hepatic vein and bile duct). Portal area (P). H and E, 100, 400x (Fig. 8).

**GROUP (2a) (fresh aqueous extract):** Sections of the liver collected from the animals in this group showed a mild to

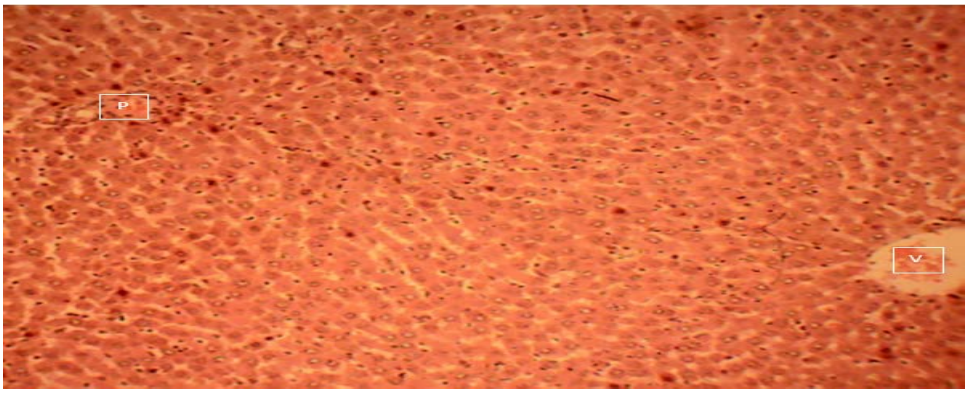


Fig. 8: Liver collected sections with normal hepatic histo-architecture

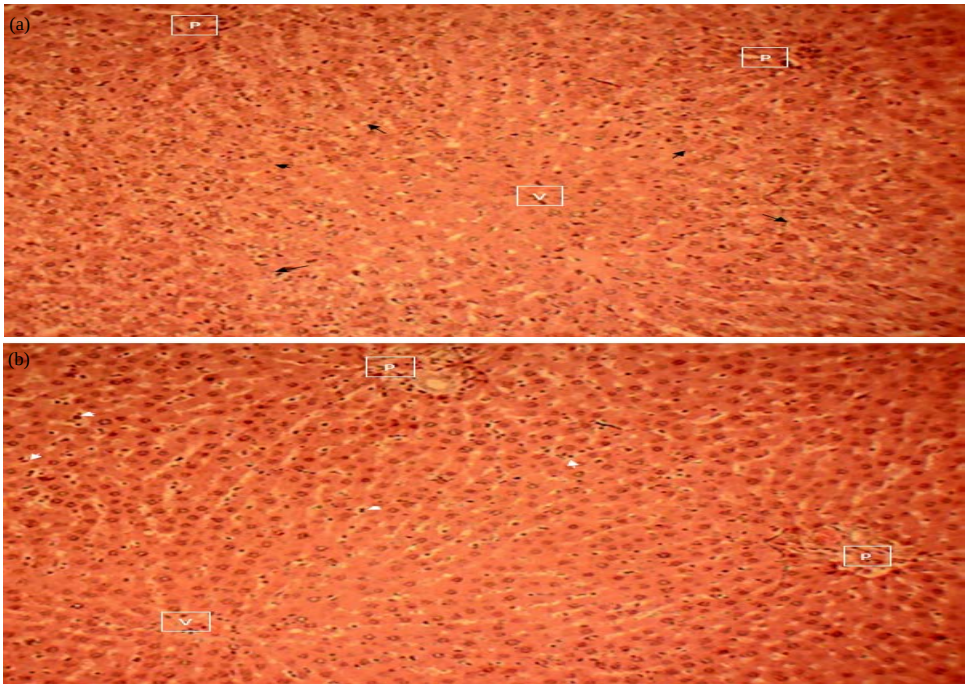


Fig. 9(a-b): (a) Liver collected sections with mild to moderate fatty degeneration of the hepatocytes and (b) Liver collected sections in fermented aqueous extract showed normal hepatic histo-architecture

moderated fatty degeneration of the hepatocytes, especially those around the portal areas (arrow). The affected hepatocytes are swollen, with multiple coalescent clear vacuoles in their cytoplasm. Notice that the hepatocytes around the central vein (V) are normal. Portal area (P). H and E, 100, 400x (Fig. 9a).

**GROUP (2b) (fermented aqueous extract):** Just as observed in group 1, the sections of the liver collected from the animals in this group showed the normal hepatic histo-architecture. The hepatic lobules show normal hepatocytes arranged in radiating chords around the central veins. However, mild widespread sinusoidal infiltration of mononuclear inflammatory cells (arrow) was observed. Central vein (V), Portal area (P). H and E, 100x (Fig. 9b).

**GROUP (3a) (fresh aqueous extract):** Sections of the liver collected from the animals in this group showed a mild widespread fatty degeneration of the hepatocytes. The affected hepatocytes show minute clear vacuoles in their cytoplasm (arrow). Central vein (V). H and E, 400, 100x (Fig. 10a).

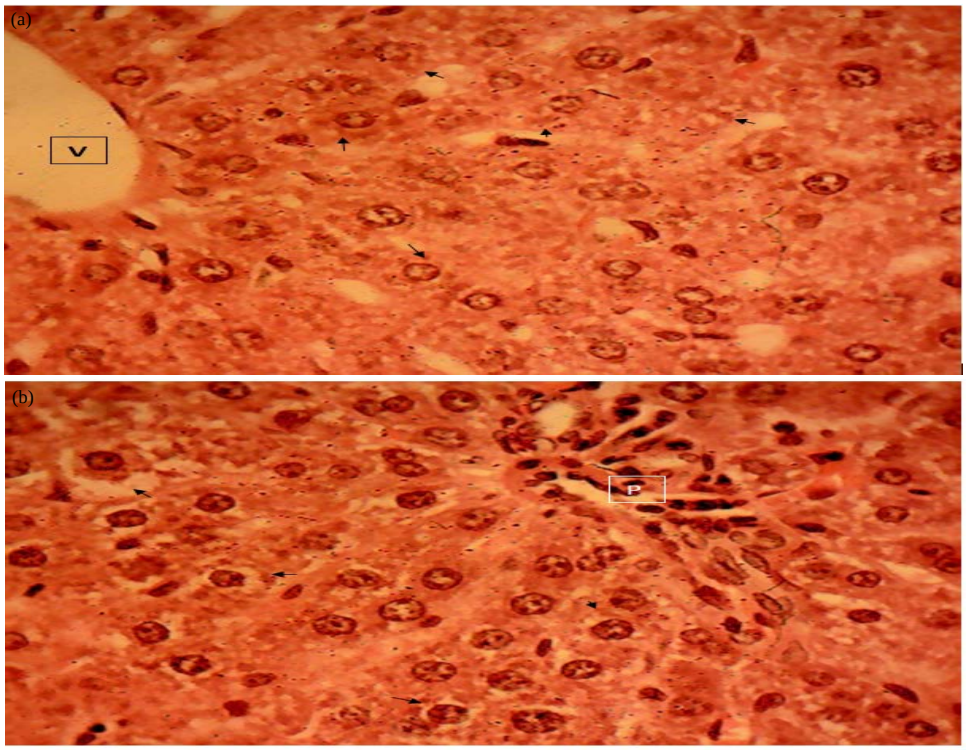


Fig. 10(a-b): (a) Liver collected sections in fresh aqueous extract with mild widespread fatty degeneration of the hepatocytes, (b) Liver collected sections in fermented aqueous extract showed mild to moderated widespread fatty degeneration of the hepatocytes

**GROUP (3b) (fermented aqueous extract):** Sections of the liver collected from the animals in this group showed a mild-moderate widespread fatty degeneration of the hepatocytes. The affected hepatocytes are swollen, with multiple coalescent clear vacuoles in their cytoplasm. Portal area (P). H and E, 400x (Fig. 10b).

**GROUP (4a) (fresh aqueous extract):** Sections of the liver collected from the animals in this group showed a mild-moderate widespread fatty degeneration of the hepatocytes. The affected hepatocytes are swollen, with multiple coalescent clear vacuoles in their cytoplasm. In addition, mild sinusoidal and periportal infiltration of mononuclear inflammatory leucocytes were observed (arrow). Central vein (V), portal area (P). H and E, 100, 400x (Fig. 11a).

**GROUP (4b) (fermented aqueous extract):** The liver sections obtained from this group of animals demonstrated mild-moderate widespread fatty degeneration of the hepatocytes, causing the hepatocytes to be swollen, with multiple coalescent clear vacuoles in their cytoplasm. Mild to moderate multifocal aggregates, sinusoidal and periportal infiltration of mononuclear inflammatory leucocytes were further observed (arrow). Central vein (V), bile duct (B), hepatic vein (HV), lymph vessel (L). H and E, 100, 400x (Fig. 11b).

**Fresh aqueous extract:** Sections of the liver collected from the animals in this group showed a mild to moderated widespread fatty degeneration of the hepatocytes. The affected hepatocytes are swollen, with multiple coalescent clear vacuoles in their cytoplasm (arrow). Central vein (V). H and E, 400x (Fig. 12a).

**GROUP (5a) (fermented aqueous extract):** Sections of the liver collected from the animals in this group showed a mild widespread fatty degeneration of the hepatocytes. The affected hepatocytes show multiple clear vacuoles in their cytoplasm. In addition, mild-moderate multifocal aggregates, sinusoidal and periportal infiltration of mononuclear inflammatory leucocytes were observed (arrow). Central vein (V), portal area (P). H and E, 100, 400x (Fig. 12b).

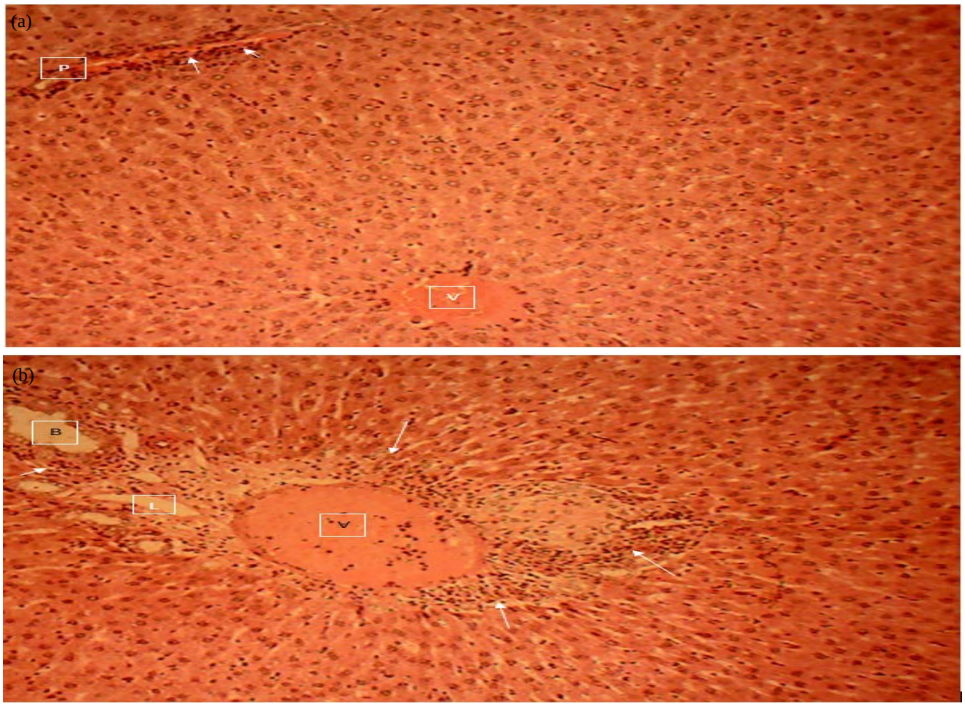


Fig. 11(a-b): (a) Liver collected sections in fresh aqueous extract showed mild to moderate widespread fatty degeneration of the hepatocytes, (b) Liver collected sections in fermented aqueous extract showed mild to moderate widespread fatty degeneration of the hepatocytes

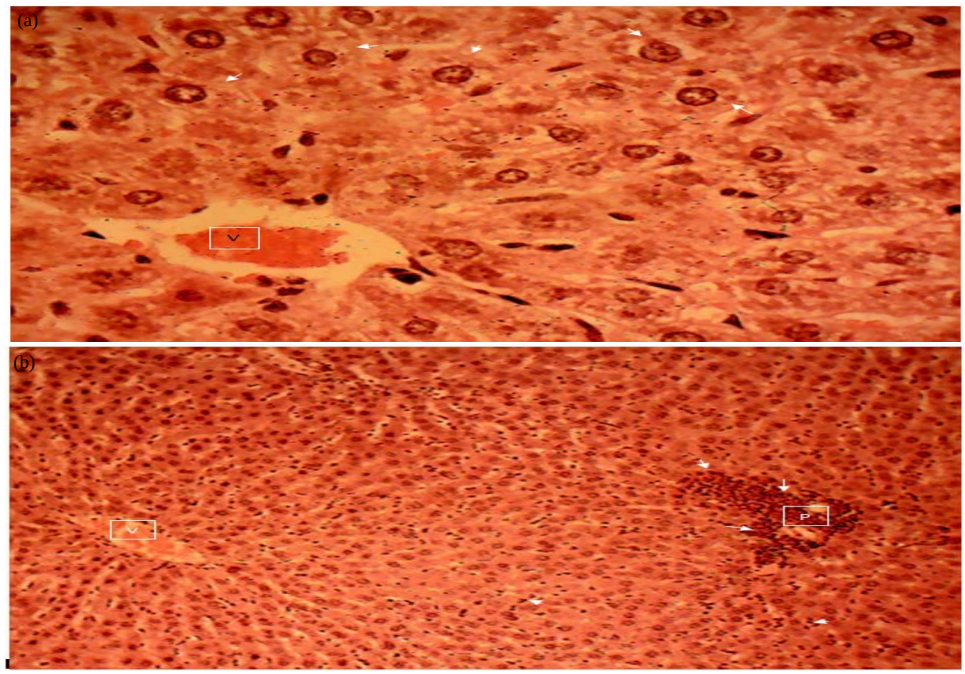


Fig. 12(a-b): (a) Liver collected sections in fresh aqueous extract showed mild to moderated widespread fatty degeneration of the hepatocytes and (b) Liver collected sections in fermented aqueous extract showed mild widespread fatty degeneration of the hepatocytes

## DISCUSSION

The liver is one of the most active organ in the human body responsible for the metabolism and detoxification of drugs and environmental chemicals[15]. In most cases, liver is the first internal organ to encounter a number of insults including ingested xenobiotics, drugs and environmental toxicants[15]. As a result, liver cells are exposed to significant concentrations of chemicals and liver functions could be adversely affected[16]. Hence, damage to the liver may elevate the concentration and subsequently activities of liver enzymes in the extrahepatic tissues as seen in various hepatic disorders. This study evaluated the effects of fresh and fermented aqueous extract of palm fruit on liver marker enzymes and selected liver function parameters.

The absence of death or adverse reactions observed when graded doses of the aqueous extracts were administered to the male Wistar albino mice may be attributed to the aqueous extracts possessing low toxicity potentials which may require higher dose and extended duration for the manifestation of toxicity or that the aqueous extracts are relatively safe.

The non-significant decrease in the ALP activity observed in group 2 and 3 rats that received low doses of fermented aqueous extract of palm fruit showed that the fermented aqueous extract is relatively safe at low concentration and may possess hepatoprotective properties at these doses. However, it could be hepatotoxic at high concentrations as depicted by significant increase in the ALP activity of group 4 and 5 that received higher doses of the fermented aqueous extract. On the other hand, the marked increase in the ALP activity of all the groups administered graded doses of the fresh aqueous extract may be attributed to the fresh extract having toxic effects on the liver, which could have compromised the liver architecture and integrity. This might have led to damage of the membrane of the liver cells resulting to increased permeability of the liver membrane which led to the increased ALP activity in the extrahepatic tissues. Fermented aqueous extract might have metabolized the toxic constituent responsible for the increased ALP activity in rat that received fresh aqueous extract of palm fruit to less toxic metabolites due to the low ALP activity observed in rats administered with graded doses of fermented extract of palm fruit.

Aspartate aminotransferase, considered as a less specific biomarker enzyme for hepatocellular injury which helps in detecting hepatocellular disorder[17]. The non-significant ($p>0.05$) increase in AST activity observed in rats which received a low dose of the fresh extract indicates that the fresh extract was relatively safe and had less hepatotoxic effect at low concentration. However, significant ($p<0.05$) increase in AST activity observed in all the groups administered graded doses of fresh and fermented aqueous extracts of palm fruit suggests hepatotoxicity which might have led to the disruption of liver integrity and architecture as reported by Nathwani *et al.*[18]. The marked increase in AST activity of all the groups administered graded doses of the fermented extract with respect to the fresh aqueous extract suggests that the fermented extract may have high toxic effects which may be due to the degradation of the less toxic metabolites in the fresh extract to more toxic metabolites. The increase in AST activity may also have been raised from damage to other organs since AST is not specific to the liver as it also signifies abnormalities in heart, muscle brain or kidney integrity and architecture[19].

Proteins are biomolecules which are vital to the function of all cells and tissues involved in the fighting of diseases, regulating body functions and transport of molecules across the cells. The non-significant increase in total protein concentration in groups 2 and 3 suggests that the fresh aqueous extract had little or no effects on the liver function at low concentrations. On the contrary, significant ($p<0.05$) decrease observed in the total protein in groups 4 and 5 that received the fresh extract and groups 2 and 3 that received low doses of the fermented extract indicates negative effects of the extract on the liver function. This effect might have resulted in marked alteration in the ability of the liver to synthesize protein which may affect regulatory and transport functions mediated by proteins. The marked decrease in the levels of total protein concentration may also be due to haemorrhage, liver damage or malnutrition as recorded by Manary and Trehan and these might have been caused by the extracts[20]. However, the significant ($p<0.05$) increase in total protein concentration observed in groups administered with high doses of the fermented aqueous extract indicates that the toxic components in the fermented extract might have been masked by some inhibitory metabolites which may be present in higher concentration in the fermented aqueous extract.

Albumin is the major plasma protein synthesized by the liver and serves as a useful indicator of hepatic function[21]. The non-significant decrease in albumin concentration observed in group 2 administered low dose of the fresh aqueous extract and group 3 administered fermented aqueous extract suggest little or no toxic effects on liver at the stated doses of the extracts. The significant ($p<0.05$) decrease in concentration of albumin observed in this study suggests altered synthesis of albumin by the liver which may alter other cellular functions such as the regulation of the colloidal osmotic pressure of the blood which is the major function of albumin as recorded by

Masaki *et al*[22]. The non-significant increase in albumin concentration observed in group 5 administered a high dose of the fresh extract depicts that the fresh extract may not be toxic at higher doses and may not have affected protein synthesis. Also, the non-significant increase in albumin concentration of group 2 administered a low dose of the fermented extract suggests little or no toxicity of the fermented extract at low doses and so may be relatively safe at the stated concentration.

High levels of total bilirubin are seen in cases of jaundice or haemolytic anaemia[23]. Bilirubin is ultimately processed by the liver to allow its elimination from the body. The results showed significant ($p<0.05$) decrease in total bilirubin concentration in all the groups administered the fresh extract and group 2 which received a low dose of the fermented extract indicating possible hepatoprotective property of the fresh fermented extracts at lower doses. It could also be as a result of poor processing of bilirubin for elimination from the body which could be due to poor breakdown of RBCs leading to the disruption of normal blood cell activities which may also lead to assault to blood haemoglobin according to the records of Farrugia[24]. While no significant increase observed in the total bilirubin concentration in groups 3, 4 and 5 administered the fermented extract depicts no or less toxic impact of the fermented extract on total bilirubin concentration even at high doses suggesting that the fresh extract was more toxic to bile function than the fermented extract.

Raised levels of direct bilirubin are indicated in various liver and bile disorders. The significant ($p<0.05$) decrease in direct bilirubin observed in all the groups that received graded doses of the fresh and fermented extracts when compared to the normal may be attributed to a liver damage or disorder leading to the inability of the liver to process bilirubin which is in line with the findings of Pratt[25]. However, the significant ($p<0.05$) increase in direct bilirubin concentration in the rats administered high doses of the fermented extract depicts that the liver was possibly conjugating bilirubin normally but was unable to excrete it which could lead to liver scarring, liver inflammation or other liver diseases as suggested by the findings of Ives *et al*.[26]. Hence, this suggests that the aqueous extract of palm fruit could be toxic on liver and could impair liver functions and integrity at both low and high doses.

## CONCLUSION AND RECOMMENDATION

The findings of this study suggests that the aqueous extracts of palm fruit have potentials of causing significant liver damage and impairing liver functions most especially the fermented aqueous extract. The use of fresh and fermented aqueous extracts of palm fruit in the production of palm oil should be discouraged in order to protect the health of palm oil consumers, who may not be aware of their use in the production of commercially available palm oils.

It is highly recommended that concerted efforts should be made by regulatory bodies to educate and protect consumers from the consumption of unhealthy and non-hygienically prepared palm oils.

## SIGNIFICANCE STATEMENTS

The study discovered the possible hepatotoxic potentials of aqueous extracts of palm fruits (*Elaeis guineensis*) that could compromise liver integrity and functions. The study help the researchers to uncover the critical area of hepatological disorders and hepatoprotection that many researchers were unable to explore. Thus, a new theory on hepatoprotection through healthy dietary practice may be arrived at.

## REFERENCES


1. Nwoko, C.O. and S. Ogunyemi, 2010. Evaluation of palm oil mill effluent to maize (*Zea mays* L.) crop: Yields, tissue nutrient content and residual soil chemical properties. Aust. J. Crop Sci., 4: 16-22.
2. Geoff, S., 2011. Edible palms: An introduction to palm fruits. Daves Garden, 1: 4-5.
3. Verla, A.W., P. Adowei and E.N. Verla, 2014. Physicochemical and microbiological characteristic of palm oil mill effluent (Pome) in Nguru: Aboh Mbaise, Eastern Nigeria. Acta Chim. Pharm. Indica, 4: 119-125.
4. Bamikole, M.A. and U.J. Ikhatua, 2009. Variety diversity effect on the chemical composition and dry matter degradation characteristics of residue and by-products of oil palm fruits. Anim. Sci. J., 80: 239-249.
5. Muhrizal, S., J. Shamshuddin, I. Fauziah and M.A.H. Husni, 2006. Changes in iron-poor acid sulfate soil upon submergence. Geoderma, 131: 110-122.
6. Madaki, Y.S. and L. Seng, 2013. Palm oil mill effluent (Pome) from Malaysia palm oil mills: Waste or resource. Int. J. Sci. Environ. Technol., 2: 1138-1155.
7. Hassan, S., L.S. Kee and H.H. Al-Kayiem, 2013. Experimental study of palm oil mill effluentand oil palm frond waste mixture as an alternative biomass fuel. J. Eng. Sci. Technol., 8: 703-712.
8. Lorke, D., 1983. A new approach to practical acute toxicity testing. Arch. Toxicol., 54: 275-287.
9. Wroblewski, F. and J.S. LaDue, 1956. Serum glutamic pyruvic transaminase in cardiac with hepatic disease. Proc. Soc. Exp. Biol. Med., 91: 569-571.

10. Tietz, N.W., A.D. Rinker and L.M. Shaw, 1983. IFCC methods for the measurement of catalytic concentration of enzymes Part 5. IFCC method for alkaline phosphatase (orthophosphoric-monoester phosphohydrolase, alkaline optimum, EC 3.1.3.1). J. Clin. Chem. Clin. Biochem., 21: 731-748.
11. Rodkey, F.L., 1965. Direct spectrophotometric determination of albumin in human serum. Clin. Chem., 11: 478-487.
12. Weichselbaum, T.E., 1946. An accurate and rapid method for the determination of proteins in small amounts of blood serum and plasma. Am. J. Clin. Pathol., 16: 40-49.
13. Jendrassik, L. and P. Grof, 1938. Determination of total bilirubin. Biochemistry, 279: 81-89.
14. IBM Corporation, 2011. IBM SPSS statistics for windows, version 20.0. IBM Corp, Armonk, New York.
15. Suk, K.T., M.Y. Kim and S.K. Baik, 2014. Alcoholic liver disease: Treatment. World J. Gastroenterol., 20: 12934-12944.
16. Ikechukwu, U.R., S.R.S. Adeyi, M.K. Hadiza and A.C. Lilian, 2015. Effect of methanol extract of Abrus precatorius leaves on male wistar albino rats induced liver damage using carbon tetrachloride (CCl4). J. Biol. Sci., 15: 116-123.
17. Ozer, J., M. Ratner, M. Shaw, W. Bailey and S. Schomaker, 2008. The current state of serum biomarkers of hepatotoxicity. Toxicology, 245: 194-205.
18. Nathwani, R.A., S. Pais, T.B. Reynolds and N. Kaplowitz, 2005. Serum alanine aminotransferase in skeletal muscle diseases. Hepatology, 41: 380-382.
19. Fernandez, N.J. and B.A. Kidney, 2007. Alkaline phosphatase: Beyond the liver. Vet. Clin. Pathol., 36: 223-233.
20. Manary, M.J. and I. Trehan, 2016. Protein-Energy Malnutrition. In: Goldman's Cecil Medicine, Goldman, L. and A.I. Schafer, Elsevier Saunders, Philadelphia, PA..
21. Marshall, W., 2012. Albumin (serum, plasma). Association for Clinical Biochemistry, pp: 1-2
22. Masaki, T., T. Matsura, K. Ohkawa, T. Miyamura, I. Okazaki, T. Watanabe and T. Suzuki, 2006. All-trans retinoic acid down-regulates human albumin gene expression through the induction of C/EBPß-LIP. Biochem. J., 397: 345-353.
23. McClatchey, K.D., 2002. Clinical Laboratory Medicine, Lippincott Williams, Wilkins, pp: 288-293.
24. Farrugia, A., 2010. Albumin usage in clinical medicine: Tradition or therapeutic? Transfusion Med. Rev., 24: 53-63.
25. Pratt, D.S, 2016. Liver chemistry and function tests. In: Gastrointestinal And Liver Disease: Pathophysiology /Diagnosis/Management. Feldman, M., L.S. Friedman and L.J. Brandt, Philadelphia Elsevier Saunders.
26. Ives, N.K., G. Mieli-Vergani, N. Hadzic, S. Newell and I. Sugarman, 2012. Gastroenterology. In: Rennie and Robertson's Textbook of Neonatology, Rennie, J.M. (Ed.)., 5th Edn., Elsevier, Philadelphia, PA.s.