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Hepatoprotective effect of methanolic leaf extract of *Boswellia dalzielii hutch* on carbon tetrachloride induced hepatotoxicity in wistar rats

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Abstract

The aqueous extract of *Boswellia dalzielii Hutch* was reported to strengthen the liver. Hence, the effect of this plant on carbon tetrachloride (CCL_4) induced hepatotoxicity was investigated. 96 male rats were divided into 7 groups of 12 rats each. 100mg/kg, 200mg/kg and 300mg/kg methanolic extract of the leaves of *Boswellia dalzielii Hutch* were administered orally for 4weeks after 0.63ml of CCl_4/kg body weight was used to induce hepatotoxicity. Reducdyn and vitamin E were used as standard control drugs. Liver functions were assessed by the assay of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total protein (TP), albumin (ALB), total bilirubin (TB) and thiobarbituric acid reactive substances (TBARS). The biochemical observations were confirmed by histological examinations of the liver sections and are comparable with the standard hepatoprotective drug, reducdyn and vitamin E, which served as positive control. The effect of the extract increased with increase in the extract concentration. When the different concentrations of the extract were compared with the drugs, they were found to mimic the hepatoprotective effect of the drugs. The overall experimental results indicate that the biologically active antioxidant phytoconstituents of the methanolic extract of *Boswellia dalzielii Hutch* could alleviate the toxic action of CCl_4 in the liver of rat.

Keywords: *Boswellia dalzielii Hutch,* carbon tetrachloride, hepatotoxicity, histopathology, liver function enzymes, Reducdyn, vitamin E, anti-oxidants.

Introduction

In Nigeria, there is a growing interest in herbal remedies because of their effectiveness, minimal side effects and relative low cost. Traditional medicine practitioner for the treatment of liver disorders for centuries (Schuppan *et al.,* 1999; Kumar *et al.,* 2011) has used plant extracts. Plants are able to synthesis a wide variety of chemical compounds of almost every class. Some of these compounds exhibit marked pharmacological activity. This is the basis of herbal medicine. Identifying bioactive dietary constituents is an active area of scientific investigation that may lead to new drug discovery.

One of the major functions of the liver is detoxification of xenobiotics and toxins (Mitra *et al*., 1998). In many cases, reactive oxygen species are produced during detoxification (Jeong *et al*., 1999). Over dose of toxins and some drugs or long time use can produce large amounts of free radicals that could cause oxidative stress and liver injury (Jeong *et al*., 1999). Liver cell injury caused by various toxic chemicals like certain antibiotics, chemotherapeutic agents, carbon tetrachloride (CCl_4), thioacetamide (TAA), excessive alcohol consumption and microbes are often associated with cellular necrosis, increase in lipid peroxidation and elevation of serum levels of most biochemical makers of the liver (Mossa *et al*., 1991; Mascolo *et al*., 1998; Kumar *et al*., 2011). Because the liver performs

many vital functions in the human body, damage to the liver cause unbearable problems (Mitra *et al*., 1998; Chattopadhyay, 2003).

Boswellia dalzielii Hutch is a tree plant of the savannah forest belonging to the family of "*Burseraceae*". It is commonly known as the "Frankincense tree". The tree has a characteristic smooth, pale brown bark that peels off in ragged papery patches, which on rapping exudes a whitish fragrant resin. It grows up to 13metre high. The small white flowers, which may appear while the tree is leafless, are fragrant. The tree is sometimes planted in the northern parts of Nigeria to prevent bad luck (hanu), hence the names "Hanu" and "Basamu" (Ethuk *et al*., 2006; Dimas *et al*., 2006; Hassan *et al*., 2009). It is locally abundant in Togo, Cote d' Ivoire, Cameroon, Benin, Ivory coast, Poland, Ghana, Burkina Faso, Nigeria and Czech Republic. In Nigeria, the tree has been found in Kebbi (Ethuk *et al*., 2006), Kano (Nwinyi *et al*., 2004), Kaduna (Hassan *et al*., 2009) and Adamawa States (Burkill, 1985).

The LD_{50} of the aqueous extract of the stem bark of *Boswellia dalzielii Hutch* has been reported to be above 3000mg per kilogram body weight and considered to be relatively safe when given orally (Ethuk *et al*., 2006). Aliyu et al. (2007) investigated the effect of aqueous bark extract of *B. dalzielii* on liver function using female Wistar albino rats, the extract was found to have no significant effect on total protein, albumin, bilirubin content and alkaline phosphate activity at the end of five days oral treatment. Their results suggest no damage to hepatocytes as a result of the exposure and that the extract may strengthen the liver. Hence this study is aimed at investigating the biochemical effect of the methanolic extract of *Boswellia dalzielii Hutch* leaves on carbon tetrachloride induced hepatotoxicity.

Materials and methods

Collection and authentication of plant leaves

The leaves of *Boswellia dalzielii Hutch* were obtained from Maitunku hill, Bambam, Dadiya district of Gombe state. The plant was identified by Mr. Thlama Daniel Mshelbwala, department of forestry technology, federal college of forestry, Job and further authenticated by Dr. S.S. Sanusi, Department of Biological Sciences, University of Maiduguri, Borno state.

Extraction of plant

The leaves were air dried and pulverized with the aid of mortar and pestle. Six hundred grams of the pulverized leaves were extracted with six litres of methanol using Soxhlet extractor for 24hours and was exposed to atmospheric air for evaporation to dryness. The resulted extract was weighed and then stored in an airtight plastic container.

Phytochemical screening

The methanolic extract of the leaves of *Boswellia dalzielii Hutch* was subjected. To preliminary phytochemical screening (Trease & Evans, 1978; Sofowera, 1984).

Experimental animals

Healthy male Wister albino rats weighing between 175gms-225gms were obtained and maintained at the animal house, University of Port Harcourt Rivers State were used for this investigation. They were kept under standard environmental conditions at 25°C with 12:12h light-dark cycle in ventilated plastic cages. The rats were fed with standard feed and clean fresh water *ad libitum* throughout the duration of this study.

Experimental design

Healthy male Wister albino rats weighing 175gms to 225gms were equalized with respect to body weight and randomly divided into seven groups of twelve rats each in separate cage.

- Group 1 (Normal control) received sterile water daily for 28 days
- Group II (Toxic control) received CCl_4: olive oil (1:1 v/v) (I.25ml/kg *i.p*) on the first day only sterile water daily for 28 days.
- Group III was administered CCl_4: olive oil (1:1 v/v) (1.25ml/kg i.p) only on the first day, and methanolic extract (100mg/kg p.o) daily for 28days.

- Group IV was administered CCl_4: olive oil (1:1 v/v) (1.25ml/kg i.p) only on the first day and methanolic extract (200mg/kg p.o) daily for 28days.
- Group V was administered CCl_4: olive oil (1:1 v/v) (1.25ml/kg i.p) only on the first day and methanolic extract (300mg/kg p.o) daily for 28 days.
- Group VI was administered CCl_4: olive oil (1:1 v/v) (1.25ml/kg i.p) only on the first day, reducdyn (4.3mg/kg p.o) daily for 28 days.
- Group VII was administered CCl_4: olive oil (1:1 v/v) (1.25ml/kg i.p) only on the first day, reducdyn (4.3mg/kg p.o) and vitamin E (14.3mg/kg p.o) daily for 28 days.

Three rats from each group were sacrificed under light ether anaesthesia 24hrs after treatment on the first day and at the end of each week for 4weeks. Blood was collected by cardiac puncture, allowed to coagulate at 37^{o}C for 30min and serum separated by centrifugation at 3000rpm for 5min. The serum was used to estimate serum AST, ALT, ALP, albumin, total protein and total bilirubin concentration using spectrophotometer. After collection of the blood, the liver was immediately excised and divided into two parts. The first was rinsed in ice-cold normal saline and stored at -20^{o}C for TBARS analysis, while the second was used for histopathological studies. *Biochemical analysis* Serum aspartate Aminotransferase (AST) and serum alanine aminotransferase (ALT) were determined colorimetrically by Reitman and Frankel method. Serum total bilirubin (TB) was determined by Jendrassik and Grof method. Total protein (TP) was determined by the biuret method. Serum albumin was determined by bromocresol green colorimetric method. Serum alkaline phosphatase (ALP) activity was determined by King and Kings method. Thiobarbituric acid reactive substances (TBARS) were determined by Ohkawa et al. method.

Histological studies

A portion of the liver tissues from control and experimental groups were fixed in 10% formalin for 12 hours. They were dehydrated through ascending grades of alcohol (70%, 80%, 90% and absolute). The tissues were cleared in xylene, infiltrated and embedded in paraffin wax for light microscopic studies. Thin sections of 5µm thickness were cut using a Reichert ultra microtome, and were mounted on slides. Each slide was stained with hematoxylin and eosin according to the routine procedures for light microscopy by Galigher and Kayloff method. They were observed microscopically and analysed by a histopathologist.

Statistical analysis

Data are expressed as means ± standard error of mean (S.E.M) the result were analyzed statistically by Analysis of Variance (ANOVA) followed by multiple comparison test of Least Significance Difference (LSD). Significance was accepted at a p-value of 0.05.

Results

The result of the preliminary screening of the crude methanolic extract of *B. Dalzielii Hutch* showed the presence of phytochemicals such as saponins, flavonoids, glycosides resins and tannins. The result of CCl_4 intoxicated group after 24H showed significant ($P \leq 0.05$) increase in the serum enzyme levels (AST, ALT, ALP) and total bilirubin and a significant decrease in serum total protein and albumin levels when compared to normal groups (Table 1). Administration of methanolic extract of B. dalzielii Hutch decreased the activities of the activities of serum hepatic enzymes and total bilirubin while total protein and albumin was significantly ($P \leq 0.05$) increased when compared to CCl_4 intoxicated groups, normal group, extract concentrations and the control drugs as shown in (Table. 2-7), respectively. The result obtained showed an increase in the level of Thiobarbituric acid reactive substances (TBARS) in CCl_4 intoxicated group when compared to the normal control group. Treatment with methanolic extract of *B.Dalzielii* Hutch significantly ($P \leq 0.05$) decreased the concentrations of TBARS (Table

Table 1.Biochemical parameters of normal and CCl_4 administered rats after 24hrs.

Experimental Groups	AST (IU/L)	ALT (IU/L)	ALP (g/dl)	ALB (g/dl)	TP (g/dl)	TB (mg/dl)
Normal	20.67±1.67	16.33±2.33	39.33±0.66	2.45±0.02	7.40±0.40	0.47±0.04
Control CCl_4	30.00±7.00	29.33±6.89	73.66±5.61	2.38±0.04	5.13±0.32	0.86±0.13

Values are expressed as mean ± S.E.M (n=6).* Represent significantly different values at 95% confidence limit (P <0.05) when compared to the normal control.

Table 2. Effect of methanolic extract of Boswellia dalzielii Hutch on AST (IU/L) in CCl_4 induced hepatotoxicity in rats.

Experimental groups	Week one	Week two	Week three
Normal control	23.00±2.31	16.00±1.73	18.00±1.00
Toxic control (ccl_4)	$36.00\pm1.67^{ac,d}$	36.00 ± 2.89^{adc}	37.33 ± 1.86^{adc}
100mg/kg extract	$31.33\pm2.60^{ac,d}$	17.66 ± 0.67^{b}	27.00 ± 2.31^{abdc}
200mg/kg extract	28.33 ± 1.76^{c}	16.00 ± 2.08^{bc}	21.67 ± 1.33^{bdc}
300mg/kg extract	$23.67\pm1.76^{a,dc}$	19.33 ± 2.03^{b}	24.33 ± 1.33^{abc}
Reducdyn	29.67 ± 1.33^{bdc}	23.00 ± 2.31^{abd}	31.33 ± 1.00^{bdc}
Reducdyn + vitamin E	21.67 ± 1.33^{bdc}	17.00 ± 1.00^{bc}	18.00 ± 1.00^{bdc}

Data represented as mean ± S.E.M of n=6. Values with different superscript letter are significantly different at 95% confidence limit (P<0.05).

Table 3. Effect of methanolic extract of Boswellia dalzielii Hutch on ALT (IU/L) in CCl_4 induced hepatotoxicity in rats.

Experimental Groups	Week one	Week Two	Week Three
Normal Control	14.67 ± 00.67	13.33 ± 01.33	11.33 ± 01.33
Toxic control (ccl_4)	$33.33\pm03.48^{a,dc}$	34.33 ± 06.67^{acd}	30.00 ± 02.08^{adc}
100mg/kg Extract	29.33 ± 02.60^{adc}	11.33 ± 00.67^{b}	15.33 ± 01.76^{bc}
200mg/kg Extract	25.67 ± 01.76^{abdc}	10.67 ± 00.67^{b}	11.33 ± 00.67^{bc}
300mg/kg Extract	20.33 ± 00.67^{abdc}	12.67 ± 01.76	12.67 ± 01.76^{bc}
Reducdyn	27.00 ± 01.15^{abdc}	16.67 ± 01.20^{b}	17.00 ± 01.00^{abdc}
Reducdyn + Vitamin E	19.33 ± 01.20^{bdc}	10.67 ± 00.67^{b}	37.33 ± 01.76^{abdc}

Data represented as mean ± S.E.M of n=6. Values with different superscript letter are significantly different at 95% confidence limit (P<0.05).

Table 4.Effect of methanolic extract of Boswellia dalzielii Hutch on ALP (IU/L) in CCl_4 induced hepatotoxicity in rats

Experimental Groups	Week one	Week Two	Week Three
Normal Control	37.33 ± 00.67	38.67 ± 00.67	37.00 ± 01.00
Toxic control (ccl_4)	46.33 ± 01.33^{adc}	58.67 ± 05.36^{adc}	56.33 ± 04.70^{adc}
100mg/kg Extract	45.33 ± 00.88^{adc}	42.67 ± 01.33^{bc}	46.33 ± 00.67^{abc}
200mg/kg Extract	42.67 ± 01.33^{dc}	39.33 ± 00.67^{bc}	43.00 ± 01.15^{bc}
300mg/kg Extract	36.67 ± 02.40^{bdc}	41.33 ± 00.88^{bc}	42.00 ± 01.00^{bc}
Reducdyn	46.33 ± 00.67^{adc}	45.67 ± 03.84^{bc}	50.00 ± 01.15^{abdc}
Reducdyn + Vitamin E	34.33 ± 02.33^{bdc}	30.33 ± 00.67^{abbc}	37.33 ± 01.76^{bdc}

Data represented as mean ± S.E.M of n=6. Values with different superscript letter are significantly different at 95% confidence limit (P<0.05).

Table 5. Effect of methanolic extract of Boswellia dalzielii Hutch on TP (g/dl) in CCl_4 induced hepatotoxicity in rats.

Experimental Groups	Week one	Week Two	Week Three
Normal Control	07.10 ± 00.40	5.63 ± 00.04	5.43 ± 00.34
Toxic control (ccl_4)	05.67 ± 00.08^{adc}	4.83 ± 00.13^{adc}	4.62 ± 00.33^{bc}
100mg/kg Extract	6.83 ± 00.02^{bc}	5.92 ± 00.67^{b}	5.68 ± 00.01^{b}
200mg/kg Extract	6.42 ± 00.02^{ab}	5.18 ± 00.25^{d}	6.04 ± 00.39^{bc}
300mg/kg Extract	6.86 ± 00.15^{bc}	5.40 ± 00.22	6.52 ± 00.03^{abc}
Reducdyn	6.36 ± 00.02^{abd}	5.53 ± 00.24^{b}	5.10 ± 00.38^{d}
Reducdyn + Vitamin E	6.80 ± 00.02^{bc}	5.37 ± 00.32	5.69 ± 00.34^{b}

Data represented as mean ± S.E.M of n=6. Values with different superscript letter are significantly different at 95% confidence limit (P<0.05)

Table 6.Effect of methanolic extract of Boswellia dalzielii Hutch on ALB (IU/L) in CCl_4 induced hepatotoxicity in rats

Experimental Groups	Week one	Week Two	Week Three
Norma Control	3.96 ± 00.38	3.30 ± 00.01	3.13 ± 00.44
Toxic control (ccl_4)	2.06 ± 00.03^{adc}	2.13 ± 00.13^{adc}	2.27 ± 00.16^{adc}
100mg/kg Extract	2.19 ± 00.09^{adc}	2.74 ± 00.19^{abc}	2.87 ± 00.03^{d}
200mg/kg Extract	2.58 ± 00.12^{a}	2.52 ± 00.07^{abc}	3.49 ± 00.17^{b}
300mg/kg Extract	3.23 ± 00.35^{bd}	2.67 ± 00.01^{abc}	4.10 ± 00.05^{abdc}
Reducdyn	3.11 ± 00.56^{bd}	2.44 ± 00.01^{ac}	2.83 ± 00.39^{d}
Reducdyn + Vitamin E	3.15 ± 00.01^{bd}	3.18 ± 00.25^{bdc}	3.21 ± 00.07^{bd}

Data represented as mean ± S.E.M of n=6. Values with different superscript letter are significantly different at 95% confidence limit (P<0.05).

Table 7. Effect of methanolic extract of Boswellia dalzielii Hutch on TB (mg/dl) in CCl_4 induced hepatotoxicity in rats.

Experimental Groups	Week one	Week Two	Week Three
Normal Control	0.25 ± 00.01	0.25 ± 00.01	0.30 ± 00.05
Toxic control (CCl_4)	0.65 ± 00.01^{adc}	0.76 ± 00.01^{adc}	1.11 ± 00.01^{adc}
100mg/kg Extract	0.43 ± 00.01^{abdc}	0.44 ± 00.01^{abdc}	0.39 ± 00.01^{b}
200mg/kg Extract	0.39 ± 00.01^{abc}	0.42 ± 00.01^{abdc}	0.52 ± 00.12^{abc}
300mg/kg Extract	0.33 ± 00.02^{abdc}	0.24 ± 00.01^{abdc}	0.45 ± 00.04^{ab}
Reducdyn	0.56 ± 00.03^{abdc}	0.64 ± 00.02^{abdc}	0.46 ± 00.01^{ab}
Reducdyn + Vitamin E	0.29 ± 00.01^{bdc}	0.42 ± 00.01^{abdc}	0.37 ± 00.01^{bd}

Data represented as mean ± S.E.M of n=6. Values with different superscript letter are significantly different at 95% confidence limit (P<0.05).

Table 8. Effect of methanolic extract of Boswellia dalzielii Hutch on TBARS (nmol of TBARS/mg protein X10^{-5}) in CCl_4 induced hepatotoxicity in rats

Experimental group	Week one	Week two	Week three
Normal control	01.92 ± 00.14	01.93 ± 00.01	02.57 ± 00.01
Toxic Control (CCL_4)	03.86 ± 00.01^{adc}	04.42 ± 00.02^{acd}	04.49 ± 00.01^{abcd}
100mg/kg Extract	02.57 ± 00.01^{abdc}	01.71 ± 00.21^{bcd}	02.77 ± 00.21^{bc}
200mg/kg Extract	01.92 ± 00.01^{bdc}	01.49 ± 00.21^{bcd}	02.55 ± 00.01^{bc}
300mg/kg Extract	01.89 ± 00.27^{bdc}	01.92 ± 00.00^{bc}	02.79 ± 00.43^{bc}
Reducdyn	02.45 ± 00.10^{abdc}	02.13 ± 00.21^{bcd}	02.78 ± 00.22^{bc}
Reducdyn + Vit E	01.31 ± 00.04^{abdc}	01.07 ± 00.42^{abcd}	01.71 ± 00.42^{abcd}

Data represented as mean ± S.E.M of n=6. Values with different superscript letter are significantly different at 95% confidence limit (P<0.05).

Plate 1a.Control

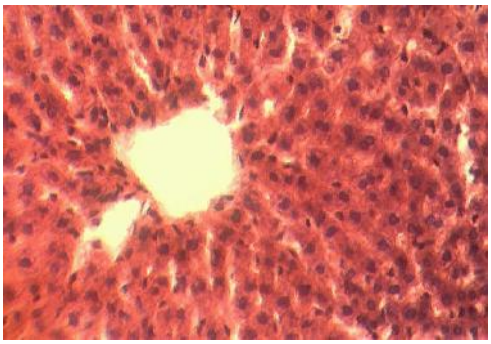


Plate1B: CCl_4 intoxicated group

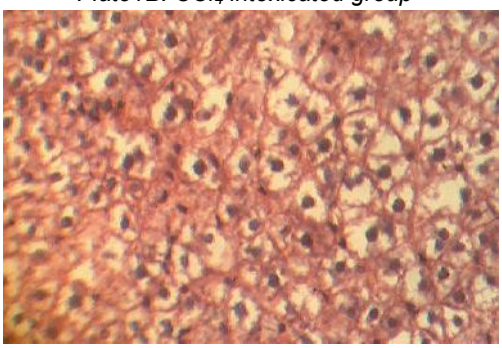


Plate 2a. 100mg/Kg BW of extract group after 3weeks.

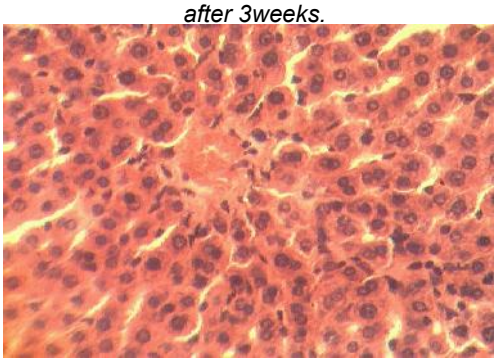


Plate 2b. 200mg/Kg BW of extract treatedroup after 3 weeks.

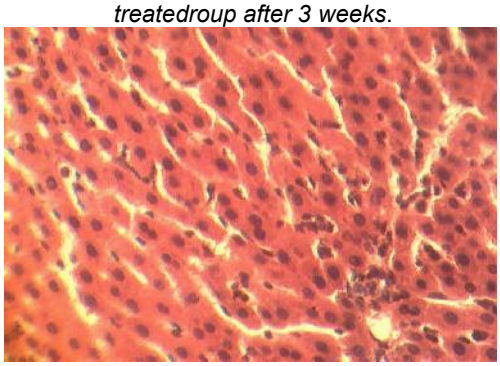


Plate 2c. 300mg/kg BW of extract treated group after 2 weeks

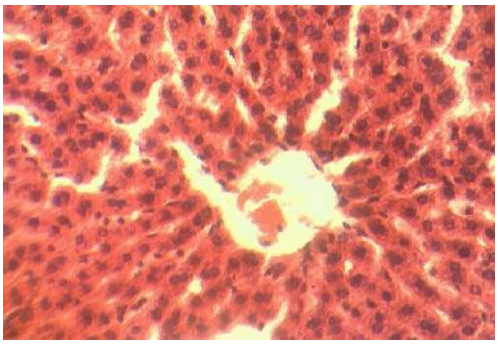
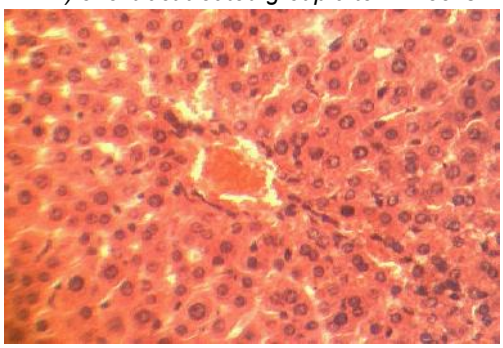


Plate 2d. Reducdyn + Vitamin E (14.28 mg/kg BW) of extract treated group after 2 weeks



8). Fig.1.Histopathological examination of the liver tissues of the control group showed normal hepatic cells with well preserved cytoplasm and nucleus (Plate 1A). CCl_4 treated group showed hepatic lesions characterized with wide spread ballooning degeneration, compression of sinusoids and mild periportal infiltration of lymphocytes (Plate 1B). Administration of methanolic extract of *B. dalzielii* Hutch showed preserved lobular architecture, moderate periportal infiltration of lymphocytes and normal portal tracts after the third week in 100mg/Kg BW group (Plate 2A) and after the second week in the 200mg/Kg BW (Plate 2B) and 300mg/Kg BW (Plate 2C) administered group. Sections of the liver taken from reducdyn+vitamine E have a near normal architecture (Plate2D).

Discussion

Carbon tetrachloride is one common hepatotoxin used in the experimental study of liver disease (Obi *et al*., 1998; Uliena *et al*., 2003; Yan-Jun *et al*., 2004). It is clearly evident that CCl_4 causes significant elevation of liver serum makers such as, AST, ALT ALP and TB (Yadav *et al*., 2011). The poison reaches its maximum concentration in the liver within 3hours of administration, there after it falls and by 24 hrs there is no CCl_4 left in the liver. The development of necrosis is associated with leakage of hepatic enzymes into the serum (Srinath *et al*., 2010). The changes associated with the CCl_4 induced liver damage in the present study is similar to acute viral hepatitis (Venukumar & Latha, 2002).

In correlation with previous researches (Gurusamy *et al*., 2010; Patrick-Iwuanyanwu *et al*., 2010; Kumar *et al*., 2011; Yadav *et al*., 2011), the result of this study show that CCl_4 elevated the serum levels of AST, ALT, ALP, TBARS and TB in rats poisoned with CCl_4. Such elevation is indicative of liver injury (Patrick-Iwuanyanwu *et al*., 2010). ALP activity is related to the functioning of hepatocytes and increases in activity due to increased synthesis in the presence of increased biliary pressure (Muriel & Garcipiana, 1992). The response of the liver to any form of biliary tree obstruction is to induce the synthesis of ALP and the main site of new enzyme synthesis is the hepatocytes adjacent to the biliary canaculi. Some of the newly formed enzymes enter the circulation to raise the enzyme level in serum (Burtis and Ashwood, 2001).

Serum bilirubin reflects the liver ability to take up, process and secrete bilirubin into the bile. Hepatobiliary disease is indicated when serum bilirubin exceeds the upper limit of normal (Crook, 2006). A rise in plasma aminotransferase activities is a sensitive indicator of damage to cytoplasmic and/or mitochondrial membranes. Raised plasma transaminase concentrations are indicative of hepatocyte damage such as drug or toxin induced or viral hepatitis (Crook, 2006). Estimating the activities of AST, ALT ALP, and TB in the serum are useful quantitative maker of the extent and type of hepatocelluller damage (Rekha *et al*., 2009).

The tendency of these enzymes to return to near normal in the extract-administered groups is a clear manifestation of hepatoprotective effect of the extract. The results of this investigation indicate that, treatment of rats with the methanolic extract of *Boswellia dalzielii Hutch* after CCl_4 administration caused a decline in hepatotoxicity of the rats. This is evidenced in the significant decrease in serum AST, ALT, ALP, TB and TBARS and increase in serum total protein (TP) and albumin (ALB) relative to the CCl_4 treated and the normal control groups as shown in the tables. The decrease in the activities of AST, ALT, ALP, TB and elevation of TP and ALB concentrations after administration of the methanolic extract of *Boswellia dalzielii Hutch* is in agreement with the work of Aliyu et al. (2007). They studied the effect of *Boswellia dalzielii Hutch* aqueous bark extract on rat liver function and they suggested that the aqueous extract of *Boswellia dalzielii Hutch* has strengthening action on the liver and other organs having significant quantities of these enzymes.

The changes in albumin and total protein levels observed in CCl_4 treated rats and

subsequent reversal caused by the administration of this different concentration of *B. dalzielii* methanolic extract toward normalization is suggestive of the stabilization of endoplasmic reticulum leading to repair of impaired protein synthesis cause by CCl_4 with concurrent improvement of Kupffer cells (Surest-Kumar & Mishra, 2008). Thus, methanolic extract of *Boswellia dalzielii Hutch* showed ability to alleviated CCl_4 induced hepatotoxicity. These findings agree with the findings of Yadav *et al*., (2011) who reported increased ALB and TP concentrations after administration of ethanolic extract of *Cissompelos periera* against CCl_4 induced hepatotoxicity in rats.

Thiobarbituric acid reactive substance (TBARS) is used as an index of lipid peroxidation (Patrick-Iwuanyanwu *et al*., 2010). The elevation of lipid peroxidation produced by CCl_4 was reverse in rats administered methanolic extracts of *Boswellia dalzielii Hutch*. This result is in agreement with Patrick-Iwuanyanwu *et al*., (2010) who reported that methanolic extract of *Tapinanthus bangwensis* reduced lipid peroxidation in CCl_4 induced hepatotoxicity in rats.

The reduction of serum AST, ALT, ALP, and TB, TBARS and increase in serum TP and ALB by the methanolic extract was observed to be dose dependent. The elevated enzymes levels were significantly reduced after the first week of administration of 300mg/kg body weight when compared to the administration of 100mg/Kg and 200mg/kg body weight administered groups. The serum concentrations of ALB and TP significantly increased with the increase in the concentration of *Boswellia dalzielii Hutch* methanolic extract.

The effect of duration of administration of the methanolic extract of *Boswellia dalzielii Hutch* on AST, ALT, ALP, TB and TBARS was observed with a greater reduction after the second week of administration. There was significant decrease in levels of AST, ALT and ALP at 100mg/kg, 200mg/kg and 300mg/kg concentrations of the extract after the first week when compared to similar concentrations after the second week. This infers that the methanolic extracts of *Boswellia dalzielii Hutch* have a time dependent therapeutic effect on the damaged liver and hence could alleviate liver damage caused by CCl_4 toxicity.

The marked decrease in AST, ALT ALP, TB and increase in TP and ALB after administration of methanolic extract of *Boswellia dalzielii Hutch* was found to be in agreement with studies carried out by other researchers on CCL_4 hepatotoxicity of other plant extracts such as *Solanum americanum* (Kumar *et al*., 2011), *Asteracantha longifilia*, *Cypenai rotundus* and *Bryophyllum pinnatum*, a polyherbal formulation (Gurusamy *et al*., 2010), *Tapinanthus bangwensis* (Iwuanyanwu *et al*., 2010), *Mimosa pudica* (Rekha *et al*., 2009), *Cissampelos spariera* (Yadov *et al*., 2011) which have shown that elevated levels of AST, ALT, ALP, TB and decreased levels of TP and ALB as a result of CCl_4 induced hepatotoxicity can be reduced and increased respectively, alleviating liver damage by administration of these plant extracts.

Lipid peroxidation was postulated as the mechanism of free radical induced tissue injury, hence free radical scavenging is established as the means by which antioxidants inhibit lipid peroxidation. Lipid peroxidation is probably the most extensively investigated process induced by free radicals and reactive oxygen species (ROS). This process and sub organelle (mitochondria/lysosomes) membrane damage is regarded as an important mechanism underlying the toxicity of several oxidative xenobiotics (Nakagawa *et al*., 1992).The ability of a hepatoprotective drug to reduce the injury effect or to preserve the normal hepatic physiological mechanisms which have been disturbed by a hepatotoxin is the index of its protective effect (Krishna *et al*., 2011). Therefore, CCl_4 induced hepatic injury is a commonly used model for the screening of hepatic drugs and the extent of damage is

assessed by level of released cytoplasmic transaminases (ALT and AST) and alkaline phosphatase in circulation (Patrick-Iwuanyanwu *et al*., 2007; Patrick-Iwuanyanwu and Wegwu, 2008).

The histological examination of hepatic tissues further validates the result of the biochemical studies. The prolonged oral administration of the methanolic extracts of *Boswellia dalzielii Hutch* of 100mg/kg, 200mg/kg and 300mg/kg concentrations produced histopathological changes. The near normal architecture of the liver tissues of rat treated with CCl_4 followed by the administration of methanolic extract of *Boswellia dalzielii Hutch* is suggestive of hepatoprotective property of this extract. This result is comparable with the standard reducdyn groups, hence confirming the significant hepatoprotective effect of the extract of *Boswellia dalzielii Hutch*.

Conclusion

The overall experimental results indicate that the biologically active antioxidative phytoconstituents of the methanolic extract of *Boswellia dalzielii Hutch* leaves could alleviate the damaging action of carbon tetrachloride in the liver of rats. The effect of the extract increased with increase in the extract concentration. When the different concentrations of the extract were compared with known drugs they were found to mimic the hepatoprotective effect of the drugs.

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