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Estimation of Lipid Profile in CCl_4 Induced Toxicity in Albino Rats

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ABSTRACT

The combination of chlorine and chloroform in the presence of light produces carbon tetrachloride (CCl_4), a colorless, volatile, non-inflammable liquid. It is a clear liquid with a sweet odor that can be perceived at low levels and does not occur naturally. It poses a significant hazard to one's health and is also one of the leading sources of toxicity in critical organs such as the lungs, kidneys, liver, and brain. **Objectives:** To determine the lipid profile with CCl_4-induced in albino rats. **Methods:** The research was conducted at the University of Okara, Department of Zoology. The experiment was conducted at the animal home of the Department of Zoology, University of Okara. Albino Rats were the intended targets. There were two groups created: a control group and an experimental group. To test the harmful effect on the lipid profile, the rats were fed 30 per cent diluted carbon tetrachloride, with normal saline as a control group. This was accomplished through a 12-day trial. Sampling or dissection was done after 12 days to determine serum Total Cholesterol, Triglycerides, high-density lipoprotein (HDL), and low-density lipoprotein (LDL). Rats were dissected, and their hearts were punctured to obtain a blood sample and organs. After sampling was taken by puncturing the Rats' hearts, the samples were examined by a machine called Micro-Lab 300. **Results:** Total Cholesterol, Triglycerides, HDL, and LDL levels were higher than usual. **Conclusions:** The study indicated that CCl_4 has a toxic effect on the lipid profile of rats.

INTRODUCTION

The photochemical reaction between chlorine and chloroform yields carbon tetrachloride (CCl_4), an odorless, colorless, volatile liquid compound in the chlorinated hydrocarbons class. Carbon tetrachloride finds its way into various domestic and industrial applications as a degreaser, fire suppressant, and refrigerant precursor. However, the production and use of the compound have been limited due to its harmful and toxic properties. Despite these regulations, some companies still use it. The most common routes of exposure are inhalation, skin contact, and ingestion to the toxic effects of CCl_4, with intentional ingestion as a suicidal agent as an additional risk factor. CCl_4 toxicity can lead to cellular damage in critical organs such as the lungs, kidneys, and liver [1, 2]. CCl_4 toxicity is primarily caused by generating the free radical CCl_3 and other metabolites, which cytochrome P450 releases. These harmful agents damage cells by altering their structure through pathways such as lipid peroxidation. Multiple organ dysfunction caused by these free radicles can lead to severe conditions [3]. Carbon tetrachloride (CCl_4) kills lipids inside the cell and the membrane. Increased membrane permeability is one sign of imminent cell death. The partial pressure of oxygen affects the formation of free radicals in CCl_4-induced hepatotoxicity [4, 5]. The liver enzyme cytochrome P450, mainly its isoenzyme CYP2E1, plays a role in metabolizing

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CCl_4 to other toxic metabolites. Additionally, CYP2E1 is an essential component of the hepatic microsomal ethanol oxidizing system (MEOS), which regulates ethanol metabolism in the liver. Excessive alcohol consumption can activate both enzymes, with even a single dose of alcohol sufficient to activate the MEOS system. In the presence of CCl_4 toxicity, an alcoholic will experience severe disease [6, 7]. In most cases of CCl_4 poisoning, the liver, kidneys, and lungs are damaged. An experiment involving CCl_4 showed that glycogen-loaded hepatocytes were more resistant to injury than those with glycogen depletion and fatty infiltration. This explains why chronic alcoholics are more susceptible to acute symptoms of CCl_4-induced hepatotoxicity. Because of glycogen depletion and fat accumulation in their liver cells, chronic alcoholics are at increased risk of experiencing severe symptoms of CCl_4-mediated hepatotoxicity [8]. This chemical activates various factors in the cell, including tumours necrosis factor (TNF), transforming growth factors (TGF) - and -ß, and nitric oxide (NO). These factors tend to cause self-destruction or fibrosis in the cell. TNF causes cells to go into apoptosis, while TGFs cause them to go into fibrosis [9-11]. In cases of severe CCl_4 toxicity, the liver and kidney show significant histopathologic changes. Specifically, the liver shows enlarged hepatic lobules, centrilobular hemorrhage, and centrilobular necrosis. Additionally, the kidneys show evidence of hydropic degeneration in the proximal convoluted tubules [12]. Elevated aspartate transaminase (AST), alanine transaminase (ALT), and glutamate dehydrogenase (GDH) levels in liver function tests (LFT) may indicate CCl_4 toxicity. The intensity and route of toxin exposure determine which enzymes are affected. The poison is consumed more quickly and in large amounts by inhalation than by ingestion. As a result, if you inhale, your AST, ALT, and GDH levels can spike quickly [13]. If the patient experiences acute renal failure, serum electrolytes and arterial blood gases (ABGs) must be monitored. The patient may have hyperkalemia and hyperphosphatemia in the early stages of acute renal failure, but hypokalemia progresses later. An ABG test indicates metabolic acidosis, which occurs when acid is retained in the body [14]. Antioxidants and radical scavengers have been used to investigate the mechanism of CCl_4 toxicity and to protect tissue cells from CCl_4-induced damage by interrupting the lipid peroxidation chain [9]. Numerous studies have shown that bananas, like other horticultural crops, contain various antioxidant properties that can protect the body from CCl_4-induced oxidative stress [15]. Lipids are an important component that regulates cellular functions and homeostasis. The liver is involved in lipid metabolism and other lipid synthesis and transportation stages. As a result, those with severe liver disease should assume an irregular lipid profile. A significant decrease in plasma cholesterol and triglyceride levels can be seen in patients with acute hepatitis and hepatic failure due to decreased lipoprotein biosynthesis. Low levels of TG and cholesterol are commonly seen in chronic liver diseases due to decreased liver biosynthesis ability [16]. Plasma lipid profiling could be useful in deciphering hepatic pathophysiology. In reality, plasma lipid profiling has already been used to understand the pathophysiology of hepatocellular carcinoma, liver phospholipidosis, and nonalcoholic fatty liver disease and recognised biomarkers [17]. When measuring a lipid profile, total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides are considered. A comprehensive lipid profile can include very low-density lipoprotein (VLDL). This is used to detect hyperlipidemia (a variety of cholesterol and triglyceride abnormalities), all known risk factors for cardiovascular disease and, in certain cases, pancreatitis [18]. In terms of size and composition, HDL particles are heterogeneous. They have the highest relative density despite being the smallest compared to other lipoproteins. [19]. Hepatic fibrosis is characterized as an accumulation of extracellular matrix proteins in the liver that forms excessive connective tissue in the presence of various etiologically diverse hepatic conditions, including alcoholic and nonalcoholic liver disease, viral hepatitis and chemical disease [20]. The liver carries out lipid metabolisms and various lipid synthesis and transportation phases. As a result, patients with significant liver dysfunction should anticipate having an aberrant lipid profile. The loss in lipoprotein production causes a significant drop in plasma total cholesterol and triglycerol levels in patients with severe hepatitis and hepatic failure. Low triglycerol and total cholesterol levels are common in chronic liver disorders due to diminished liver biosynthetic ability. Certain pharmaceuticals, chemicals, and herbal therapies can harm the liver and kidneys. Today, plants are used to make a large number of medications that are effective against a variety of disorders [16].

METHODS

For this analysis, carbon tetrachloride CCl_4 was used. The tested chemical, carbon tetrachloride CCl_4, was purchased locally and stored in the Department of Zoology laboratory at the University of Okara. The chemical has been diluted by 30%. Distilled water was used to make the stock solutions. All of the working solutions were freshly prepared from stock solutions. All other chemicals and solutions were of pro-analysis quality and collected from standard commercial sources. The rats used in this study were

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healthy adult Wistar albino rats weighing180 ± 200g. The rats were purchased from a local market and housed in the University of Okara Department of Zoology animal house. All experimental rats were kept at a constant temperature (25 ± 3°C) and relative humidity and were given unlimited access to average forage, tap water, and libitum. All of the animals' weights were measured twice a week. Both doses were administered in the morning. Rats were weighed before and after treatment. The animals were housed in these facilities for at least a week before the experiment. The rats were randomly divided into two groups: a control group (Co) and an experimental group that received 30 per cent CCl_4 via oral gavage for two weeks. The control group comprised four animals, while the experimental group comprised six, as given in Table 1.

Table 1: List of Groups, Doses, Days, and Amount of Dose

Groups	Doses	Days	Amount
Group 1	Normal Saline	12 Days	1 ml
Group 2	30 % CCl_4	12 Days	200mg/kg

The rats were placed in a desiccator with chloroform, and a small incision was made in the abdominal wall with sharp scissors to anesthetize them. The internal organs were then exposed by cutting the muscular coating on the sides. To keep the exposed organs of the animal from drying out, a 0.9% pyrogen-free sodium saline solution was poured on them. Rats were fed regular food for 24 hours before being dissected. Chloroform was used to euthanize the rats. Before dissection, the rats were weighed. Blood samples were obtained in vacutainers using 23 G1 syringes after the rats were dissected and cardiac punctured. The liver and brain are dissected, and debris is washed away with ice-cold saline. For tissue homogenate tests, organs were weighed and stored at -20°C. Centrifuge the blood samples at 10,000rpm for 15 minutes at 4 ◦C. Serum was separated and stored at -20 ◦C. The diagnostic kits were used to estimate the levels of AST and ALT in serum samples taken from rats. Randox kits were used to determine the lipid profile parameters. Cholesterol, triglycerides TG low-density lipoprotein cholesterol (LDL-C), and High-density lipoprotein cholesterol (HDL-C) were measured. For ALT take 100ul of sample and 800ul of reagent (R1). After 1 minute, mix and apply 200l reagent (R2). After 1 minute, measure the absorbance at 340nm. Start the stopwatch. After 1, 2, and 3 minutes, recheck the absorbance. Calculate AA/min from the absorbance reading and multiply by the appropriate factors (1745) as shown in the formula; ΔA/min x factor =ALAT(GPT)activity [U/1]. For AST mix 800ul of Reagent (RI) and 100pl of the sample. After 1 minute, mix and apply 200pl reagent (R2). After 1 minute, read the absorbance at 340 nm and start the stopwatch. After 1, 2, and 3 minutes, recheck the absorbance. Calculate A/min from absorbance readings and multiply by the appropriate factor (1745) as given in the formula ΔA/min x factor = ASAT (GOT) activity [U/l]. For Biuret Method for Protein Quantification prepare a stock solution of BSA containing 5mg/ml in distilled water. Prepare dilutions using 0.1, 0.2, -, and 1.0 ml of BSA solution and make the volume of 4 ml using distilled water. Add 6ml of biuret reagent. Mix and incubate at 37^0 or room temperature for 10min. Prepare dilutions of unknown samples. Make the volume of 4ml using distilled water and add 6ml of biuret reagent. Read the absorbance of the solutions at 562 nm.

RESULTS

CCl_4 is a hazardous compound, and it harms the lipid profile. In this experiment, CCl_4 exposure disrupted normal physiology, causing abnormal cholesterol, triglyceride, HDL, and LDL levels in the blood of the treated group. Significant changes in Haematologica parameters were found between the control and treatment groups, as given in Table 2 and Figure 1.

Table 2: Statistical Analysis of TC, TG, HDL, and LDL Diseased Value with Normal Values

	N	Minimum	Maximum	Mean ± SD
Total Cholesterol	15	184.00	231.00	202.0000 ± 19.07504
Triglycerides	15	189.00	258.00	222.8000 ± 24.87167
HDL	15	43.00	62.00	52.6000 ± 6.94674
LDL	15	115.00	148.00	132.8000 ± 12.58230
Valid N (list-wise)	15	-		

To calculate the confidence interval of mean differences in total cholesterol, triglycerides, HDL, and LDL, a one-sample t-test was used, as given in Table 4.

Table 4: One-Sample Test show the interval difference of T.C, triglycerides, HDL, and LDL

	Test Value = 0					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
Total Cholesterol	41.014	14	.000	202.00000	191.4366	212.5634
Triglycerides	34.694	14	.000	222.80000	209.0265	236.5735
HDL	29.326	14	.000	52.60000	48.7530	56.4470
LDL	40.877	14	.000	132.80000	125.8322	139.7678

Total cholesterol correlates with HDL and LDL; triglycerides only indicate a correlation between HDL and LDL. HDL shows the correlation between cholesterol and triglycerides, while LDL shows the correlation between cholesterol and HDL, as given in Table 5.

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Table 5: Correlations analysis among the T.C., triglycerides, HDL, and LDL

		Total Cholesterol	Triglycerides	HDL	LDL
Total Cholesterol	Pearson Correlation	1	.304	.699**	-.974**
	Sig. (2-tailed)		.271	.004	.000
	N	15	15	15	15
Triglycerides	Pearson Correlation	.304	1	.726**	-.215
	Sig. (2-tailed)	.271		.002	.441
	N	15	15	15	15
HDL	Pearson Correlation	.699**	.726**	1	-.680**
	Sig. (2-tailed)	.004	.002		.005
	N	15	15	15	15
LDL	Pearson Correlation	-.974**	-.215	-.680**	1
	Sig. (2-tailed)	.000	.441	.005	
	N	15	15	15	15

**. At the 0.01 level, the correlation is significant (2-tailed)

DISCUSSION

This study aimed to determine the toxic effects of CCl_4 on the lipid profile of Albino Rats. Rats were fed with 30% diluted CCl_4. Total Cholesterol, Triglycerides, HDL, and LDL, were all measured throughout this research. According to this finding, the parameters were significantly higher in the CCl4-treated rats than in the normal rats. In the Albino Rats, CCl_4 consumption disrupts the body's normal lipid levels, resulting in toxicity. The lipid profile and serum levels of total cholesterol, TG, LDL, and LDL exhibited significant increases in CCl_4-treated rats. CCl_4 exposure induced an imbalance in lipid profile cholesterol, triglycerides, HDL, and LDL levels. The amount of lipid profile imbalance was observed in this study. Similar results were obtained by Boll *et al.*, CCl_4 poisoning causes a rise in cholesterol synthesis because the liver plays an essential role in lipid metabolism, including several stages of lipid synthesis and transportation [17]. As a result, an abnormal lipid profile is to be observed. Similar observations and results were obtained by Althnaian *et al.*, Abdel Moneim *et al.*, according to these results, the Lipid profile, as well as serum levels of total cholesterol, TG, LDL, and LDL, are abnormal due to CCl_4 toxicity. Fernandez and West obtained similar results [18-20]. According to them, injecting CCl_4 caused a significant increase in triglyceride, total cholesterol, and LDL levels and decreased HDL levels. Protein synthesis could be inhibited, and phospholipid metabolism could be affected, resulting in abnormal lipoprotein levels and a messed-up lipid profile. CCl_4 raised cholesterol, triglycerides, and LDL levels in the blood while decreasing HDL levels significantly. One of the leading causes of hepatic lesions caused by CCl_4 is cellular oxidative stress, which is mediated by the free radicals created by this poisonous chemical. Increased oxidative stress increases the effect of non-essential fatty acids, which raise cholesterol and triglyceride levels in the blood and tissues. In this investigation, the amount of lipid profile imbalance was observed; CCl_4-induced elevated levels of low-density lipoprotein (LDL), total cholesterol, triacylglycerol and increased high-density lipoprotein (HDL). In this investigation, an abnormal lipid profile is to be observed. In this study, we observed the abnormal lipid profile, and their parameters also disturb. Similar results were obtained by Turner and Lysiak these findings show that lipid peroxidation in the testes is linked to male reproductive system failure caused by steroidogenesis impairment [21]. Hyperlipidemia was caused by CCl_4 exposure [22, 23]. Intoxication with carbon tetrachloride increased triglycerides, LDL, and cholesterol levels while decreasing HDL levels. We discovered aberrant lipid profiles and associated values in our investigation. Similar results were obtained by Islam *et al.*, that serum lipid profiles such as total cholesterol, triglycerides, and LDL were elevated [24]. At the same time, HDL was lowered, indicating a decline in hepatic function due to CCl_4 treatment and an aberrant lipid profile. Honma obtained similar results [25] that the lipid profile and serum levels of total cholesterol, TG, LDL, and LDL are disturbed due to CCl_4 toxicity. In our research, we found aberrant lipid profiles as well as their parameters. Similar results were obtained by West *et al.* [26]; the quantity of lipid profile imbalance was determined using serum cholesterol, triglycerides, HDL, and LDL. The rate of protein synthesis is slowed. Phospholipid metabolism may be disturbed, resulting in aberrant lipoprotein levels in the blood serum. Similar results were obtained by Noguchi *et al.*, according to these findings, the increase in blood lipid profile in CCl_4-intoxicated rats alone predicts cardiovascular risk [27]. TAG, TC, LDL-C, and HDL-C levels were lower in the treatment groups. During our examination, we detected abnormal lipid profiles and corresponding elevated values.

Authors Contribution

Conceptualization: SM
Methodology: MFB
Formal Analysis: MJK
Writing-review and editing: SM, M, MKAK

Author have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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