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Hematobiochemical, antioxidant, and lipid alterations in mice feed with thermally oxidized coconut oil

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Abstract

In the present study, the effects of recycled oxidized coconut oil were assessed on hematobiochemical, antioxidant and cardiac markers in albino mice. In all, 24 mice were divided into three groups: group I, II, and III; animals in each group received a normal diet as well as fresh and deep-oxidized coconut oil. The outcomes demonstrated that group III mice fed with thermally oxidized coconut oil revealed a significant alteration in the form of decreased levels of alkaline phosphatase, alanine transaminase, aspartate transaminase, total white blood corpuscle, platelet count, hemoglobin (Hb), Hb concentration, mean corpuscular hemoglobin, and hematocrit (HCT) ($p > 0.05$). Likewise, levels of triglyceride, cholesterol, and low-density lipoprotein in group III were high, while level of high-density lipoprotein was weakened. Moreover, it was observed that administration of oxidized coconut oil (group III) caused significant changes in the levels of creatinine, uric acid, serum urea, total proteins, globulin, albumin, blood urea nitrogen, and serum glucose as well as concentrations of serum electrolytes, such as calcium, magnesium, potassium, and sodium. This study also showed that group III mice had low levels of glutathione, superoxide dismutase, and radical scavenging capacity and high levels of thiobarbituric reactive substances. However, animals in group II, fed with diet of fresh coconut oil, showed normal levels of all the above-mentioned hematobiochemical, antioxidant, and lipid markers, compared to control mice (group I) and group-III animals. The histological findings of the liver and heart further confirmed the findings of the current investigation, that is, deep-oxidized coconut oil has negative consequences and ought to be avoided.

Keyword: oxidized coconut oil; hematology; lipid profile; serum electrolytes; histology

Introduction

Coconut tree (*Cocos nucifera*) is known as the "tree of life." Belonging to the family *Aracaceae* (palm family), coconut is considered as an integral part of human diet and livelihood (Henrietta *et al*., 2022). Coconut oil contains about 91% saturated fats and 8% unsaturated fats. Medium chain fatty acids, such as lauric acid, make up more than half of the lipids in coconut oil. The main natural source of lauric acid is coconut oil (Arias *et al*., 2023).

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Coconut oil is also a predominant source of different combinations of triacylglycerols (TAG), fatty acids, phospholipids, and unsaponifiable components (Gao *et al*., 2022). Since ancient times, coconut oil has been utilized as a food in both fresh and thermally oxidized forms (de Paiva Azevedo *et al*., 2021) (Meireles *et al*., 2022). However, over time, thermal oxidation has shown a negative effect on the quality of dietary oil (Ganesan *et al*., 2018) Saleem *et al.,* 2023; Sana *et al.,* 2022; (Venkata and Subramanyam, 2016). Additionally, if thermally oxidized oil is consumed, development of concomitant by-products occurs, which is extremely cytotoxic to cells, tissues, and organs (Bacou *et al*., 2021). It is hypothesized that oxidized oils are absorbed to decrease crucial fatty acid deficit (Cui *et al*., 2021), but they increased the growth of fatty livers, retardation in growth, and atherosclerosis (Savic *et al*., 2020). As coconut oil is oxidized thermally, distinct free radicals are created in the body. These free radicals could be hazardous to the liver, kidneys, and heart, and thus contribute to a number of disorders, including diabetes, cataract development, arthritis, and cancer (Abdallah *et al*., 2020).

In order to maintain homeostasis, the liver and kidneys excrete and reabsorb a variety of substances, including alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), creatinine (CR), serum urea (URE), and uric acid (UA) (Rosner, 2011). Thus, the organs are exposed to various toxicants produced as a result of metabolism (Gupta, 2020). Damage to these tissues is also related to alterations in glutathione (GSH), superoxide dismutase (SOD), and malondialdehyde (MDA). As a result, reactive oxygen species (ROS) are produced, causing oxidized stress, thus leading to apoptosis because of the peroxidation of lipids, nucleic acids, and proteins. This also changes hematological markers, such as total leucocyte count (TLC), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular volume (MCV), hemoglobin (Hb), and packed cell volume (PCV). The primary catalogue for determining toxicity is serum biochemical characteristics, which show the good functioning of organs (Li, Z-H *et al.*, 2011). The current study aimed to determine the effects of recycled edible coconut oil on hematobiochemical, antioxidant, and lipid alterations, in addition to changes in the histology of the liver and heart in albino mice.

Materials and Methods

Chemicals

Utilizing the methodology described below, biochemical kits were used to estimate or count total cholesterol, triglyceride, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) levels (Addanki and Reddy, 2023).

Oil sample

The study was conducted at the Department of Zoology, University of Malakand, Pakistan. Fresh coconut oil was utilized in 1:1 ratio, and albino mice were fed with the oil at a dose of 100 mg/kg body weight, and the remaining coconut oil was oxidized thermally for 9–10 h in a stainless steel vessel. Food and water were provided to the animals at will in cages while they were acclimatized to surroundings.

Experimental design

The animals were divided into three groups (group I–III). Each group received a sample of coconut oil via oral administration. Mice in group I (control group) received normal food and water. Group II mice were fed with fresh coconut oil (100 mg/kg body weight). Group III mice were fed with thermally oxidized coconut oil (100 mg/kg body weight).

Blood Collection

Albino mice were weighed twice, before and after the experiment. On the final day of the experiment, blood was drawn from the jugular vein of mice and placed in a test tube for biochemical examination and estimation. Clear serum was obtained from the blood samples by centrifuging them in a bench centrifuge for 10 min at 3,000 revolutions per hour. This serum was then utilized to evaluate the hematobiochemical and lipid profile function tests (Adham *et al*., 2011).

Biochemical analysis

Utilizing the approach described by Al-Daghri, *et al.* (2017), serum was used to perform renal function test. Serum electrolytes were also assessed using the method described by Chen, Y., *et al.* (2018). According to Forouzandeha H *et al.* (2013), serum was used for liver function test utilizing an auto-analyzer (Olympus AU 600, Japan).

Antioxidants analysis

The total reduced thiol contents (GSH), radical scavenging activity (RSA), and thiobarbituric acid reactive substances (TBARS) of liver tissues were measured according to the method described by Ajuwon *et al.* (2014).

Histopathological analysis

Histopathology of the liver and heart was performed using the technique described by Alsaad *et al.* (2018). All the animals were dissected at the end of the experiment, and tissues were removed and preserved in a solution containing 10% formalin and 0.9% NaCl. A light microscope (BX50; Olympus; Tokyo, Japan) was used to study the tissues placed in paraffin; the tissues were sectioned using a microtome, and stained with hematoxylin and eosin (H&E) for a more traditional morphological analysis. Photographs were taken using a microscope-mounted digital camera system (Pixcera Co., Osaka, Japan) (Ovalle and Nahirney, 2013).

Data analysis

Statistical Package for the Social Sciences (SPSS) was used for presenting and analysis of data, demonstrated as mean values + standard deviation (SD). Results were statistically significant at $p > 0.05$.

Results

To look at how lab-raised albino mice (Mus. Musculus) Linnaeus 1758 react to oxidized coconut oil. The albino mice that were fed coconut oil that had undergone thermal oxidation displayed a marked rise in body weight. Histological research has revealed changes in the liver and cardiac cells that further support the oxidized coconut oil's (group III) toxicity. The current study also examined the effects of thermally oxidized coconut oil on serum biochemical markers, such as ALT, AST, ALP, URE, UA, CR, urea total protein (TP), albumin (ALB), globulin (GB), and blood urea nitrogen (BUN)

Blood hematological analysis

Deep-oxidized coconut oil (100 mg/kg body weight) significantly ($p > 0.05$) decreased the blood levels of hemoglobin, red blood cells, MCV, MCH, and MCHC in group III mice while increasing the levels of white blood cells (WBC), platelets, lymphocytes, and monocytes. The ingestion of fresh coconut oil (100 mg/kg body weight) maintained standardized hematological factors as shown in Table 1.

Serum biochemical analysis

Mice in group III fed with deep-oxidized coconut oil (100 mg/kg body weight) demonstrated statistically increased levels of AST, ALT, and ALP values ($p > 0.05$), compared to the control group 1 (Table 2). Group III mice also demonstrated changes in the concentrations of blood URE, UA, serum CR, and BUN, compared to the control group (group I) as shown in Table 3. Similarly, mice in group III showed lower serum levels of total protein, albumen, and globulin and higher levels of bilurobine, compared to the control group (Table 4). Administration of fresh coconut oil (100 mg/kg body weight) had more long-lasting effects, as observed in mice.

Analysis of lipid profile

When compared to the control (group I), levels of total cholesterol, triglycerides, HDL, and LDL were normal in group II mice fed with fresh coconut oil (100 mg/kg

Table 1. Effects of deep-oxidized coconut oil on hematological parameters in mice expressed as mean ± SD values.

Dosages		RBC (M/µL)	HB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	PLT (g/dL)	WBC (×10^3/µL)	MONO%
Group I	Control	7 ± 2.8	11 ± 3.4	37 ± 2.6	64 ± 2.6	27 ± 3.1	32 ± 3.4	130 ± 3.1	15 ± 1.3.	6 ± 3.1
Group II	Fresh coconut oil	12 ± 4.4	13 ± 5.2	40 ± 2.3	72 ± 3.2	32 ± 2.1	33 ± 2.9	142 ± 2.1	9 ± 3.1.	5 ± 1.1
Group III	Deep-oxidized coconut oil	8.2 ± 0.44	8 ± 4.2	17 ± 2.3	35 ± 2.6	18 ± 0.84	18 ± 2.1	273 ± 6.1	17 ± 0.6	9 ± 3.1

Note: RBC= Red blood cell; HB= hemoglobine; HCT= hematocrit; MCV= mean corpuscular volume; MCH= mean corpuscular hemoglobin; MCHC= mean corpuscular hemoglobin concentration; PLT= platelet; WBC= white blood cells; MONO = monocytes

Table 2. Effects of deep-oxidized coconut oil on liver-related serum markers in mice expressed as mean ± SD values.

Dosages		Serum ALT (U/L)	Serum AST (U/L)	Serum ALP (U/L)	Serum glucose (mg/dL)
Group I	Control	43 ± 2.6	38 ± 3.1	39 ± 1.6	66 ± 2.1
Group II	Fresh coconut oil	47 ± 4.2	40 ± 1.3	41 ± 1.3	63 ± 3.2
Group III	Deep-oxidized coconut oil	176 ± 3.4	119 ± 3.4	169 ± 1.6	134 ± 5.1

Table 3. Effects of deep-oxidized coconut oil on kidney-related serum markers in mice (expressed as mean ± SD values).

Dosages		Creatinine (mg/dL)	Serum urea (mg/dL)	Uric acid (mg/dL)	BUN (mg/dL)
Group I	Control	0.97 ± 0.74	32 ± 0.66	66 ± 2.1	21 ± 1.3
Group II	Fresh coconut oil	0.3 ± 1.1	29 ± 0.46	63 ± 3.2	18 ± 3.2
Group III	Deep-oxidized coconut oil	2.3 ± 0.3	63 ± 1.3	134 ± 5.1	47 ± 4.1

Table 4. Effects of deep-oxidized coconut oil on serum markers in mice expressed as mean ± SD values.

Dosages		T. Bilirubin (mg/dL)	Albumin (g/dL)	Total protein (g/dL)	Globulin (mg/dL)
Group I	Control	0.5 ± 0.2	2.3 ± 2.2	4.4 ± 0.2	1.59 ± 0.01
Group II	Fresh coconut oil	0.3 ± 0.3	2.0 ± 1.6	2.9 ± 1.1	1.89 ± 1.06
Group III	Deep-oxidized coconut oil	2.6 ± 0.8	3.8 ± 2.0	3.9 ± 1.2	1.31 ± 0.02

Table 5. Effects of thermally oxidized coconut oil on serum lipid markers in group III mice (expressed as mean ± SD values).

Dosages		Cholesterol (g/dL)	Triglycerides (mg/dL)	HDL (mg/dL)	LDL (mg/dL)
Group I	Control	112.62 ± 2.87	29.31 ± 3.47	66.12 ± 5.92	23 ± 2.1
Group II	Fresh coconut oil	109.54 ± 3.1	29.17 ± 5.92	45.81 ± 4.42	20 ± 2.3
Group III	Deep-oxidized coconut oil	132.13 ± 4.3	87.13 ± 5.9	24.62 ± 2.72	44 ± 1.4

Table 6. Effects of deep-oxidized coconut oil on serum electrolytes in group III mice (expressed as mean ± SD values).

Dosages		Serum Na (mmol/L)	Serum K (mmol/L)	Serum Mg (mmol/L)	Serum Ca (mmol/L)
Group I	Control	137.1 ± 0.54	5.1 ± 0.04	0.99 ± 0.06	6.4 ± 0.02
Group II	Fresh coconut oil	136.2 ± 0.21	5.9 ± 0.07	1.01 ± 0.03	7.0 ± 0.01
Group III	Deep-oxidized coconut oil	114.1 ± 2.12	4.2 ± 1.07	0.87 ± 0.02	4.7 ± 0.03

body weight). However, the lipid profile of mice in group II showed a notable increase. Similarly, group III mice demonstrated significantly altered lipid markers, that is, increase was observed in cholesterol levels, triglycerides, LDL levels, although decrease was observed in HDL concentrations, signifying the toxicity of thermally oxidized coconut oil (Table 5).

Analysis of serum electrolytes

Normal levels of serum sodium, potassium, and magnesium were determined in group I mice (control group). However, all of these blood electrolytes showed lower levels ($p > 0.05$) in group III mice, fed with thermally oxidized coconut oil. The treatment of fresh coconut oil at a dose 100 mg/kg body weight demonstrated stabilizing effects on serum electrolytes concentration as shown in Table 6.

Analysis of tissue antioxidants

Significantly lower levels of antioxidant parameters of liver tissues, such as GSH, RSA, and SOD, were observed, while TBRAS level was significantly high, in group III animals, compared to the control group, as shown in Table 7.

Analysis of body weight

The body weight of albino mice (*M. musculus Linnaeus* 1758 (is the scientific name of mice identified first time by Linnaeus taxonomist in 1758) was monitored in the current study. Initial body weights of animals in control (group I), fresh coconut oil (group II), and thermally oxidized coconut oil (group III) groups were 24 g, 36 g, and 64 g, respectively. However, the ultimate body weights of mice in groups I and II were 68 g and 66g, respectively, and group III mice had 97 g body weight. After comparisons with group I (a control group) this study revealed that mice in group III showed a noticeably increased ($p > 0.05$) in weight respectively (Table 8).

Histological examination

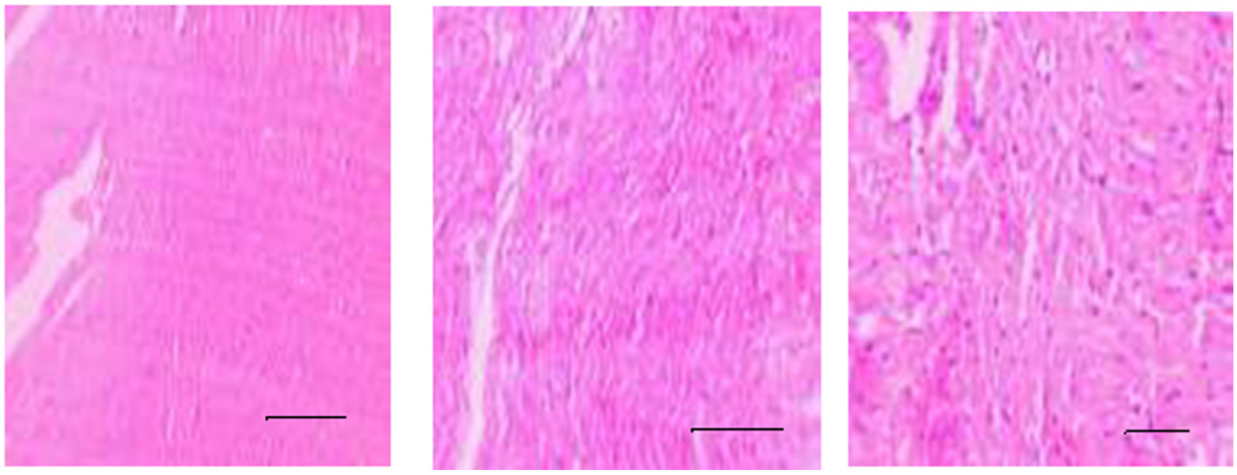
Histology of the liver and heart in group III mice showed that papillary muscles had few vacuolizations and a congested myocardial state (Figures 1 and 2).

Table 7. Effects of deep-oxidized coconut oil on liver antioxidant enzymes in group III mice (expressed as mean ± SD values).

Dosages		GSH (mmol/dL)	RSA (mmol/dL)	TBARS (mmol/dL)	SOD (mmol/dL)
Group I	Control	39.12 ± 0.71	43.69 ± 1.0	14.23 ± 1.4	11.23 ± 1.2
Group II	Fresh coconut oil	41.25 ± 1.3	47.73 ± 1.1	14.11 ± 1.2	16.12 ± 2.3
Group III	Deep-oxidized coconut oil	19.35 ± 1.3	22.2 ± 1.2	29 ± 2.0	9.23 ± 2.1

Table 8. Effects of deep-oxidized coconut oil on the body weight of albino mice.

Dosages		Primary body weight (g)	Final body weight (g)	Weight gain (g)
Group I	Control	44 ± 4.95	68 ± 2.9	24 ± 3.56
Group II	Fresh coconut oil	30 ± 6.05	66 ± 12.01	36.5 ± 5.02
Group III	Deep-oxidized coconut oil	33 ± 11.90	97 ± 13.30	64.11 ± 8.86



Group-I = A **Group-II = B** **Group-III = C**

Figure 1. Effect of oxidized lipid on the heart tissues of albino mice. Group A: control; group B: congested myocardial condition with fresh coconut oil feed; group C: papillary muscles and few vacuolizations with thermally oxidized coconut oil feed.

Discussion

Diet plays a key role in inhibiting contagious diseases (Wiertsema *et al*., 2021). Nutritional issues are widespread in Asian nations, and various industrialized countries have geared up nutritional policies to address health issues. The current study examined the effects of oxidized coconut oil in albino mice. Various serum biomarkers, such as liver- and kidney-related serum markers, lipid profile, and antioxidant marker, and histology of the liver and heart were examined. These parameters were considered being the subject of health and infection to be analyzed (Siong *et al*., 2020, Adeleke and Babalola, 2020). The results showed an alteration in the levels of hematological, biochemical, lipid, and antioxidant markers in group III mice fed with thermally oxidized coconut oil. Microbes and their metabolites can also cause toxicity in animals. (Rauf *et al.,* 2023; Wilson and Nicholson *et al.,* 2017). According to Ogueji, Nwani *et al.* (2020), toxicity is the degree of harm caused to an organism by the exposed substance. The liver and kidneys are highly vascularized organs and more vulnerable to damage than other body parts; hence, the degree of toxicity varies from organ to organ (Sümer *et al*., 2020). Hepatocellular changes are related with changes in blood parameters (Mitra *et al*., 2019). Blood markers are used to determine the range of lethal influence of any exogenous substance on the blood of an animal (Ahmed *et al*., 2020).

Results revealed that significant deviations in hematological markers, such packed cell volume, Hb, TLC, MCH, MCHC, and MCV, were observed in group III mice. These results were in agreement with the findings of (Maleki *et al*., 2016), who investigated thermal decomposition of crude oil, and its fractions were studied by differential scanning calorimetry using mice as a

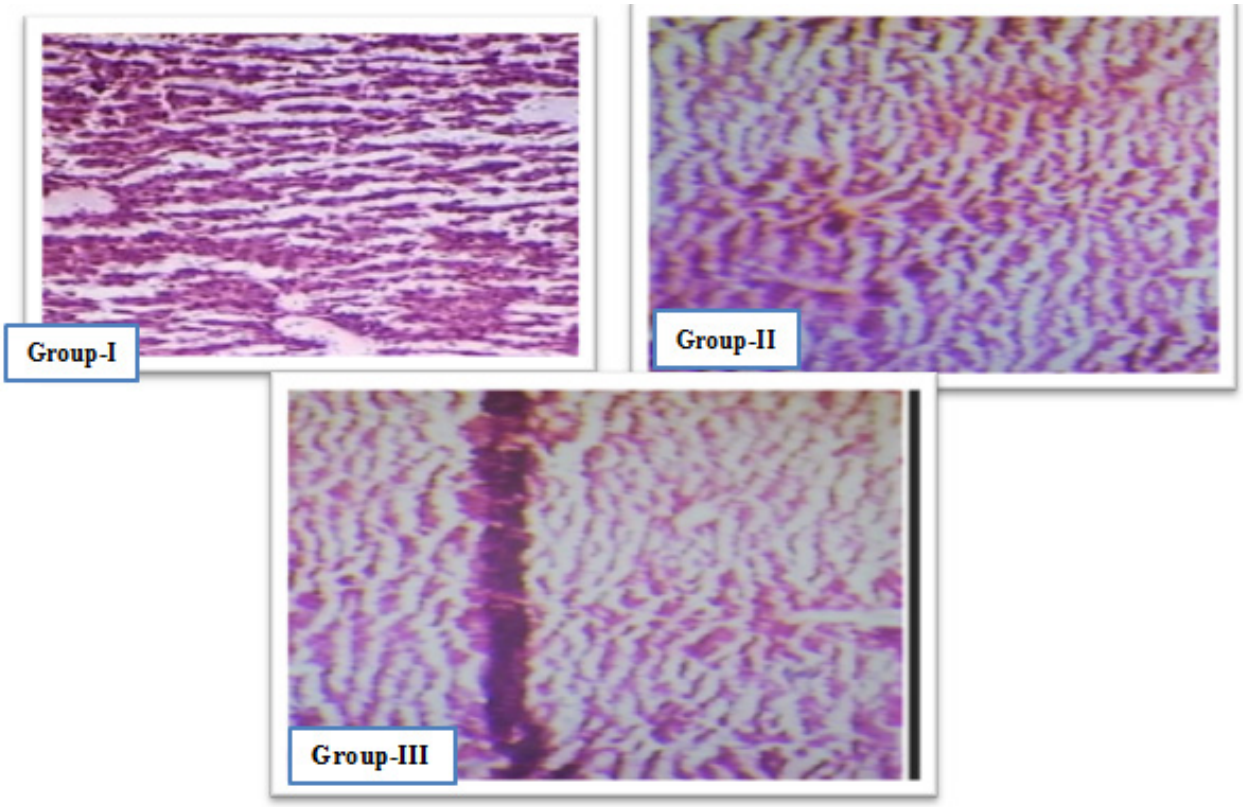


Figure 2. Histology of the liver in group I, II, and III mice. Group I: control group; group II: mild necrosis and swelling; group III: inflammation, necrosis, and welling.

model. However, group II mice fed with fresh coconut oil demonstrated no changes in the normal levels of hematological indices, as observed in the third week of treatment.

The liver, a homeostatic organ in the body, is exposed to toxic substances, and the toxicity could be calculated by liver function tests, such as AST, ALT, and ALP (Lozano-Paniagua *et al*., 2021). High levels of these enzymes are symptomatic of cellular leakage and loss of hepatic cell functional integrity (López-Otín and Kroemer, 2021). The present study also analyzed the adverse effects of thermally oxidized recycled coconut oil on the functioning of liver enzymes. In this study, we observed an insignificant ($p > 0.05$) increase in the levels of ALT, AST, and ALP after ingestion of coconut oil. This revealed the toxic effect of oxidized recycled coconut oil on the liver. A study conducted by (Ambreen *et al*., 2020) concluded that ingestion of thermally oxidized mixed vegetable oil for a longer period could damage the liver and impair its histological architecture. Our study is comparable to the study done by (Aziz *et al*., 2023b), who studied the effects of oxidized sunflower oil on various hematobiochemical markers as well as liver histopathology in rabbit. The present study also revealed the effects of thermally oxidized coconut oil on lipid profile. Thermally oxidized coconut oil-fed mice (group III) showed decreased HDL level and increased LDL, triglycerides and cholesterol levels, compared to normal mice (group I) and mice fed with fresh coconut oil (group II). A similar study conducted by (Feleke *et al*., 2022) postulated that intake of deep-fried oil resulted in higher levels of total cholesterol and LDL cholesterol, but reduced HDL cholesterol. Such adverse health effects are very risky with oils rich in unsaturated fats, such as sunflower oil. The levels of total cholesterol, triglycerides, and LDL mounted with increase in the length of coconut oil's thermo-oxidation process. The total cholesterol level ascended unevenly with increase in the time spent frying; high-density lipid and cholesterol levels decreased, while those of other cholesterols such as low-density lipoproteins increased. A parallel study conducted by (Selani *et al*., 2016) also confirmed that levels of different lipids expanded in the body due to coconut oil.

In the present work, we examined the effect of oxidized recycled coconut oil on renal functions. The kidneys remove metabolic waste products from the body; therefore, these are liable to chemical injury (Kellum *et al*., 2021). The current research showed that nephrotoxicity caused by chemical substances is the result of the accumulation of certain metabolites in the kidneys (Miners *et al*., 2017). According to the literature, marked increase in the levels of serum CR, URE and UA indicates certain

forms of infection (Skrzypczyk *et al*., 2021). Increase in blood urea nitrogen, serum CR, URE, UA, and glucose levels with reduced levels of total protein, albumin, and globulin along with changes in serum electrolyte concentrations, such Na, K, Mg, and Ca, show tissue toxicity and damage to visceral organs. Similarly (Kwek *et al*., 2022) reported that regular intake of deep-fried corn oil and lard could affect gut health (Aziz *et al*., 2024, Aziz *et al*., 2023a). A previous research conducted by (Baig *et al*., 2022) also demonstrated similar results. Oxidative stress and toxicity causes impairment in blood, serum biomarkers also deteriorates renal function (Arani and Whecsler *et al*, 2023). It was observed in the present study that changes in blood urea nitrogen, serum URE, UA, and CR as well as other markers, such as total protein, globulin, albumin, and total bilurobine, are due to frequent use of oxidized recycled coconut oil.

It is clear from previous studies that damage to visceral organs is the leading cause of oxidized stress and impairment, which contribute to the imbalance of tissues antioxidants, such as GSH, SOD, and TBRAS which play main role in our immune system by defending our body from the harmful action of free radicals otherwise they lead to various chronic illness. (Carmo de Carvalho e Martins *et al*., 2022).

In the present study, the effects of thermally oxidized coconut oil on the concentration of tissue antioxidants were analyzed. Results showed that feeding of deep-oxidized oil reduced the levels of GSH, RSA, and SOD but increased TBARS levels. However, usage of fresh coconut oil maintains the normal levels of these antioxidants. Several analogous studies, such as (Abdelnour *et al*., 2022)), (Gopinath *et al*., 2021), and (Narayanankutty *et al*., 2022), reported similar results.

In the present study, increase in weight and nourishment was observed by using thermally oxidized coconut oil in mice. Results showed that maximum weight gain was observed in group III mice, fed with thermally oxidized coconut oil. However, the diet of fresh oil maintained normal body weight. This increase in body weight could be due to the accumulation of unchanged metabolites in body tissues. The accumulation of these unchanged metabolites causes subcellular damage and thus effect the cell metabolism, which increase the body weight (obesity) is a leading cause several disorders.

Conclusion

Intake of deep-oxidized coconut oil has adverse effects on hematobiochemical markers, alters lipid profile, and disturbs the liver, kidney and cardiac functions. Finally, weakening of the immune system produces free radicals that react with membrane lipids of cells (peroxidation), causing oxidized stress, abnormality, and toxicity, resulting in various disorders.

Recommendation

It is advised to never or sparingly use recycled oxidized coconut oil. More research is required to understand its effects on genomes, proteome, and at subcellular levels that result in acute and chronic damage to vital organs and sicknesses.

Conflict of interest

There was no conflict of interest to declare.

Ethical Approval

Ethical approval for the study was obtained from the Department of Pharmacy, University of Malakand, Pakistan (Reference No. Pharm/23/4169).

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