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Lipid Lowering Potency of *Phoenix dactylifera*, *Cyperus esculentus*, *Cocos nucifera* Mixed Extract on Male Wistar Albino Rat Model

[1]Sarah Kelechi Enebeli, [2]Tamuno-Boma Odinga, [1]Cletus Barizoge Lemii, [1]Iyaeneomi Ransome Daka, [3]Christine Umanu Gabriel-Brisibe, [1]Iyingiala Austin-Asomeji and [1]Felicia Ucheawaji Edward

[1]Department of Pharmacology and Therapeutics, Faculty of Basic Clinical Sciences, College of Medical Science, Rivers State University, Port Harcourt, Nigeria

[2]Department of Biochemistry, Faculty of Science, Rivers State University, Port Harcourt, Nigeria

[3]Department of Medical Biochemistry, Faculty of Basic Medical Sciences, College of Medical Science, Rivers State University, Port Harcourt, Nigeria

[4]Department of Community Medicine, Faculty of Clinical Sciences, College of Medical Sciences, Rivers State University, Port Harcourt Nigeria

ABSTRACT

Background and Objective: Lipids and lipoproteins metabolism have been associated with cardiovascular diseases and their complications due to their ability to regulate blood cholesterol. This study evaluated the potential of the synergistic aqueous extract of *Phoenix dactylifera*, *Cyperus esculentus* and *Cocos nucifera* (STCD) commonly taken as a healthy drink in Nigeria on the lipid profile of male Wistar rats. **Materials and Methods:** Acute oral toxicity LD_{50} of STCD extract was analyzed and interpreted according to OECDE (Organization for Economic Co-operation and Development) guidelines. Fifteen male albino rats were grouped into three groups with 5 rats in each group, control, 200 and 400 mg kg^{-1} STCD. The rats were administered STCD extract orally 24 hourly, for 21 days, with feed and water *ad libitum*. At the end of the experiment, blood samples were collected for lipid profile analysis using standard laboratory methods. One-way ANOVA and Turkey's Test were performed. The $p \leq 0.05$ was considered statistically significant. **Results:** The LD_{50} of STCD extract was ≥ 2404.2 mg kg^{-1} body weight, thus being non-toxic. The percentage of body weight difference increased significantly. The extract at 200 and 400 mg kg^{-1} caused a decrease in the serum TG, TC, VLDLC and LDLC levels, with the most effect at 200 mg kg^{-1}. The administered concentrations were observed to cause a non-significant increase in the serum HDLC level in comparison to the control group at $p \leq 0.05$. **Conclusion:** The antilipidemic and anti-cholesterolaemic potency of the extract. This may hence be of advantage in the management and prophylaxis of lipid peroxidation and cardiovascular disorders.

KEYWORDS

Tigernuts (*Cyperus esculentus),* date fruits *(Phoenix dactylifera),* coconut *(Cocos nucifera),* lipid profile, cardiovascular disorders, male albino rats

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INTRODUCTION

A lipid profile is a complete cholesterol test that measures the amount of cholesterol and triglycerides in the blood. It is also called a lipid panel. This test typically includes: Low-Density Lipoprotein (LDL), High-Density Lipoprotein (HDL), triglycerides (TG), total cholesterol (TC), Very Low-Density Lipoprotein Cholesterol (VLDLC), etc. and is used to assay for dyslipidaemia, cardiovascular diseases and rarely pancreatitis[1]. The lipid profile indices can affect the health of an individual if they are relatively higher or lower than normal. This may cause cardiovascular diseases in the body if not taken care of properly.

Cyperus esculentus (also called tiger nut, chufa, atadwe, yellow nutsedge and earth almond) is a crop of the sedge family widespread worldwide. It is found in most of the Eastern Hemisphere, including Southern Europe, Africa, as well as the Middle East and the Indian Subcontinent[2]. In Nigeria, tiger nut is called "Ofio" by the Yorubas, "Akiausa" by the Igbos and "Aya" by the Hausas[3]. It is cultivated for its edible tubers, called earth almonds or tiger nuts, as a snack food and for the preparation of horchata de chufa, a sweet, milk-like beverage. Tiger nut is a good source of calcium, iron, magnesium, phosphorus, ascorbic acid (vitamin C), tocopherol (vitamin E), dietary fibre as well as fats like oleic acid[3]. Tiger nut milk compared with any other soft drink is very healthy. It contributes to the reduction of cholesterol by diminishing Low-Density Lipoprotein (LDL) and increasing High-Density Lipoprotein (HDL)[4].

Phoenix dactylifera, is a monocotyledon that belongs to the family of Arecaceae (Angiosperms), it consists of about 200 genera with over 2,500 species. *Phoenix* (Coryphoideae phoeniceae) is a genera with approximately 14 species. It is native to Africa and Asia[5,6]. The fruits are nutritious, high-energy food and an important part of the diets of people in Asia, the Middle East and African countries. Dates are a rich source of nutrients such as carbohydrates (44-88%), dietary fibers (6.4-11.5%), fats (0.2-0.5%) and proteins (2.3-5.6%)[7]. The dried fruit of *Phoenix dactylifera* contains over 50% of sugar by weight. It also consists of about 2% of protein, fat and mineral matter, 20-70 calories[8]. The date fruit extract contains natural antioxidants such as vitamins, riboflavin, vitamin C and thiamine depending on size and variety and phenolic compounds including flavonoids, ferulic acid, p-coumaric and anthocyanins[9]. Dates have been reported to be rich in minerals such as calcium, iron, magnesium, selenium, copper, phosphorus, potassium, zinc, sulfur, cobalt, fluorine, manganese and boron. It also contains palmitoleic acid, oleic, linoleic and linolenic acid. Dates are observed to be distinct from some fruits such as apples, oranges and bananas due to their amino acid contents. They also contain vitamins A, B1 and B2 and nicotinic acid are constituents of dates[7].

Cocos nucifera is a member of the palm tree family (Arecaceae) and the only living species of the genus *Cocos*. The term "coconut" (or the archaic "coconut") can refer to the whole coconut palm, the seed, or the fruit, which botanically is a drupe, not a nut. The coconut tree provides food, fuel, cosmetics, folk medicine and building materials, among many other uses. The milk extracted from Coconuts serves as a regular part of diets in many habitats of tropic and subtropic areas. It is an excellent source of calories, carbohydrates, protein, fats, fibre, potassium, manganese and selenium[10].

Plants rich in phytochemicals such as flavonoids and tannins have been reported to have antioxidant potencies and play a significant role in lipid lowering activity[11]. The aqueous extract of *Phoenix dactylifera* fruits, *Cocos nucifera* nuts and *Cyperus esculentus* (STDC) is a common drink in Nigeria due to its assumed health benefits. Odinga *et al*.[12] reported its benefits to the liver and kidney in male albino rats as part of this project. This is the first report on the health benefits of the STCD extract. However, several studies have reported the health benefits of the individual plants. This study evaluated the potential of the synergistic aqueous extract of *Cyperus esculentus*, *Phoenix dactylifera* and *Cocos nucifera* (STCD) commonly taken as a healthy drink in Nigeria on the lipid profile of male rodents.

MATERIALS AND METHODS

This study was undertaken at the Department of Biochemistry, Rivers State University, Port Harcourt, Nigeria from November, 2022 to March, 2023.

Plant material and preparation of extract: Fresh seeds of tiger nuts, dates and coconut were purchased from mile 1 market in Port Harcourt and authenticated at the herbarium of the Plant Science and Biotechnology department of Rivers State University. Tiger nuts (400 g) were cleaned to remove impurities, washed and put in a bowl. The dates (120 g) were cut into two so as to remove the seeds, then washed and put in a bowl. The coconut (200 g) was removed from the shell, diced and washed. All were pulverized with a manual blender, adding 150 mL of water until a uniformed mixture was obtained. The mixture was filtered using a sieve and the resulting filtrate was put into a bottle until use. This synergistic mixture was prepared daily for the 21 days of administration.

Acute toxicity studies (LD_{50}) of STCD: The acute toxicity of STCD extract was determined by the OECD[13] procedure outlined by Lorke[14] as reported by Adefisayo *et al.*[15]. The rats were fasted overnight prior to experiment. The experiment was carried out in 2 phases: In phase 1, 9 rats were used, they were grouped into 3, with 3 rats in each group. The STCD extract was administered via gavage at the doses of 10, 100 and 1000 mg kg^{-1}. In the second phase, 8 rats were divided into 4 groups of 2 rats each and they were administered with STCD extract by gavage at the doses of 850, 1700, 3400 and 6800 mg kg^{-1}. The general behavior of the animals was observed continuously for 1 hr after administration, then intermittently for 4 hrs and finally hourly for the next 24 hrs.

The LD_{50} was determined using the formula by Odinga *et al.*[12]:

$$LD_{50} = \sqrt{a \times b}$$

Where:

a = Least dose that killed any rat

b = Highest dose that did not kill any rat

Experimental protocol: After acclimatization of the experimental rats, they were properly grouped, group 1: Experimental rats acting as the control group were administered with normal rat feed and distilled water, group 2: Experimental rats acting as the low dose, were administered 200 mg kg^{-1} of the STDC extract and group 3: Experimental rats which was the high dose were administered 400 mg kg^{-1} of the STDC extract. The administration in both group 2 and 3 was done orally using an oral gavage tube. The administration lasted for 21 days and animals were sacrificed.

Collection of blood samples: Sacrifice was done in three batches; the first was carried out after 7 days, the second after 14 days and the third after 21 days. Blood samples (5 mL) were collected through cardiac puncture from each rat and put in plain sample bottles for biochemical analysis of TG, TC, LDLC, VLDL, HDLC using the methods as described by Ighodaro and Omole[16]. The LDLC-HDLC ratio for each group was estimated mathematically using the Friedewald's equation[17].

Statistical analysis: The results obtained were expressed as Mean±Standard Deviation. Data were analyzed using one-way analysis of variance followed by a *post hoc* Test using Turkey's Test and a p-value less than 0.05 was considered statistically significant. The statistical analysis was performed with the aid of IBM SPSS, version 25.

Ethical consideration: Handling and treatment of the rats were in conformation to the guidelines of the National Institute of Health (NIH publication 85-23, 1985)[18] for laboratory animal care and use. All animals in this study adhered to the Institutional Animal Ethical Committee according to guidelines given by the Committee for Control and Supervision of Experiments on Animals (CPCSEA). This study received approval from the Ethical Committee of Rivers State University.

RESULTS

Figure 1 revealed a decrease in the serum level of TG in the experimental groups after 14 and 21 days when compared to the 7 days Wistar rats. The most decrease in TG was observed in the group administered 400 mg kg^{-1} body weight STDC extract.

Figure 2 showed the concentration of LDLC of experimental rats exposed to STDC extract for 7, 14 and 21 days. A decrease in the serum level of LDLC was also observed in the experimental rats for the groups administered 200 and 400 mg kg^{-1} body weight STDC extract.

A decrease was observed in the total cholesterol (TC) serum level in all the experimental rats administered 200 and 400 mg kg^{-1} body weight STDC extract. However, 400 mg kg^{-1} body weight STDC had the most effect after 14 and 21 days of administration in comparison to the 7 days of administration of STDC extract as shown in Fig. 3.

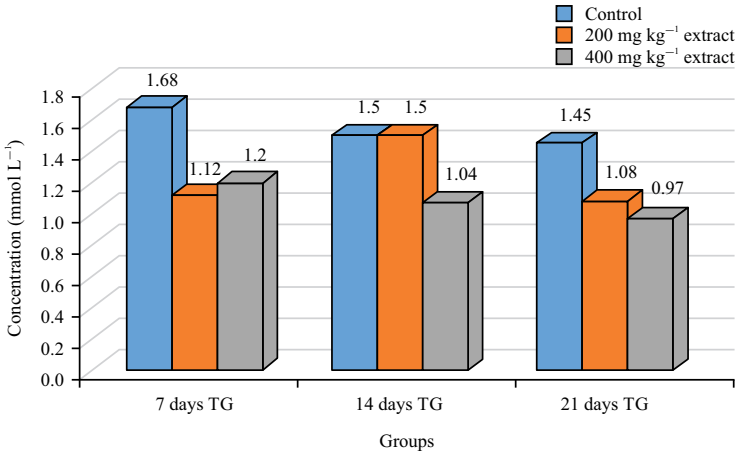

Fig. 1: Concentration of triglyceride (TG) of experimental Wistar rats administered STDC extract for 7, 14 and 21 days

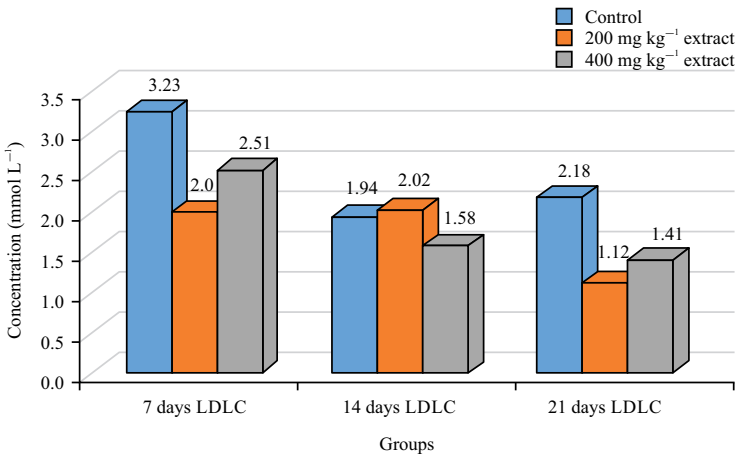

Fig. 2: Concentration of LDLC of experimental Wistar rats administered STDC extract for 7, 14 and 21 days

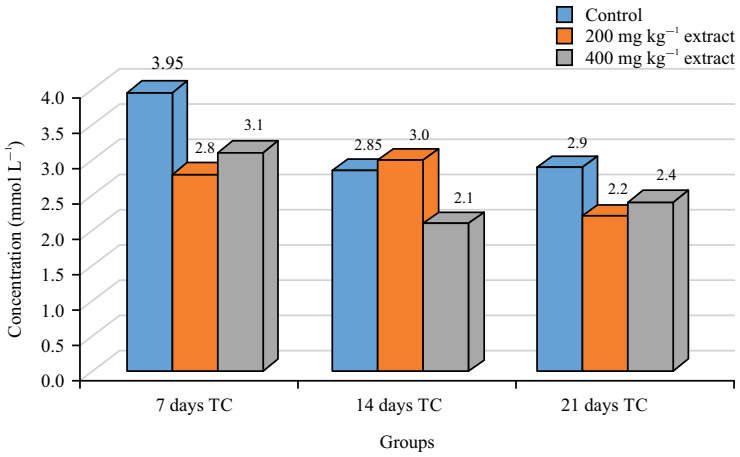

Fig. 3: Concentration of TC of experimental Wistar rats administered STDC extract for 7, 14 and 21 days

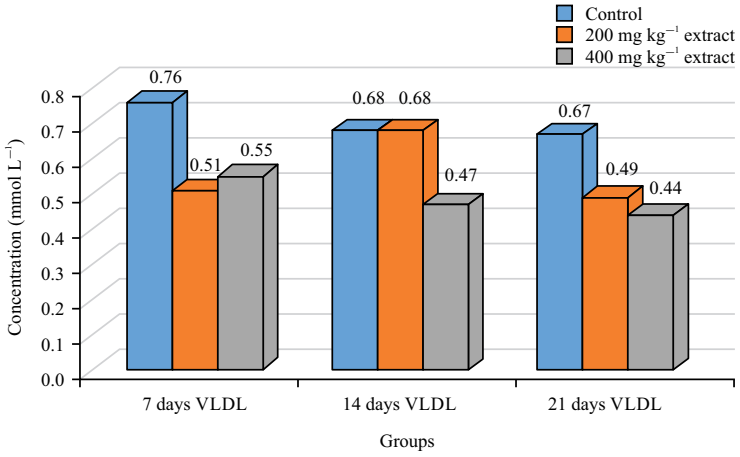

Fig. 4: Concentration of VLDL cholesterol of experimental Wistar rats administered STDC extract for 7, 14 and 21 days

Figure 4 revealed the serum VLDL level. A decrease was observed in the experimental groups administered 200 and 400 mg kg^{-1} STDC extract with the most decrease at 400 mg kg^{-1} after 14 and 21 days of administration of STDC extract in comparison to 7 days.

An increase in the HDLC serum level was observed in all the experimental rats administered 200 and 400 mg kg^{-1} body weight STDC extract after 14 and 21 days when compared to 7 days of administration as revealed in Fig. 5.

Table 1 gives the percentage body weight difference in the experimental wistar rats administered 200 and 400 mg kg^{-1} STDC. An increase in the percentage of body weight of 8.39% was observed in the group administered 200 mg kg^{-1} STDC extract while the 400 mg kg^{-1} STDC extract group had a percentage of increase of 2.86. The control group had a 30.95% increase in percentage of the body weight of the experimental Wistar rats.

Table 2 gives the lipid profile of the experimental Wistar rats administered 200 and 400 mg kg^{-1} body weight STDC extract. A decrease in the TC, LDLC, TG and VLDL serum levels were observed in all experimental wistar rats administered 200 and 400 mg kg^{-1} body weight STDC extract. The decrease observed in the lipid profile indices were however, not significantly different at $p \leq 0.05$ when compared to the control group. Serum HDLC had a non-statistical significant increase at $p \leq 0.05$ in all groups administered STDC extract in comparison to the control group.

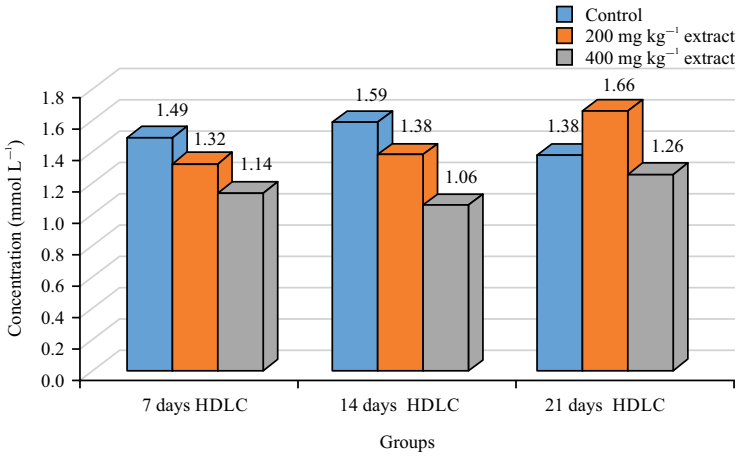

Fig. 5: Concentration of HDLC cholesterol of experimental rats administered STDC extract for 7, 14 and 21 days

Table 1: Body weight difference (%) of experimental Wistar rats administered STDC extract

Groups	Initial body weight (g)	Final body weight (g)	Body weight difference (%)
Group 1 (control)	69.80±7.50	121.00±30.83	30.95
Group 2 (200 mg kg^{-1} STDC extract)	88.20±5.12	121.20±29.20	8.39
Group 3 (400 mg kg^{-1} STDC extract)	111.80±6.72	123.00±11.68	2.86

Values are expressed as Mean±Standard Deviation

Table 2: Lipid profile of experimental male Wistar rats administered STDC extract

Group	TC (mmol L^{-1})	HDLC (mmol L^{-1})	LDLC (mmol L^{-1})	TG (mmol L^{-1})	VLDL (mmol L^{-1})
Group 1 (control)	3.30±0.62^{a}	1.13±0.08^{a}	2.50±0.67^{a}	1.55±0.11^{a}	0.70±0.50^{a}
Group 2 (200 mg kg^{-1} STDC extract)	2.76±0.41^{a}	1.50±0.18^{a}	1.88±0.62^{a}	1.26±0.23^{a}	0.57±0.10^{a}
Group 3 (400 mg kg^{-1} STDC extract)	2.56±0.55^{a}	1.50±0.13^{a}	1.83±0.47^{a}	1.08±0.14^{a}	0.49±0.06^{a}

Values are Mean±Standard Deviation, values with the same superscripts are not significant at p≤0.05. TC: Total cholesterol, HDLC: High Density Lipoprotein Cholesterol, LDLC: Low Density Lipoprotein Cholesterol, TG: Triglyceride and VLDL: Very Low Density Lipoprotein

DISCUSSION

This study evaluated the potential of the synergistic aqueous extract of *Cyperus esculentus*, *Phoenix dactylifera* and *Cocos nucifera* (STCD) extract commonly taken as a healthy drink in Nigeria on the lipid profile of male Wistar rats. In a previous publication as part of this study, Odinga *et al.*[12] reported the result of the acute toxicity test of the extract. They reported that the acute toxicity (LD_{50}) of STCD was ≥2404.2 mg kg^{-1} body weight in adult male albino rats.

Table 1 which shows the mean weight difference of the experimental Wistar rats is as reported by the part study of Odinga *et al.*[12] on the synergistic mixture of *Cyperus esculentus*, *Phoenix dactylifera* and *Cocos nucifera* aqueous extract: Its liver and kidney benefits in male albino rat model. An increase in the percentage of body weight of all the experimental rats, with the most increase in the control group. This could be attributed the nutrient composition of the feed of the rats. The decrease in the weight of the rats administered 200 and 400 mg kg^{-1} STDC extract in comparison to the control group can be associated to the undulate effect on experimental rats when administered extracts via oral gavage method[12].

A decrease in triglycerides concentration was observed in the experimental rats administered 200 and 400 mg kg^{-1} STDC extract. The TG serve as an energy source and insulator in the body, they are formed when excess glucose in the body is stored in the adipose tissue. High levels of TG have been linked to an increased risk of heart disease. This is evidenced by the contribution of TG to the buildup of plaques in the arteries, thus leading to heart failure, cardiovascular diseases and stroke[19,20]. Figure 1 shows that the administration of the STDC extract at 200 and 400 mg kg^{-1} caused a decrease in the TG level after 14 and 21 days. The reduction in the TG levels on administration of the extract could be consequent to the

presence of some metabolites and bioactive components of the extract. Studies have reported the Antihyperlipidemic potency of *Ricinodendron heudelotii* seed extract stated that the TG reducing potency of extract is due to the presence of the inherent phytochemicals in the extract[19]. The study of Phunikhom *et al*.[21] also agreed with the findings of this study. A study by Laufs *et al*.[22] suggested that low TG levels are beneficial in healthy individuals, however, in unhealthy people.

The LDLC, VLDLC and TC have been reported to buildup on the walls of the blood vessels when it is in high concentration in the blood. Although, cholesterol has its benefits in the body, which includes its involvement in the synthesis of hormones, Vitamin D and digestive fluids, higher than normal levels in the blood can interfere with and build in the arteries, clogging them and making them less flexible. This could result in Atherosclerosis, heart disease and stroke[23,24]. The reduction in the serum level of the experimental Wistar rats administered 200 and 400 mg kg^{-1} STDC extract implies the potency of the extract to reduce the risk of stroke and heart diseases.

Figure 5 shows the HDLC level of the experimental rats. An increase in the HDLC serum level was observed in the groups administered 200 and 400 mg kg^{-1} STDC extract after 14 and 21 days. A consistent increase in the serum HDLC level was observed after 14 and 21 days of administration of 200 mg kg^{-1} extract. However, a decrease was observed after 14 days of administration of 400 mg kg^{-1} extract. On the 21st day, an increase was observed in comparison to the 7 days' administration. The HDLC is saddled with the responsibility of getting rid of excess cholesterol in the blood, thereby making the excess cholesterol to be less likely in the arteries. Healthy levels of HDLC has been suggestive to have protective effect against heart attack and stroke. Albeit, some studies have reported the disadvantageous implication of high HDLC. Kjeldsen *et al*.[25], in their study reported that high plasma HDLC levels are associated with cardiovascular diseases, infectious diseases, age-related macular degeneration and increased mortality.

Table 2 shows the lipid profile in experimental Wistar rats administered STDC. Here the serum levels of TC, LDLC, TG and VLDL decreased in the groups administered with 200 and 400 mg kg^{-1} of STDC extract as compared to the control group. However, the HDLC level in the serum increased in these groups as compared to the control. Except for HDLC, high serum level of every other lipid analyzed in this study (TG, TC, LDLC and VLDLC) implies a possible onset of cardiovascular disorder. Downes *et al*.[26] reported high serum levels of TG and LDLCs results in atherosclerosis and coronary heart diseases. Mohammed *et al*.[27] reported that hypercholesterolemic rats treated with 10, 15 or 25% *Cyperu succulents*, showed significant decreases ($p \leq 0.05$) in the levels of serum total cholesterol, TG, LDL-cholesterol, VLDL and LDL-cholesterol while showing a most significant increase ($p \leq 0.05$) in the values of serum HDL-cholesterol compared to the control group. A previous study by Vogel *et al*.[28] further confirms these result in their research where they stated that *Phoenix dactylifera* and *Cocos nucifera* contains high fibers and unsaturated fatty acids which helps to boost metabolism and reduced inflammation as seen in obesity. The elevated level of HDLC and concurrent decrease in the TG, TC, LDLC and VLDLC in the experimental Wistar rats administered STDC extract can be attributed to the phytochemicals present in the extract, responsible for definite pharmacological effects exerted on the human body when taken. Some health benefits of phytochemicals, anti-oxidant, anti-inflammatory, anti-obesity etc., have been reported by Odinga *et al*.[29]. *Phoenix dactylifera*, *Cocos nucifera* and *Cyperu sesculentus* have been reported to contain Alkaloids, glycosides, flavonoids, crude fibres, tannins, carotenoids, phenolics, terpenoids and steroids[30-32].

This study therefore recommends the synergistic extract of *Phoenix dactylifera*, *Cyperus esculentus* and *Cocos nucifera* as a valuable natural and healthy drink for the management and prevention of hyperlipidemia and cardiovascular disorders due to its lipid lowering potency, however, a moderation in daily intake is recommended.

This study did not assess the effect of the extract in hyperlipidemia induced rats, it only assessed the lipid lowering potency of the extract, thus is recommended for further studies.

CONCLUSION

The findings of this study evidenced by the data obtained in the study suggest that the synergistic aqueous extract of *Phoenix dactylifera*, *Cyperus esculentus* and *Cocos nucifera* (STCD) extract had Lipid lowering activity on the experimental Wistar rats. This is due to the reduction in the serum TG, TC, LDLC, VLDLC level and the increase in the serum HDLC level. The reduction in TG, TC, LDLC, VLDLC have the potential to protect against the accumulation of triglycerides and cholesterol in the blood, thus, giving prophylaxis against cardiovascular disorders. The LD_{50} results suggest that the STDC extract should be taken in limits that will not pose toxicity to the body system.

SIGNIFICANCE STATEMENT

This study uncovered the health benefits of *Phoenix dactylifera*, *Cyperus esculentus* and *Cocos nucifera* (STCD) extract on the lipid profile, thus its lipid lowering activity and consequent protective activity on the cardiovascular system. It is therefore recommended to be taken as part of nutrition in dose limits not toxic to the body system.

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