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EXPLORING THE THERAPEUTIC POTENTIAL OF *CURCUMA LONGA* RHIZOME EXTRACT TO MITIGATE DYSLIPIDEMIA

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ABSTRACT

Various researches have publicized that different parts of *Curcuma longa* plant possess therapeutic potential to tackle dyslipidemia and associated inflammatory issues which is one of the key contributory factors leading to the oxidative stress, cardiovascular diseases and other associated metabolic problems. The current study was done to explore the ability of *Curcuma longa* rhizome extract to regulate lipids in rabbits with induced dyslipidemia. The Soxhlet method was used to create the ethanolic extract of *Curcuma longa* rhizome. The obtained extract was applied on experimental rabbits in this trial. For this purpose, 25 healthy rabbits were arranged to accomplish the trial. These rabbits were then divided into five groups, with five rabbits in each group; the healthy rabbits were fed a regular diet, while the NC (Negative Control) rabbits were given a normal diet. The remaining 20 rabbits were given a high-fat diet on a regular basis for 28 days, and then they received a dose-dependent ethanolic extract of *Curcuma longa* rhizome on a regular basis for two months. This caused dyslipidemia in the rabbits. Rabbits in the PC (Positive Control) group had dyslipidemia and were fed a normal diet, whereas the G1, G2, and G3 groups also had dyslipidemia but were given varying dosages of *Curcuma longa* rhizome extract (50, 100, and 150 mg per kilogram of body weight, respectively). Every 15 days, blood samples were taken and analyzed to determine the serum lipid profile in order to assess the effectiveness of the prescribed medication. A significant reduction in low-density lipoprotein (49.01±2.1mg/dL), total cholesterol (80.18± 3.4mg/dL) and triglycerides (49.01±2.1mg/dL) was seen in G2 ($P<0.05$), on the other hand there was a significant improvement in the high-density lipoprotein level (40.39±1.7mg/dL) of G2 in comparison to that of other groups. Findings of this study suggest that giving the ethanolic extract of *Curcuma longa* rhizome (at 100 mg/kg) orally to G2 on a regular basis for 60 days reduced the lipid profile of dyslipidemic rabbits by significantly lowering their low-density lipoprotein (LDL), total cholesterol (TC), and triglycerides (TG) levels and raising their high-density lipoprotein (HDL) levels.

1. INTRODUCTION

Turmeric, or *Curcuma longa*, a part of the family Zingiberacea, is widely considered a popular herbal medicine with a range of pharmacological properties (Nikbakht et al., 2008). Due to its potent lipid-regulating qualities, *Curcuma longa* rhizome is frequently utilized in the treatment of cardiovascular diseases (Kwon et al., 2014). *Curcuma longa's* active biological components have anti-dyslipidemic potential because they lessen oxidative stress and apoptotic effects on hepatic tissues (Xia et al., 2020). Digalloyl-hexoside, Caffeic acid hexoside, Curdione, Coumaric, Caffeic acid, Sinapic acid, Qurecetin-3-D-galactoside, Casuarinin, Bisdemethoxycurcumin, Curcuminol, Demethoxycurcumin, Isorhamnetin, Valoneic acid bilactone, Curcumin, and Curcumin-O-glucuronide are the main phytochemicals found in the rhizome of *Curcuma longa*. Bioactive compounds responsible for major therapeutic effect include curcumin, demethoxycurcumin and bisdemethoxycurcumin (Bozkurt et al., 2022a,b; Taha et al., 2015a,b; Verma et al., 2018a,b;Sabira et al., 2020a,b; Panahi et al., 2017a,b; Ling et al., 2012; Kim et al., 2016,). Anti-oxidants present in *Curcuma longa* rhizome enhance the efficacy of enzymes like catalase (CAT) superoxide dismutase (SOD) and glutathione dependent antioxidant species that ultimately increase antioxidant status and prevent the lipids peroxidation (Zhu et al., 2022). The lipid lowering potential and management of blood glucose by *Curcuma long* is attributed to its bioactive components (Akter et al., 2019). Several investigations revealed that in streptozotocin-induced diabetic rabbits, alternating doses of *Curcuma longa* rhizome extract raised concentration of HDL in blood and decreased the amount of LDL, VLDL, TC, and triglycerides (Park et al., 2019; Karthikesan et al., 2016; Yunes et al., 2017; Razavi et al., 2021; Salehi et al., 2019; Torres-Ascota et al., 2020).

The cases of coronary heart diseases (CHD) caused by hyperlipidemia are increasing rapidly. Worldwide about 35% of total population is suffering from abnormal lipids level. The current surveys of urban and rural regions of Pakistan revealed that almost 62.9% of total Pakistani people are suffering from anomalous serum lipid profile (Sucato et al., 2020). It involves raised TC, LDLs, triglycerides (TG) and decline in HDL that leads to cardiac ailments (Lind et al., 2021). The major causes of abnormal lipid profile are associated with insulin insensitivity and commonly identified in the preliminary phases of metabolic disorders (Kaze et al., 2020). To overcome various physiological abnormalities in body, a variety of therapeutic mediations may be use involving the application of active constituents of different remedial florae (Frankova et al., 2020; Sibeko and Johns et al., 2021). Different kinds of natural therapies including Berberibne, Ephedra sinica, Poriacocos, Mulberry leaf fiber and black garlic used in different research trials that revealed an effective action potential to control fatness. But most of studies used the aqueous extracts of medicinal herbs that possess a variety other water soluble compounds in extract capable of interacting with the chemical of interest (Li et al., 2021; Pineda-Lozano et al., 2021). In least developed states, the expensive traditional remedial practices is a major issue, so people prefer to use herbal sources as a way to treat lifestyle related disorders (Hassanin et al., 2021; Mclntyre et al., 2021;).

In present age, people must move towards the utilization of natural sources regarding their cost effectiveness and fewer side effects, to treat and cure the dyslipidemia and cardiovascular ailments by the adequate management the anomalous serum lipid concentrations. This research trial has been planned to examine the therapeutic potential of *Curcuma longa* rhizome extract in normal and dietary induced dyslipidemic rabbits. This study on rabbits provides evidence-based results to support the effectiveness of rhizome extract from *Curcuma longa* in controlling dyslipidemia.

2. MATERIALS AND METHODS

The National Institute of Food Science and Technology (NIFSAT), University of Agriculture Faisalabad (UAF), Pakistan, was the site of this study trial.

2.1. Preparation of sample

Turmeric rhizomes (*Curcuma longa* L.) of good quality were acquired from Ayub Agriculture Research Institute Faisalabad, Pakistan. Turmeric was washed with sterilize water to remove the adherent soil and other organic matter then it was peeled to remove the outer skin. The rhizomes were dehydrated, ground and homogenized to form a fine powder for further experimental use. Turmeric powder was utilized for the extract preparation by using Soxhlet's apparatus applying ethanol as solvent adopting the procedure of (Kulkarni et al., 2012) then rotary evaporator was used to removethe extra solvent (Mottahedin et al., P 2017).

2.2. Induction of disease

To induce the experimental dyslipidemia in rabbits, they were fed regularly on high-fat diet (normal diet augmented with 8% lard and 10% vegetable oil) for the duration of 28 days. Hyperlipidemia induced by this method sustained for the time period of one year and remains suitable for long term studies (Lin et al., 2022; Arias-Mutis et al., 2018).

2.3. Efficacy study plan

The anti-dyslipidemic potential of prepared ethanolic defatted extract of turmeric was evaluated in this experimental trial. All experimentation was performed following the ethical guidelines of the International Association and the standard guidelines for animal use. 25 rabbits (n=5) weighing between 2500 and 3000 grams on average were chosen at random from the National Institute of Food Science and Technology's animal room at UAF for the efficacy trial. For seven days, these rabbits were acclimated by giving them regular food and beverages. The animals' room temperature was kept between 20 and 32 degrees Celsius, while the relative humidity ranged between 60 and 75 percent. The rabbits were divided into five groups based on the diet they were given. Each group had five rabbits (n=5). The groups included NC, PC, and diseased rabbits eating a normal diet. G1, G2, and G3 rabbits ate a normal diet that contained varying amounts of *Curcuma longa* rhizome extract, which were 50, 100, and 150 mg/kg, respectively. The rabbits' grouping and diet administration are shown in Table 1.

2.4. In-vivo analyses

Blood samples were routinely drawn from each rabbit's ear vein at 15-day intervals for the course of this study experiment. Following the steps outlined by Loaiza et al. (2020), these samples were photometrically analyzed to measure the serum lipid profile involving LDL, HDL, TC, and triglycerides (TG). To avoid denaturing the proteins, 0.1 mL/100 mL sodium azide, 0.1 mL/100 mL phenylmethylsulfonyl fluoride, and 0.5 mL/100 mL aprotinin were added to the samples prior to the photometric analysis.

Table 1: Different groups of rabbits treated with *Curcuma longa* rhizome extract.

Group	Treatment
NC	Normal Rabbits fed on Normal Diet
PC	Diseased Rabbits fed on Normal Diet
G_1	Normal Diet + 50 mg/kg Extract
G_2	Normal Diet + 100 mg/kg Extract
G_3	Normal Diet + 150 mg/kg Extract

NC= Negative Control; PC= Positive Control; G1= Group 01; G2= Group 02; G3= Group 03.

2.5. Statistical analysis

All of the collected data (n=5) was subjected to a general linear model (GLM) approach using the two-way analysis of variance (ANOVA) in the Statistical Analysis System (Statistix 8.1 Software). The results for each lipid profile parameter, such as TC, triglycerides, LDL, and HDL, were expressed as mean+SD. The Tukey HSD test was used to compare the treatment means, and the results were considered significant at $P<0.05$ (Montgomery et al., 2017).

3. RESULTS

3.1. Low-Density Lipoprotein (LDL)

Table 2 displays the results of the significant ($P<0.05$) decreases in LDL levels of the several rabbit groups that were given different dosages of *Curcuma longa* rhizome extract. Comparing G2 to G1, G3, NC, and PC, these results demonstrated a considerable impact. Samples from the control groups (PC and NC) had considerably ($P<0.05$) greater levels of LDL, while samples from groups that received alternate extract concentrations had significantly ($P=0.05$) lower levels. But from day 0 to day 60, the concentration of LDL decreased the most in group 2, which was given the dose of 100 mg/kg (from 49.23±2.4 mg/dL to 49.01±2.1 mg/dL). Groups G2 and G3 received extract at doses of 50 mg/kg and 150 mg/kg, respectively, and their LDL levels decreased from 49.2±1.9 mg/dL to 49.1±0.7 mg/dL.

Table 2: Impact of rhizome extract from *Curcuma longa* on low-density lipoprotein (mg/dL) levels in blood samples from various rabbit groups.

Treatments					
Days	**NC**	**PC**	**G_1**	**G_2**	**G_3**
0	40.1±1.37	40.26±1.21	40.2±1.6	40.21±2.0	40.23±0.97
15	40.1±0.81	40.25±0.60	40.2±1.4	40.25±0.9	40.26±0.85
30	40.15±0.77	40.23±0.60	40.2±1.7	40.30±1.4	40.29±1.81
45	40.2±0.85	40.18±0.76	40.3±0.6	40.36±1.7	40.33±1.49
60	40.23±0.85	40.1±0.76	40.3±0.6	40.39±1.7	40.37±1.49

Mean+SD has been used to express the results. Superscripted alphabets have demonstrated significant (P<0.05) changes, with a > b > c > d.

3.2. High-Density Lipoprotein (HDL)

Table 3 displays the information regarding the changes in blood HDL levels of multiple rabbit groups fed on different amounts of *Curcuma longa* rhizome extract. These findings showed that HDL levels were significantly (P<0.05) lower in blood samples from the PC and NC control groups. On the other hand, blood HDL levels increased in the other three groups.The blood samples from the G2 group had the most (P<0.05) increase in HDL levels from day 0 to day 60 (from 40.21±2.0 mg/dL to 40.39±1.7 mg/dL). On the other hand, groups G1 and G2 saw only modest improvements in their HDL levels, which ranged from 40.23±0.97 mg/dL to 40.37±1.49 mg/dL and 40.2±1.6 mg/dL to 40.3±0.6 mg/dL, respectively. Between G1 and G3, there was no statistically significant difference.

Table 3: Impact of rhizome extract from *Curcuma longa* on high-density lipoprotein (mg/dL) levels in blood samples from various rabbit groups.

Treatments					
Days	**NC**	**PC**	**G_1**	**G_2**	**G_3**
0	49.1±1.67	49.2±1.48	49.2±1.9	49.23±2.4	49.16±1.18
15	49.1±0.98	49.26±0.74	49.2±1.7	49.19±1.1	49.14± 1.03
30	49.13±0.93	49.29±0.74	49.2±2.1	49.12±1.8	49.08 ± 2.21
45	49.15± 1.0	49.31± 0.9	49.1±0.7	49.08±2.1	49.05 ± 1.81
60	49.16± 1.0	49.36±0.94	49.1±0.7	49.01±2.1	49.01 ±1.81

Mean+SD has been used to express the results. Superscripted alphabets have demonstrated significant (P<0.05) changes, with a > b > c > d.

3.3. Total cholesterol (TC)

The results pertaining to the differences in blood sample total cholesterol levels across the rabbit groups fed varying amounts of *Curcuma longa* rhizome extract are shown in Table 4. The findings unequivocally demonstrated that the blood samples from both control groups (PC and NC) had considerably higher total blood cholesterol levels (P<0.05). However, over time, the total blood cholesterol level in the samples from the other three groups exhibited a declining tendency. From day 0 to day 60, it dropped more precipitously in the G2 group (from 82.59±4.1 mg/dL to 80.18± 3.4 mg/dL). Comparing groups G1 and G3 to G2, it was discovered that their total blood cholesterol levels decreased at low rates, from 82.7± 3.3 mg/dL to 80.6±1.2 mg/dL and 81.76 mg/dL± 1.96 to 80.29 ±2.97 mg/dL, respectively.

Table 4: Impact of rhizome extract from *Curcuma longa* on blood samples from various rabbit groups' levels of total cholesterol (mg/dL).

Treatments					
Days	NC	PC	G_1	G_2	G_3
0	49.1±1.67	49.2±1.48	49.2±1.9	49.23±2.4	49.16±1.18
15	49.1±0.98	49.26±0.74	49.2±1.7	49.19±1.1	49.14± 1.03
30	49.13±0.93	49.29±0.74	49.2±2.1	49.12±1.8	49.08 ± 2.21
45	49.15± 1.0	49.31± 0.9	49.1±0.7	49.08±2.1	49.05 ± 1.81
60	49.16± 1.0	49.36±0.94	49.1±0.7	49.01±2.1	49.01 ±1.81

Mean+SD has been used to express the results. Superscripted alphabets have demonstrated significant (P<0.05) changes, with a > b > c > d.

3.4 Triglycerides

The data pertaining to the variations in triglyceride levels in blood samples from rabbits given varying amounts of *Curcuma longa* rhizome extract are shown in Table 5. These findings demonstrated that the blood triglyceride levels in samples from both control groups (PC and NC) increased significantly (P<0.0.5). Nevertheless, blood samples from groups that received varying amounts of *Curcuma longa* rhizome extract showed a significant (P<0.05) decrease in triglyceride levels. From day 0 to day 60, group G2 experienced the greatest decrease in triglyceride levels (from 49.23±2.4 mg/dL to 49.01±2.1 mg/dL). However, after receiving 50 mg/kg and 150 mg/kg of extract, respectively, G1 and G2 saw a decrease in their triglyceride levels from 49.2±1.9 mg/dL to 49.1±0.7 mg/dL and 49.16±1.18 mg/dL to 49.01±1.81 mg/dL. There was no statistically significant difference between G1 and G2.

Table 5: Impact of rhizome extract from *Curcuma longa* on triglyceride levels (mg/dL) in blood samples from various rabbit groups.

Treatments					
Days	NC	PC	G_1	G_2	G_3
0	80.01± 2.7	80.1± 2.40	82.7± 3.3	82.59±4.1	81.76± 1.96
15	80.17± 1.6	80.89±1.2	82.5±1.9	82.21±1.9	81.41± 1.23
30	80.91±1.54	81.71± 1.2	81.9±3.5	81.57± 3.0	81.04 ± 3.65
45	81.10± 1.7	82.69± 1.5	81.7±1.2	81.13±3.5	80.63 ± 2.98
60	81.24± 1.7	83.03± 1.5	80.6±1.2	80.18± 3.4	80.29 ±2.97

Mean+SD has been used to express the results. Superscripted alphabets have demonstrated significant (P<0.05) changes, with a > b > c > d.

4. DISCUSSION

The study's findings demonstrated that the ethanolic extract of *Curcuma longa* rhizome had significant (P<0.05) anti-hyperlipidemic efficacy to treat dyslipidemia in experimentally produced hyperlipidemic rabbits fed a high-fat diet. The results of earlier investigations confirmed the considerable (P<0.05) decrease in LDL, TC, and TG levels. The regular oral intake of ethanolic extract of *Curcuma longa* rhizome caused reduction in blood concentrations of LDL, TC and TG, simultaneously the amount of HDL in blood was also enhanced in same experimental rabbits. The present results indicating the variation in LDL, HDL, TC and TG levels are closely matched with the conclusions of different studies stated in the literature. Previous research has unequivocally shown that one of the main risk factors that eventually cause diabetes to result in neuropathy, retinopathy, and cardiovascular complications is the elevated level of free fatty acids in the blood (Xiao et al., 2020). The bioactive elements found in *Curcuma longa* rhizome extract have ability to regulate the anomalous blood lipid profile. They demonstrated that the oral intake of curcumin at dose of 50-150mg/kg regular for the period of four weeks have significant potential to reduce the blood concentration of LDL, TC, triglycerides and even very LDL while there was a noticeable rise in the HDL concentration (Kumar et al., 2011). By lowering blood lipids in patients at risk for CVDs, another study conducted by Qin et al. (2017) shown that the extract of *Curcuma longa* rhizome exhibited significant ($P<0.05$) cardioprotective effect. The proposed mechanism of action by which *Curcuma longa* decreases the lipids involves the reduction of serum insulin level that ultimately dilutes the blood lipids and increases the utilization of fats. The suppression of hepatic fatty synthesis is a possible mechanism of action to moderate the excessive blood lipids concentration (Pingali et al., 2020). In the same way, results reported by (Ling et al., 2012), revealed the lipid lowering effect of oil extracted from *Curcuma longa*. The oral administration of this oil significantly ($P<0.05$) lowered the level of LDL, TC, TG and simultaneously improved the level of HDL in experimental subjects. The histopathological findings also reported the hepatoprotective potential of *Curcuma longa* oil. The proposed mechanism refers to the enhanced activity of superoxide dismutase and glutathione peroxidase followed by the depression of maleic dialdehyde activity. In a related study, Hussein et al. (2014) found that giving hypercholesterolemic rats a diet supplemented with curcumin for six weeks significantly reduced their serum LDL levels. Additionally, they noted the reduction in Apo B, which stands for the overall quantity of LDL particles. Blocking the transfer of cholesteryl ester from HDL to LDL by delaying cholesteryl ester transferases is the mechanism of action responsible for the reduction of LDL. Scavenger receptor-B1 activation increases the hepatic cholesterol reverse reflux. The present results are matching with the findings of (Chandrakala and Tekulapally et al., 2014) they estimated the hypolipidemic activity of turmeric polyphenols. They described that turmeric as well as curcumin, both have ability to decrease the amounts of triglycerides, LDL and total blood cholesterol along with concurrent increase in amount of HDL as compared to the control. When compared to whole turmeric, curcumin showed a noticeable improvement in the lipid profile. In another bio evaluation trial, (El-Bahr and Al-Azraqi et al., 2014) recorded 54.91% lessening of triglycerides concentration in the rats relying on turmeric extract. The inactivation of the enzyme fatty acid synthase, which is in charge of producing long-chain fatty acids, is one of the molecular approaches pertaining to turmeric's cardioprotective properties. In the meantime, it increases β-oxidation by activating carnitylpalmityl transferase-1, which in turn regulates acyl-CoA's entry into the mitochondria for fat metabolism. In a bio-efficacy trial, hypercholesterolemic rats were fed on the 2% turmeric containing diet for the period of 56 days consequently modulation in the HDL level was recorded (Al-Nawazi and El-Bahr et al., 2012). They observed the therapeutic role of curcumin in regulation of serum lipids and other diabetes associated metabolic parameters. HMG CoA reductase was activated by curcumin that reduced the cholesterol in diabetic rats. Afterwards (Qin et al., 2017) also delineated the cholesterol lowering potential of curcumin in animals. They noticed the steady decline in total plasma cholesterol with the amplification in dietary curcumin. The trial's findings are consistent with those of a study by Pari et al. (2007) that examined the impact of tetrahydrocurcumin (THC), an active form of curcumin, on the regulation of serum cholesterol in rats with diabetes caused by streptozotocin.

5. CONCLUSION

It is well explained by epidemiological investigations that eating behaviors have an undeviating influence on the wellbeing and overall health status of people and scientists revealed that there exists an association between health and dietetic status. Many diet related disorders are directly linked to intake of refined foods and changing life styles. For improving mental and physical health of consumers as well as to avoid nutrition related disorders, food is used besides satisfying appetite. A variety of plants and their extracts have already been used in animal trials but their results were uncertain due to the unwanted chemical interactions among bioactive ingredients and other reagents used in biochemical assays. Similarly the economic issues act as hurdle while selecting the herbal extracts as most of the herbs are very rare and costly so it is very difficult to procure them. Globally, hyperlipidemia is basic cause of obesity and increasing prevalence of cardiovascular diseases. *Curcuma longa* is a cheap and commonly found herb all around the world that makes it easy to procure and utilize in study trials in a cost effective way. In order to investigate the therapeutic and functional qualities of *Curcuma longa* rhizome extract by lowering hyperlipidemic situations in blood and improving the lipid profile, the present study trial was conducted on rabbits. The ethanolic extract of *Curcuma longa* rhizome has anti-hyperlipidemic potential in rabbits with high-fat diets, according to the study's findings. LDL, TC, and TG levels decreased after repeated oral administration of an ethanolic extract of *Curcuma longa* rhizome; at the same time, HDL levels increased throughout the research. Our results suggest that *Curcuma longa* rhizome ethanolic extract could be useful in the management of hyperlipidemia.

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