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Efficacy of *Circuma longa Linn.* Extract in the Management of Type-2 Diabetes Mellitus associated Hypercholesterolemia in Mice Diabetic Model

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A B S T R A C T

The majority of Type-2 DM patients suffer from visceral obesity and they often have high circulating levels of lipids including cholesterol, triglycerides, low levels of high density cholesterol, which also contribute to the development of vascular complications. In the present investigation the efficacy of *Circuma longa* extract on serum lipid profile of diabetic mice was studied. The results clearly indicated that Diabetic mice treated with *C. longa* extract (DT_{150}) the Diabetic mice treated with lower dose of *C. longa* extract (DT_{150}) showed significantly lower values of serum TC (-26.5%; $p<0.001$) and TGs (-55.6%; $p<0.001$), when compared with the DC counterparts. The DT_{250} treatment showed superior lowering effects compared with the DC counterparts as well as DT_{150} group mice by (-34.7%; $p<0.001$) on serum TC levels and (-50%; $p<0.001$) on TGs levels. Contrarily, treatment with Pioglitazone (DT_{PGZ}) showed (-33.2%; $p<0.001$) on TC levels and (-09.6%; $p<0.001$) on TGs levels compared with diabetic control mice. Relative to normal control, the diabetic mice had higher value of low density lipoprotein (LDL) (+256%; $p<0.001$) while diminished value of high density lipoprotein (HDL) (-55%; $p<0.001$). Diabetic mice treated with lower dose of *Circuma longa* extract (DT_{150}) showed significantly lower values of serum LDL (-50%; $p<0.001$) and higher value of HDL (-45.4%; $p<0.001$), when compared with the DC counterparts. All over again, the DT_{250} treatment showed even better lowering effects on LDL (-53%; $p<0.001$) compared with the DC counterparts and improved level of HDL (+56%; $p<0.001$). In contrast, treatment with Pioglitazone (DT_{PGZ}) showed a considerable diminished level of LDL (-58%; $p<0.001$) while improved level of HDL (+59%; $p<0.001$) compared with diabetic control mice.

Introduction

Type-2 Diabetes Mellitus (DM) is a heterogeneous disease with both genetic and environmental causative factors. Gerich (1996) has summarized the pathophysiology of Type-2 DM as follows. Initially the pancreatic beta cells are not able to respond with appropriate insulin secretion to glucose challenge. At the same time, an increased

demand for insulin due to environmentally induced insulin resistance has also act. At this juncture, a compensatory increase of the insulin secretion is still sufficient to maintain a normal glucose level. By gradual decrease of insulin secretion and increase of insulin resistance, a reduced suppression of hepatic glucose output and impaired glucose tolerance appear. With further increase in insulin resistance, an absolute increase in hepatic glucose output occurs which leads to fasting hyperglycemia. At the same time, pancreas fail to compensate for the increased demand of insulin any further and hyperglycemia sets in. If untreated, hyperglycemia and insulin resistance in Type-2 DM increase the risk of several macro and micro vascular complications such as, hypertension, coronary vascular disease, cardiomyopathy, stroke and retinopathy, neuropathy, nephropathy (Kannel and McGee, 1979; Garcia, 1974). The majority of Type-2 DM patients suffer from visceral obesity and they often have high circulating levels of lipids including cholesterol, triglycerides, low levels of high density cholesterol, which also contribute to the development of vascular complications. Independent of coronary artery complications, complex changes in the mechanical and electrical properties of the heart may contribute to diabetic cardiopathy. The devastating consequences of these complications include lower-limb amputation, end stage renal failure, loss of vision and myocardial infarction.

It is clear that the contributory abnormalities in Type-2DM are insulin deficiency, insulin resistance and increased hepatic glucose output. The current therapies used to treat patients with these complications are aimed at correcting one or more of these physiological abnormalities. The diabetes control and complications study (DCCT, 1996) and the United Kingdom Prospective Diabetes Study (UKPDS, 1998) demonstrated that good metabolic control through intensive drug therapy and strict lifestyle management could reduce the risk of developing diabetic complications.

Phytochemicals have played an important role in the development of chemotherapeutic agents. Phytochemicals have multiple beneficial activities including manipulation of carbohydrate metabolism by various mechanisms, preventing and restoring integrity and functioning of β-cells, insulin releasing activity, improving glucose uptake and utilization, and antioxidant properties. Furthermore, natural products are widely viewed as templates for optimization programs with the goal of creating new drugs.

The pharmacological treatment of disease began long ago with the use of herbs (Schulz *et al*., 2001). India is a vast repository of medicinal plants that are used in traditional medical treatments (Chopra *et al*., 1956). The various indigenous system such as Siddha, Ayurveda, Unani and Allopathy use several plant species to treat different ailments (Rabe and Staden, 1997). Medicinal plants play an important role in the development of potent therapeutic agents. Many traditional medicines in use are derived from medicinal plants, minerals and organic matter. Presently, there is growing interest in herbal remedies due to the side effects associated with the oral hypoglycemic agents (therapeutic agents) for the treatment of diabetes mellitus. So the traditional herbal medicines are mainly used which are obtained from plants, it plays important role in the management of diabetes mellitus. In recent years, herbal medicines have started to gain importance as a source of hypoglycemic agents. Biological action of the plant products used as alternatives medicines to treat diabetes are

related to their chemical composition. Herbal products or plant products are rich in phenolic compounds, flavonoids, terpenoids, coumarins, and other constituents which show reduction in blood glucose levels. Due to their perceived effectiveness, fewer side effects in clinical experience and relatively low costs, herbal drugs are prescribed. The use of herbal medicine becoming popular due to toxicity and sie effects of allopathic medicines. This led to sudden increase in the number of herbal drug manufactures (Agarwal, 2005). The practices of herbs as medicine continue today because of its biomedical benefits as well as place in cultural beliefs in many parts of world and have made a great contribution towards maintaining human health. The current review focuses on herbal drug preparations and plants used in the treatment of diabetes mellitus.

Curcuma longa Linn. (Circuma domestica Wall.), belonging to the Zingiberaceae family, is a perennial herb that measures up to 1 m high with a short stem, distributed throughout tropical and subtropical reions of the world, being widely cultivated in Asiatic countries, mainly in India and China. In India is popularly known as 'Haldi', in Malaysia, Indonesia and India has been well studied due to is economic importance. Its rhizomes are oblong, ovate, pyriform, often short-branched and they are a household remedy in Nepal (Eigner & Scholz, 1999). As a powder, called turmeric, it has been in continuous use for its flavoring, as a spice in both vegetarian and non-vegetarian food preparations and it also has digestive properties (Govindarajan, 1980). Current traditional Indian medicine claims the use of its powder against biliary disorders, anorexia, coryza, cough, diabetic wounds, hepatic disorder, rheumatism and sinusitis (Ammon *et al*., 1992). The coloring principle of turmeric was isolated in the 19th century and was named curcumin, which was extracted from the rhizomes of *C. longa*, with yellow color and is the major component of this plant, being responsible for the anti-inflammatory effects.

Photograp showing dried rhizome of Turmeric (*Circuma longa*)

Photograph showing row rhizome of Turmeric (*Circuma longa*)

The active constituents of turmeric are the flavonoids curcumin (diferuloylmethane) and various volatile oils, including tumerone, atlantone, and zingiberone. Other constituents include sugars, proteins, and resins. The best-researched active constituent is curcumin, which comprises 0.3–5.4 percent of raw turmeric. The major constituent, curcumin (diferuloylmethane) is in the most important fraction of *C. longa* and its chemical structure, was determined by Roughley and Whiting (1973). It melts at 176-177°C and forms red-brown salts with alkalis. Curcumin is soluble in ethanol, alkalis, ketone, acetic acid and chloroform; and is insoluble in water. In the molecule of curcumin, the main chain is aliphatic, unsaturated and the aryl group can be substituted or not. Curcumin is the principal curcuminoid of the popular Indian spice turmeric, which is a member of the ginger family (Zingiberaceae). The other two curcuminoids are desmethoxycurcumin and bis-desmethoxycurcumin. The curcuminoids are polyphenols and are responsible for the yellow color of turmeric. Curcumin can exist in at least two tautomeric forms, keto and enol. The enol form is more energetically stable in the solid phase and in solution. Curcumin can be used for boron quantification in the so-called curcumin method. It reacts with boric acid forming a red colored compound, known as rosocyanine. Curcumin is brightly yellow colored and may be used as a food coloring.

The Phytochemicals from *Circuma longa* are known to possess following activities

Anti-inflammatory activity

The volatile oils and curcumin of *Curcuma longa* exhibit potent anti-inflammatory effects. In rats with Freund's adjuvant-induced arthritis, oral administration of *Curcuma longa* significantly reduced inflammatory swelling compared to controls. In monkeys, curcumin inhibited neutrophil aggregation associated with inflammation. C. longa's anti- inflammatory properties may be attributed to its ability to inhibit both biosynthesis of inflammatory prostaglandins from arachidonic acid, and neutrophil function during inflammatory states. Mukophadhyay *et al*., (1982) demonstrated the activity of curcumin and

other semi-synthetic analogues (sodium curcuminate, diacetyl curcumin, triethyl curcumin and tetrahydro curcumin) in carrageenin- induced rat paw edema and cotton pellet granuloma models of inflammation in rats. Arora *et al*., (1971) investigated the anti-inflammatory activity in different fractions of the petroleum ether extract of the rhizomes of turmeric (two constituents) in animals. They found that the extracts reduced the granuloma growth and no toxic effects were observed. Chandra and Gupta (1972) demonstrated the anti-inflammatory and anti-arthritic actions of volatile oil of *C. longa* L. Ghatak and Basu (1972) showed the action of sodium curcuminate as an anti-inflammatory agent, being better than curcumin and hydrocortisone acetate, in experimental inflammation induced by carrageenin and formalin in albino rats (ED50 = 144 μg/kg), its more soluble in water than curcumin and no side effects were observed.

Antioxidant activity

Water- and fat-soluble extracts of turmeric and its curcumin component exhibit strong antioxidant activity, comparable to vitamins C and E. A study of ischemia in the feline heart demonstrated that curcumin pretreatment decreased ischemia-induced changes in the heart. An *in vitro* study measuring the effect of curcumin on endothelial heme oxygenase-1, an inducible stress protein, was conducted utilizing bovine aortic endothelial cells. Unnikrishnan and Rao (1995) studied the antioxidative properties of curcumin and its three derivatives (demethoxy curcumin, bisdemethoxy curcumin and diacethyl curcumin). Curcumin is a good antioxidant and inhibits lipid peroxidation in rat liver microsomes, erythrocyte membranes and brain homogenates (Pulla Reddy & Lokesh, 1994). The lipid peroxidation has a main role in the inflammation, in heart diseases, and in cancer. Turmeric can lower lipid peroxidation by maintaining the activities of antioxidant enzymes like superoxide dismutase, catalase and glutathione peroxidase at higher levels. These enzymes play an important role in the regulation of lipidperoxidation (Pulla Reddy & Lokesh, 1992). Pulla Reddy and Lokesh (1992) observed that curcumin is capable of scavenging oxygen free radicals such as superoxide anions and hydroxyl radicals, which are important to the initiation of lipid peroxidation.

Antimicrobial activity

Turmeric extract and the essential oil of Curcuma longa inhibit the growth of a variety of bacteria, parasites, and pathogenic fungi.

Anti-protozoal activity- Rasmussen *et al*., (2000) reported the efficacy of an ethanolic extract from *C. longa* against *Plasmodium falciparum* and *L. major*, which was able to inhibit the in vitro growth of these parasites.

Nematocidal activity- Kiuchi *et al*., (1993) demonstrated the activity of fractions (methanolic and chloroformic) of turmeric against *Toxocara canis*.

Anti-bacterial activity- Bhavani Shankar and Murthy (1979) investigated the activity of turmeric fractions against some intestinal bacteria in vitro. In this work, total inhibition of growth of *Lactobacilli* in the presence of whole turmeric was observed (4.5-90 μl/100 ml). The other fraction, the alcoholic extract, was effective too (10-200 mg/ml), but the inhibition was not equal as the whole turmeric. Curcumin (2.5- 50 mg/ml) only inhibited *S. aureus*. Curcuma oil was tested against cultures of *Staphylococcus albus*, *S. aureus* and

Bacillus typhosus, inhibiting the growth of *S. albus* and *S. aureus* in concentrations up to 1 to 5,000 (Chopra *et al*., 1941).

Antivenom activity

A potent antivenom was tested against snakebite. The fraction consisting of ar-turmerone, isolated from *C. longa* L., neutralized both the hemorrhagic activity and lethal effect of venom in mice. In this study ar-turmerone was capable of abolishing the hemorrhagic activity of *Bothrops* venom and about 70% of the lethal effect of *Crotalus* venom. Ar-turmerone can act as an enzymatic inhibitor in the case of venom enzymes, with proteolytic and hemorrhagic activities (Ferreira *et al*., 1992).

Hepatoprotective Effects

Turmeric has been found to have a hepatoprotective characteristic similar to silymarin. Animal studies have demonstrated turmeric's hepatoprotective effects from a variety of he-patotoxic insults, including carbon tetrachloride (CCl4), galactosamine, acetaminophen (paracetamol), and Aspergillus aflatoxin. Turmeric's hepatoprotective effect is mainly a result of its antioxidant properties, as well as its ability to decrease the formation of pro-inflammatory cytokines. In rats with CCl4-induced acute and subacute liver injury, curcumin administration significantly decreased liver injury in test animals compared to controls. Turmeric extract inhibited fungal aflatoxin production by 90 percent when given to ducklings infected with Aspergillus parasiticus. Turmeric and curcumin also reversed biliary hyperplasia, fatty changes, and necrosis induced by aflatoxin production.

Anticarcinogenic Effects

Animal studies involving rats and mice, as well as *in vitro* studies utilizing human cell lines, have demonstrated curcumin's ability to inhibit carcinogenesis at three stages: tumor promotion, angiogenesis, and tumor growth. The anticarcinogenic effects of turmeric and curcumin are due to direct antioxidant and free-radical scavenging effects, as well as their ability to indirectly increase glutathione levels, thereby aiding in hepatic detoxification of mutagens and carcinogens, and inhibiting nitrosamine formation. Ozaki *et al*., (2000), examining the action of curcumin on rabbit osteoclast apoptosis, demonstrated that curcumin drastically inhibits bone resorption in parallel with its stimulation of apoptosis in the cells. Since cancer and bone inflammation are diseases that increase bone resorption, the authors suggest that curcumin may be useful in the therapy of these pathogenies.

Anti-HIV

Mazumber *et al*., (1995) demonstrated that curcumin has an antiviral activity, being a HIV-1 integrase inhibitor (IC50 = 40 μM) and suggested that curcumin analogs may be developed as anti-Aids drugs. Data showed that curcumin inhibited the replication of HIV-1 integrase protein. Eigner and Scholz (1999) reported that curcumin was claimed for anti-HIV-1 and HIV-2 activities in a recent patent application.

Cardiovascular Effects

Turmeric's protective effects on the cardiovascular system include lowering cholesterol and triglyceride levels, decreasing susceptibility of low density lipoprotein (LDL) to lipid peroxidation, and inhibiting platelet aggregation. These effects have been noted even with low doses of turmeric. A study of 18 atherosclerotic rabbits given low-dose (1.6–3.2 mg/kg body weight daily) turmeric extract demonstrated decreased susceptibility of LDL to lipid

peroxidation, in addition to lower plasma cholesterol and triglyceride levels. The higher dose did not decrease lipid peroxidation of LDL, but cholesterol and triglyceride level decreases were noted, although to a lesser degree than with the lower dose.

Gastrointestinal Effects

Constituents of *Curcuma longa* exert several protective effects on the gastrointestinal tract. Sodium curcuminate inhibited intestinal spasm and p-tolymethylcarbinol, a turmeric component, increased gastrin, secretin, bicarbonate, and pancreatic enzyme secretion. Turmeric has also been shown to inhibit ulcer formation caused by stress, alcohol, indomethacin, pyloric ligation, and reserpine, significantly increasing gastric wall mucus in rats subjected to these gastrointestinal insults.

Enhances immunity

Curcumin can also help the body fight off cancer should some cells escape apoptosis. When researchers looked at the lining of the intestine after ingestion of curcumin, they found that CD4+ T-helper and B type immune cells were greater in number. In addition to this localized immune stimulation, curcumin also enhances immunity in general. Researchers in India have documented increased antibodies and more immune action in mice given curcumin.

Other activities

Curcumin can decrease high cholesterol levels like statine and have antimutagenic activity (Scartezzini and Speroni, 2000). Chuang *et al*., (2000) showed that curcumin at concentrations of 200 mg/kg or 600 mg/kg could effectively inhibit diethyl nitrosamine-induced liver inflammation in rats. Other interesting action of this substance was demonstrated by Park *et al*., (2000), when acute hepatotoxicity was induced by intraperitoneal injection of carbon tetrachloride in rats. After these animals had been treated with curcumin and the results showed that the liver injury was inhibited.

The efficacy of *Circuma longa* methanol extract on lipid profile of Streptozotocin induced diabetic mice has not been investigated so far and hence the present study was undertaken.

Materials and Methods

Methanol extract of *Circuma longa* Linn. (Zingiberaceae) was used for assaying the serum lipid profile in Streptozotocin induced mice diabetic models. The whole plant of *Circuma longa* was washed under running tap water, blotted with filter paper and was dried in the shade at room temperature. The dried plant sample (2.6 kg) was then soaked with absolute methanol under reflux condition for the methanolic extract preparation. The sample was then homogenized with extraction buffer and the supernatant collected after three rounds of extraction. The solvent was evaporated under reduced pressure in a rotary evaporator at 40 ^{0}C. To this thick paste colloidal silicon dioxide was added and dried in vacuum tube dryer. The obtained methanol extract was stored in deep freezer at $^{-}20^{0}$ C until further test.

The mice were allowed to acclimatize for 15 days in an environmentally controlled room under standard environmental conditions (21±2°C, 55±5%Relative humidity, 12 hr Light: Dark cycle) and fed on diet consisted of wheat grains-1Kg, Choker wheat-250gm, Gram grains-250gm,

Maize grains-250gm, Soybean grains-250gm, Sundrop oil-50gm, Milk powder-2 table spoon and Jaggery-50gm. This diet provided carbohydrate 48.3%, crude protein 23.5%,crude fat5.9% crude ash5.9% and crude fibre 3.9% (W/W).

The animal model for the present study was based on multiple administration of low dose of freshly prepared streptozotocin (STZ). For induction of diabetes, initially the normal mice were kept 24 hours without food and water. The weight of normal mice was determined. Diabetes was induced by multiple intra-peritoneal injection of freshly prepared STZ solution in 0.05 M sodium citrate (pH 4.5) at the dose of 35 mg/kg body weight followed by an hour of fasting. The mice were then allowed to access the respective food and water *ad libitum*. Mice with fasting blood glucose level of 200 mg/dl (7.8 mmol/l) or higher were considered to be diabetic and were used in the study. A parallel set of control mice (non-diabetic) were injected with citrate buffer only.

The mice were grouped into five categories viz., Normal control (NC), Diabetic Control (DC), Diabetic Treated (DT_{150}), Diabetic Treated$_{250}$) and Diabetic Treated (DT_{PGZ}). NC received only citrate buffer solution. DC group was STZ induced which received citrate buffer only. DT_{150} and DT_{250} received 150mg/Kg and 250mg/Kg body weight of methanol extract respectively. DT_{PGZ} received Pioglitazone at a dose of 2mg/Kg of body weight. All the mice were fed with common pellet diets for 2 weeks after arrival, and then randomly divided into two groups. One group continued to receive common pellet diets and constituted the normal group; the other was fed with diets high in fat and fructose, in order to induce type-2 diabetes. All the mice had free access to food and water.

For the experiment, the mice were divided into five groups having six mice in each group: DC group (diabetic control mice), NC group (non-diabetic control mice) and three DT group (diabetic mice treated with two different doses of extract as well as rosiglitazone/ kg body weight). Body weights were recorded weekly during the experimental period. Treatment with extracts was started after one week of STZ treatment, which was considered as the 1st day of treatment. Blood samples were taken after 8 hrs fasting from the retro-orbital sinus vein prior to the administration of test substances or the buffer and 4 weeks after the treatment under mild ether anesthesia and allowed to clot for 30 minutes at room temperature. Blood samples were centrifuged at 3000 rpm for 20 minutes. Serum was separated and stored at -20°C until biochemical estimations were carried out.

The total cholesterol, total triglyceride, Cholesterol-HDL, Cholesterol- LDL and HDL/TC values were assayed and the results obtained have been presented in Table-1. Data were statically analyzed by mean ± S.E and by one-way ANOVA.

Results and Discussion

From the results it is evident that the diabetic mice had higher total cholesterol (TC) (138%; $p<0.001$) and TGs (+74%; $p<0.001$) values in comparison to normal control (Table-1 and Fig-1).These changes in biochemical parameters are as expected, as when the uncontrolled diabetic status progresses, substantial changes in total cholesterol and triglycerides values are predictable. Diabetic mice treated with lower dose of *C. longa* extract (DT_{150}) showed significantly lower values of serum TC (-26.5%; $p<0.001$) and TGs (-55.6%; $p<0.001$), when compared with the DC

counterparts. The DT_{250} treatment showed superior lowering effects compared with the DC counterparts as well as DT_{150} group mice by (-34.7%; $p<0.001$) on serum TC levels and (-50%; $p<0.001$) on TGs levels. Contrarily, treatment with Pioglitazone (DT_{PGZ}) showed (-33.2%; $p<0.001$) on TC levels and (-09.6%; $p<0.001$) on TGs levels compared with diabetic control mice (Table-1 and Fig-1).

Relative to normal control, the diabetic mice had higher value of low density lipoprotein (LDL) (+256%; $p<0.001$) while diminished value of high density lipoprotein (HDL) (-55%; $p<0.001$).This is because when the unrestrained diabetic condition advances, considerable changes in these biochemical parameters are as expected and predictable. Diabetic mice treated with lower dose of *Circuma longa* extract (DT_{150}) showed significantly lower values of serum LDL (-50%; $p<0.001$) and higher value of HDL (-45.4%; $p<0.001$), when compared with the DC counterparts. All over again, the DT_{250} treatment showed even better lowering effects on LDL (-53%; $p<0.001$) compared with the DC counterparts and improved level of HDL (+56%; $p<0.001$). In contrast, treatment with Pioglitazone (DT_{PGZ}) showed a considerable diminished level of LDL (-58%; $p<0.001$) while improved level of HDL (+59%; $p<0.001$) compared with diabetic control mice.

Chronic oral administration of the extract also reduced total cholesterol and triglyceride levels in diabetic and normoglycaemic albino mice consistent with the hypolipidemic effect earlier reported (Khanna *et al*., 2002). Diabetic dyslipidemia is marked by elevated triglycerides, cholesterol and low density lipoprotein (LDL) particles of altered composition and decreased high density lipoprotein (HDL), and constitutes an important cardiovascular risk factor in diabetics (Agrawal *et al*., 2006). Reduction in total cholesterol and triglycerides through dietary or drug therapy has been found beneficial in preventing diabetic complications as well as improving lipid metabolism in diabetic patients (Brown *et al*., 1993; Ahmed *et al*., 2001). Experimentally, streptozotocin-induced diabetic hyperglycemia is accompanied by increase in serum cholesterol and triglyceride levels (Ahmed *et al*., 2001) and mimics overt diabetes disease. Thus, in addition to glycaemic control, extract of this plant may further reduce mortality from complications of the disease by ameliorating diabetes induced dyslipidemia. Lipid lowering activity of *P. niruri* alcoholic extracts in triton induced hyperlipidaemia was examined by Chandra *et al*., (2000) and Santwana rani and Baidyanath Kumar (2015). It was observed that administration of triton in mice caused increase in serum cholesterol by 3.5 fold, phospholipids 2 fold and triglyceride 1.2 fold. Administration of *C. longa* at the dose of 200mg/kg simultaneously with triton lowered the level of total cholesterol, phospholipids and triglyceride by 27, 25 and 24 percent respectively. In an experiment with cholesterol fed rats, *C. longa* at a dose of 100 mg/kg lowered the elevated level of low-density lipoprotein lipids in hyperlipidemic and drug fed animals (Chandra *et al*., 2000).

In the present study, STZ induction to mice resulted in dyslipidemic changes as illustrated by increasing triglycerides (TGs) and total cholesterol (TC), a finding in accordance with that of Woo *et al.,* (2008). Treatment with pioglitazone or *C. longa* extract produced significant decreases in serum TGs and TC in diabetic mice. These results are in agreement with those of Okoli *et al*., (2010) who reported that treatment with *Phyllanthus. niruri* extract improves

dyslipidemia and decreases oxidative stress, with reduction of cardiac parameters. The results are also in agreement with those of Santwana Rani and Baidyanath Kumar (2015) who reported a more or less similar efficacy of *Phyllanthus niruri* methanol extract on lipid profile of Streptozotocin induced mice diabetic model.

Treatment with *C. longa* extract to diabetic mice reduces serum hypertriglyceridemia *via* decreased synthesis of triglycerides by the liver or by inhibition of triglyceride release from the liver. The treatment with *C. longa* extract also induced marked reductions in total serum cholesterol in diabetic mice (Table- 1; Fig- 1).

Unnikrishnan and Rao (1995) studied the antioxidative properties of curcumin and its three derivatives (demethoxy curcumin, bisdemethoxy curcumin and diacethyl curcumin). Curcumin is a good antioxidant and inhibits lipid peroxidation in rat liver microsomes, erythrocyte membranes and brain homogenates (Pulla Reddy & Lokesh, 1994). The lipid peroxidation has a main role in the inflammation, in heart diseases, and in cancer.

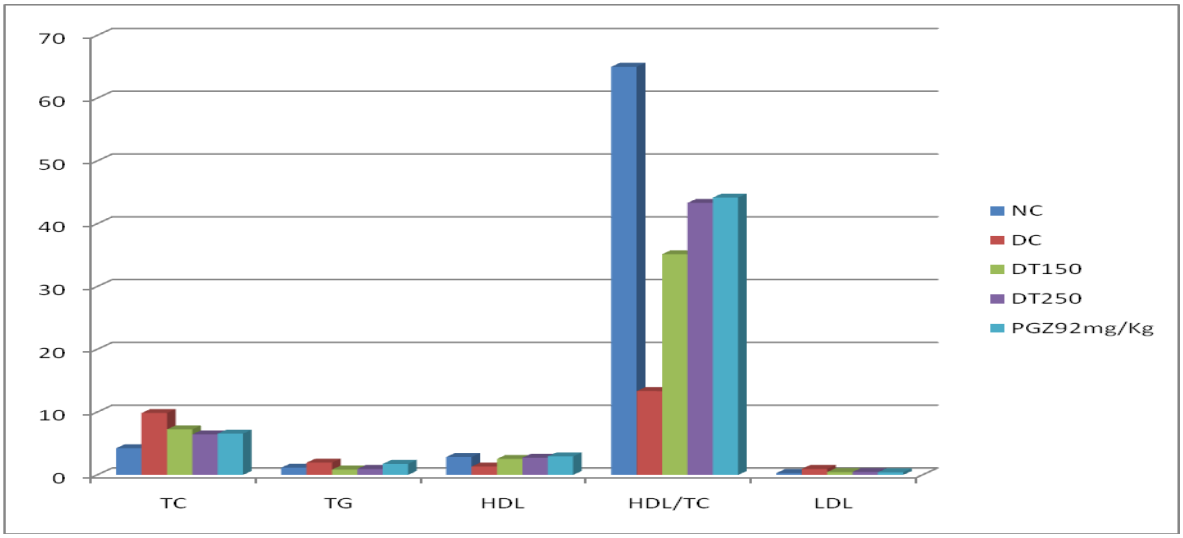
Turmeric can lower lipid peroxidation by maintaining the activities of antioxidant enzymes like superoxide dismutase, catalase and glutathione peroxidase at higher levels. These enzymes play an important role in the regulation of lipidperoxidation (Pulla Reddy & Lokesh, 1992). Pulla Reddy and Lokesh (1992) observed that curcumin is capable of scavenging oxygen free radicals such as superoxide anions and hydroxyl radicals, which are important to the initiation of lipid peroxidation.

Table.1 Showing effects of Different doses of *Circuma longa* extract and Pioglitazone on serum lipid profile in STZ induced mice diabetic model

Groups	**TC (mmol/lit)**	**TG (mmol/lit)**	**HDL (mmol/lit)**	**HDL/TC (%)**	**LDL (mmol/lit**
Normal control (NC)	4.25±0.85**	1.15±0.19**	2.85±0.24**	65±4.55**	0.29±0.03**
Diabetic control (DC)	9.85±1.54*	1.95±0.25*	1.33±0.54*	13.35±1.97*	0.95±0.13*
C. longa extract (150mg/kg) (DT_{150})	7.25±0.45**	0.85±0.07**	2.55±0.35**	35.15±3.33**	0.45±0.07**
C. longa extract (250mg/kg) (DT_{250})	6.45±0.62**	0.94±0.15**	2.73±0.45**	43.32±4.16**	0.47±0.05**
Pioglitazone 92mg/kg (DT_{RGZ})	6.57±1.33**	1.75±0.16**	2.95±0.51**	44.17±5.56**	0.42±0.12**

P<0.05 as compared with normal control. **p<0.01 as compared with diabetic control. TC=Total cholesterol; TG= Triglycerides; HDL= High density lipoprotein; LDL= Low density lipoprotein

Fig.1 Effect of *Circuma longa* extract on lipid profile in different mice group



The pharmacological activities of Curcuma longa extract are reported to have significant effects on the human body. It is anti-oxidant, anti-arthritic, anti alzheimer's, anti cancerous, anti viral, anti fungal, abortificient, anti amoebic, anti asthmatic, anticoagulant, anticonvulsant, anti edematic, anti hepatotoxic, anti hyper cholesterolemic, anti hyperlipemic, anti inflammatory, anti spasmodic, CNS depressant, diuretic, phagocytosis capacity enhancer, plasma bilirubin decreaser, platelet aggregation inhibitor and weight gain inhibitor. (Wikipedia, 2000; Ross Ivan, 2003; CCRAS.Vol. II, 2000). *Circuma longa* is a powerful blood purifier in reducing excessive cholesterol. It is very safe and has been used in Chinese and Ayurvedic medicine for more than 4000 years.

Curcuminoids are cytotoxic, inhibiting mitosis and leading to chromosome changes. However, nothing is known about the oral toxicity of Curcuminoids in man; the cytotoxic effects have been observed in cell cultures. In mice, chronic administration leads to significant changes in heart and lung weights and fall in the red and white blood corpuscles count. Curcuminoids cause the formation of stomach ulcers. It is contraindicated in patients with bile duct obstruction, gallstones, hyperacidity, and stomach ulcers. Care should be taken in women who wish to conceive or a patient complaining of alopecia as it leads to infertility and loss of hair (Bisset Norman, 2001; Duke James, 2006).

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