

# Anti-Hyperlipidaemia impact of *Costus speciosus* against atherogenic diet induced Hyperlipidaemia in Wister Rats

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## ABSTRACT

*Costus speciosus*, often referred to as crepe ginger, is an Indian ornamental plant belonging to the Costaceae family. The plant has been discovered to have a number of beneficial properties, including antibacterial, antifungal, antioxidant, antihyperglycemic, anti-inflammatory, antidiuretic, and estrogenic effects. Data regarding the distribution, morphology, chemical components, and traditional, pharmacological, and medicinal applications of crude drug is revealed in the current review. The goal of this study was to determine the antihyperlipidemic effect of 200 mg/kg of ethanolic extract from the rhizome of *Costus speciosus* between hyperlipidaemic Wistar rats that were induced and atherogenic diet. In a dose-dependent way, the ethanolic extract was found to raise HDL levels while lowering serum triglycerides, total cholesterol, LDL, and VLDL levels, according to the study.

**Keywords:** *Costus speciosus*, Antihyperlipidemic, Wistar rat, medicinal uses, atherogenic.

## INTRODUCTION

An increase in the quantity of lipids in the blood, such as cholesterol and triglycerides, is known as hyperlipidaemia. These increases might result in pancreatitis and heart illness. Hyperlipidaemia is characterized by unusually high concentrations of any or all lipids and/or lipoproteins in the blood. The main lipids in the body are cholesterol, triglycerides, and phospholipids, which are carried in the form of lipoprotein complexes made up of lipids and proteins. Recent clinical trials attempting to increase HDL have failed to show clinically significant decreases in cardiovascular end points, calling into question the significance of raising HDL fractions and Apo A-I. [1] Numerous tests and research have continuously demonstrated that high LDL cholesterol levels raise one's risk of developing atherosclerotic plaques, which can lead to vascular illness. On the other hand, high-density lipoprotein (HDL) cholesterol helps control cholesterol levels to avoid imbalances that would raise the chance of developing atherosclerotic vascular illness. Medical treatment should be customized to each patient, and

each patient's LDL cholesterol target should be based on their total cardiovascular risk. Primary prevention is the term used to describe the management of risk factors like hyperlipidaemia in order to lower the risk of atherosclerotic cardiovascular disease. Extensive epidemiological evidence, demonstrating a consistent and beneficial association between LDL cholesterol levels, cardiovascular events, and patient mortality, forms the basis for lowering LDL cholesterol. [2]

**Cholesterol:** It is a necessary ingredient in the mammalian cell membrane of all tissues, serving as a precursor to steroid hormones and bile acids. It is found in all animal cells, either in its free form or in the form of numerous fatty esters, but not in plant fats.

**Triglycerides:** This is the most prevalent of all lipids. Adipocytes are full of it. These are important constituents of storage fats in the cells of plants and animals. Excess calories, alcohol, and sugar are converted by the body into triglycerides, which are then stored in fat cells throughout the body [3].

**Lipoproteins:** These large, spherical particles are composed of an inner core of nonpolar lipids (triglycerides' cholesteryl esters) and an outer polar layer of phospholipids, unbound cholesterol, and apoproteins.

**Chylomicrons:** These are the biggest particles in terms of both size and density, and its concentration is precisely related to the quantity of triglycerides in the diet.

**VLDL:** Very low-density lipoproteins are smaller particles that are released by the liver and have lower triglyceride content than chylomicrons. Cholesterol is transported by VLDL from the liver to the body's organs and tissues. They are produced by the mixing of triglycerides and cholesterol [4].

**LDL:** Low-density lipoprotein is produced in part in the intestinal chylomicrons and in part following the lipolysis of VLDL. It is directly related to CHD [5].

**HDL:** High-density lipoproteins are produced by the liver, and HDL is frequently known as "good cholesterol." It transports cholesterol and other lipids from tissues back to the liver for breakdown. The function of HDL is antiatherogenic. [6]

**Lp (a):** It is produced by the liver. According to Berg, lipoprotein (a) is a cholesterol-rich plasma lipoprotein that is immediately associated with atherosclerosis [7]. A higher level of Lp(a) in the plasma increases the risk of CHD by a factor of 2 to 5.

According to research by Nago et al., women have greater Lp (a) levels than men, and there is a statistically significant increase in the concentration of Lp (a) plasma with age. They also found, contrary to non-drinkers, that alcohol drinkers had lower levels of Lp(a) in their plasma [8].

### Types of Hyperlipidemia:-

- 1. Hyperlipidemia that is acquired-** possibly as a result of your actions (or lack thereof). The ailment can also be brought on by medical issues or other health issues. Some individuals inherit it from their parents.
- 2. Familial hypercholesterolemia-** is a kind of inherited hyperlipidemia. The gene that normally transports cholesterol outside the body is altered, causing it to accumulate on the artery walls.
- 3. Familial hypertriglyceridemia-** is a different kind of genetic hyperlipidemia. It raises triglyceride levels to dangerously high levels.

### Classification of hyperlipidemia:

Frederickson's classification, which is based on lipoprotein patterns, is used to categorize hyperlipidemias. The World Health Organization (WHO) later embraced it.

**Table 1: Classification of hyperlipidemia [9]**

Sr. No.	Hyperlipoproteinemia	Synonym	Occurrence	Defect	Enhanced lipoprotein
1	Type I	Primary hyperlipoproteinaemia or Familial hyperchylomicronemia	Very rare	Decreased lipoprotein lipase (LPL)	Chylomicrons
2	Type IIa	Polygenic hypercholesterolemia or Familial hypercholesterolemia	Less common	LDL receptor deficiency	LDL
3	Type IIb	Combined hyperlipidemia	Commonest	Decreased LDL receptor and Increased ApoB	LDL and VLDL
4	Type III	Familial dysbetalipoproteinemia	Rare	Defect in Apo E 2 synthesis	IDL
5	Type IV	Familial hyperlipidemia	Common	Increased VLDL production and Decreased elimination	VLDL
6	Type V	Endogenous hypertriglyceridemia	Less common	Increased VLDL production and Decreased LPL	VLDL and Chylomicrons

## Causes of hyperlipidemia

- A high intake of saturated fat and cholesterol increases blood cholesterol and triglyceride levels.
- Hyperlipidemia is more likely to occur in people with conditions like obesity, diabetes mellitus, and hypothyroidism.
- Hyperlipidemia can be caused by smoking and lack of exercise.
- Hyperlipidemia is also more likely to occur when alcohol is consumed in excess.
- Hyperlipidemia may be brought on by some medications, like steroids and  $\beta$ -blockers.
- Hyperlipidemia can also be caused by a hereditary component.
- Hyperlipidemia can sometimes develop during pregnancy.

## Hyperlipidemia signs and symptoms

Hyperlipidemia often manifests itself asymptotically and is frequently identified during regular screening for atherosclerotic cardiovascular disease [10].

1. A heart attack, stroke, or chest discomfort (angina) is possible symptoms.
2. Cholesterol may be deposited in tendons or just beneath the skin under the eyes when levels are very high.
3. Swelling of organs like the liver, spleen, or pancreas.
4. Blockage of the brain and heart's blood arteries.
5. Greater incidence of obesity and glucose intolerance.
6. Pimple-like lesions all over the body.

## **MATERIALS & METHOD**

### **Plant material**

An Indian decorative plant of the *Costus speciosus* Keon belonging to family Costaceae. Excluding the dry and semi-arid regions of Punjab, Haryana, Rajasthan, Gujarat, and peninsular India, the plant is widely distributed in India in the tropical or sub-tropical climate from sea level to the Himalayas. It can be found all over the nation, up to 1200 meters above sea level, in humid tropical evergreen forests. [11] The rhizomes have expectorant, astringent, anthelmintic, and bitter characteristics. The rhizome extract is used as a tonic and is beneficial for treating fever, asthma, bronchitis, leprosy, constipation, anemia, and other skin conditions. The Leaves also lower blood sugar levels, have hypoglycemic effects, and enhance insulin activity. The rhizome has antihelminthic, antipyretic, anti-inflammatory, anticholinesterase, and antifertility effects. According to pharmacological research, the rhizomes of *C. speciosus* have hydrochloric, diuretic, cardiotonic, and CNS depressant effects [12].

The Zingiberaceae, a family of medicinal plants with around 1300 species and 52 genera, is found throughout tropical Africa, Asia, and the Americas. Cardamom (*Amomum elettaria*), turmeric (*Curcuma longa*), ginger (*Zingiber officinale*), torch ginger (*Etlingera elatior*), ginger lily (*Hedychium*), summer tulip (*Curcuma alismatifolia*), and shell gingers (*Alpinia*) are all included in it [13].

## **MORPHOLOGY**

With a succulent, upright, perennial, decorative, herbaceous plant, a tuberous rootstock stem, a sub-woody base, and thick, creeping rhizomes (120-300 cm height) reaching a height of 2-2.7 m, *Costus speciosus* has fragrant white flowers in terminal groups and long, lanceolate leaves. It is a tall, striking landscape plant with huge, dark green, subsessile, elliptic, or obovate leaves that grow in a spiral pattern along the stem. [14] The plant then grows vegetatively until September and October, at which point flowering continues until the end of October. The plant eventually dies, after the fruit has ripened and all the leaves have fallen. However, the underlying rhizome stays dormant from December to March, and during the month of April of the following year, new shoots once again appear (Maji et al. 2020).



**Figure 1.1:** plant *Costus speciosus*



**Figure 1.2 Rhizome**

Kingdom	Plantae
Subkingdom	Tracheobionta
Super division	Spermatophyta
Division	Mangoliophyta
Class	Liliopsida
Family	Costaceae/ Zingiberaceae
Order	Zingiberales
Species	speciosus
Genus	Costus

### TAXONOMIC CLASSIFICATION [15]

#### CHEMICAL CONSTITUENT

Diosgenin is primarily derived from rhizomes. The primary chemical constituents are curcumin, curcuminoids, and diosgenin. In addition to quinines, gracillin, dioscin, sitosterol- $\beta$ -D-glucoside, and  $5\alpha$ -stigmasten-3 $\beta$ -ol, costus roots and tubers also contain dioscin's prosapogenins A and B. The rhizomes, which also include seeds and roots, were also found to contain saponins. Diosgenin and tigogenin (2.6%) have been isolated from rhizomes, and palmitates of various compounds, including  $\alpha$ -amyrinsterate,  $\beta$ -amyrin, and lupeol, have been isolated from leaves. Two novel quinonesdihydrophytylplastoquinone and its 6-methyl derivatives and  $\alpha$ tocopherol were isolated from seeds.[16]

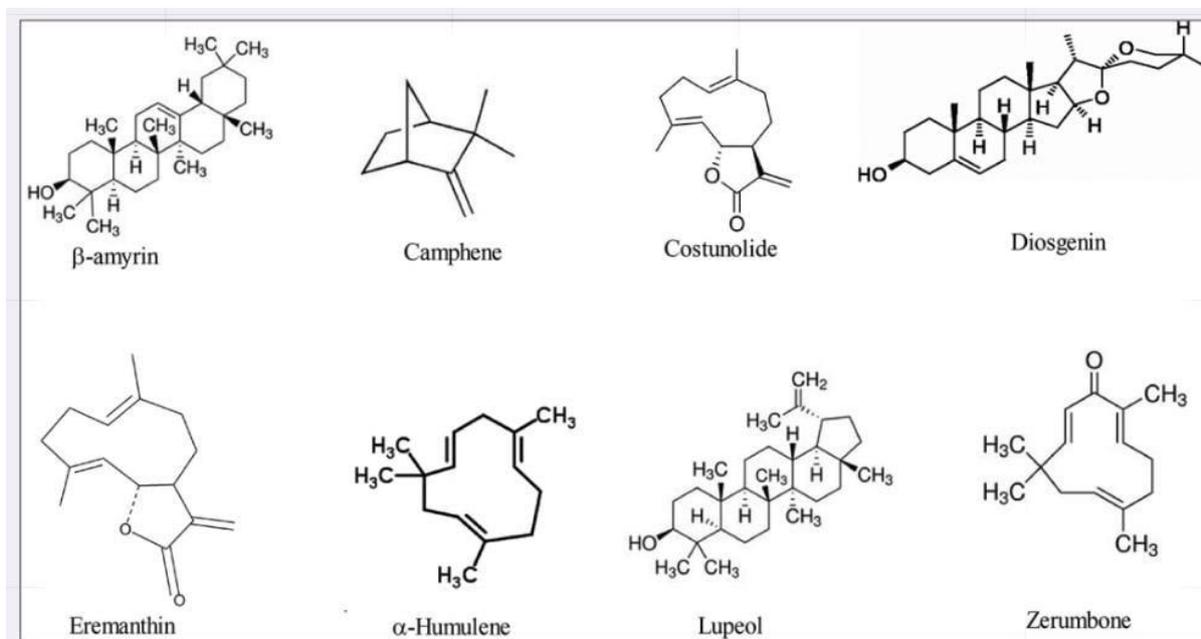


Figure 1: Chemical structures of some *Costus speciosus* active ingredients

## Therapeutic Efficacy

The rhizome of *Costus speciosus* has been shown to contain up to 3.37% diosgenin. Juice from the rhizome of the plant parts is applied to the head to cool and relieve headaches; bruised leaves are applied to treat fever; a stem decoction is used to cure dysentery and fever; patients with high fever utilize leaf infusion or decoction as a sudorific or in a bath; sap from the leaves and young stems is used to treat diarrhea cough, cuts, wounds, scabies, antidote for snake bites, jaundice, arthritis, burning sensation, constipation, leprosy, skin diseases, asthma, bronchitis, inflammations, anemia, intestinal warm, worm infection, rashes, nose pain, and to stop vomiting spermatorrhoea. It is also employed as an anti-vermin and for abortion [17].

## DRYING

Plant materials are first rinsed in water for five minutes, and then they are dried in an oven at a predetermined temperature (110°C for eight hours). The dried rhizome is crushed into a coarse powder using wood grinders.

## Setup for the experiment

The experimental investigation made use of Wistar rats of both sexes, weighing between 180 and 250 grams. The animals were split up into four groups, with six animals in each group. Group I was given food and standard saline for the rats because it was the care control group. The reference drug lovastatin, at a dose of 50 mg/kg, was administered to Group II. Groups III received 100 mg/kg of ethanolic extract of

Costus speciosus rhizome, while Group IV received 200 mg/kg of the same extract. All extracts were taken orally once daily. For 28 days, oral gavage was used to administer all treatments on a daily basis.

**Table 1: Protocol for Antihyperlipidemic Activity**

Group(N=6)	Treatment	dose
I	Vehicle control (Normal Saline)	10ml/kg
II	Lovastatin	50mg/kg
III	Ethanollic extract of Costous speciosus rhizome	100mg/kg
IV	Ethanollic extract of Costous speciosus rhizome	200mg/kg

### Laboratory studies

Before conducting in vivo studies, a laboratory analysis was conducted after the 28-day treatment period. Blood samples were taken from the creature's overnight using glass capillaries and light ether anaesthesia. The serum was then separated and analysed biochemically.

### Blood sampling and serum separation

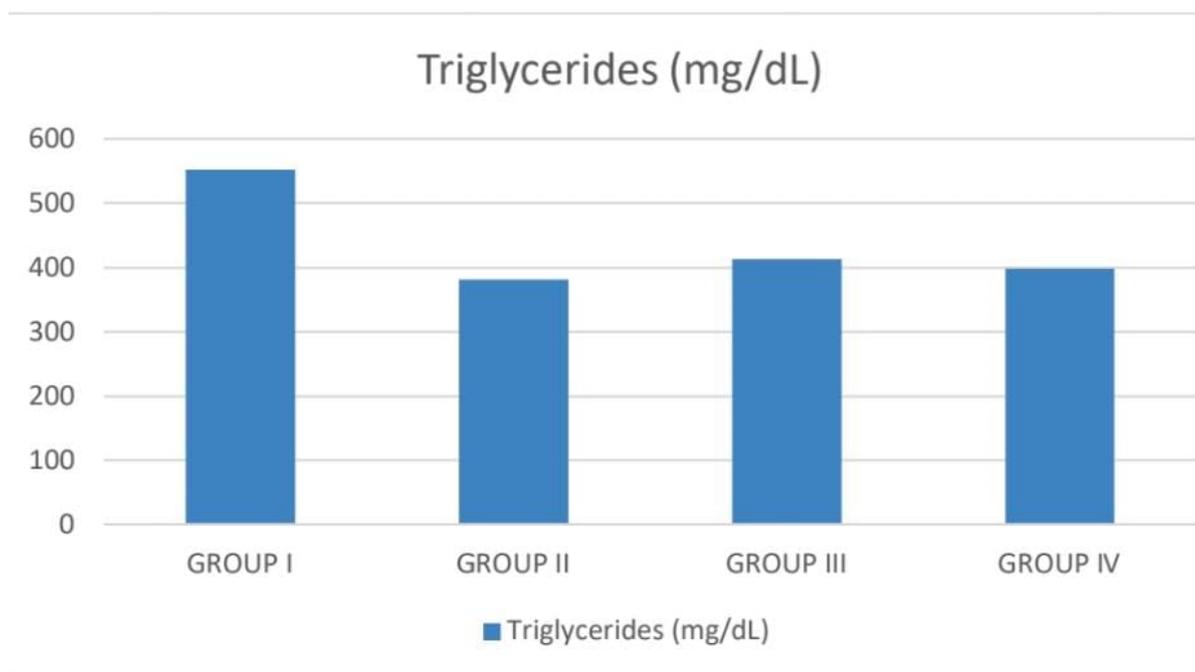
Blood was collected from the animals' clean tail tips and orbital sinuses in Eppendorf tubes without being haemolysed. To isolate the serum, the blood was centrifuged at 3000 rpm for 10 minutes at room temperature (37°C), and then it was biochemically assessed.

## RESULT

**Table 5.1: Impact of ethanolic extract of Rhizome of Costus speciosus on Triglycerides (mg/dL)**

GROUPS	Triglycerides (mg/dL)
GROUP I (VEHICLE CONTROL)	551.09 ± 47.12*
GROUP II (LOVASTATIN)	382.01 ± 2.39**
GROUP III (Ethanolic extract Of Costus speciosus rhizome 100 mg/kg)	413.19 ± 11.72**
GROUP IV (Ethanolic extract of Costus speciosus rhizome 200 mg/kg)	398.80 ± 11.72**

Values are expressed as mean ± SD (n=6). Values comparisons were made between Group I Vs Group II, III, IV (\*\*\*\*p



**Fig 1: Impact of ethanolic extract of Rhizome of Costus speciosus on Triglycerides (mg/dL).**

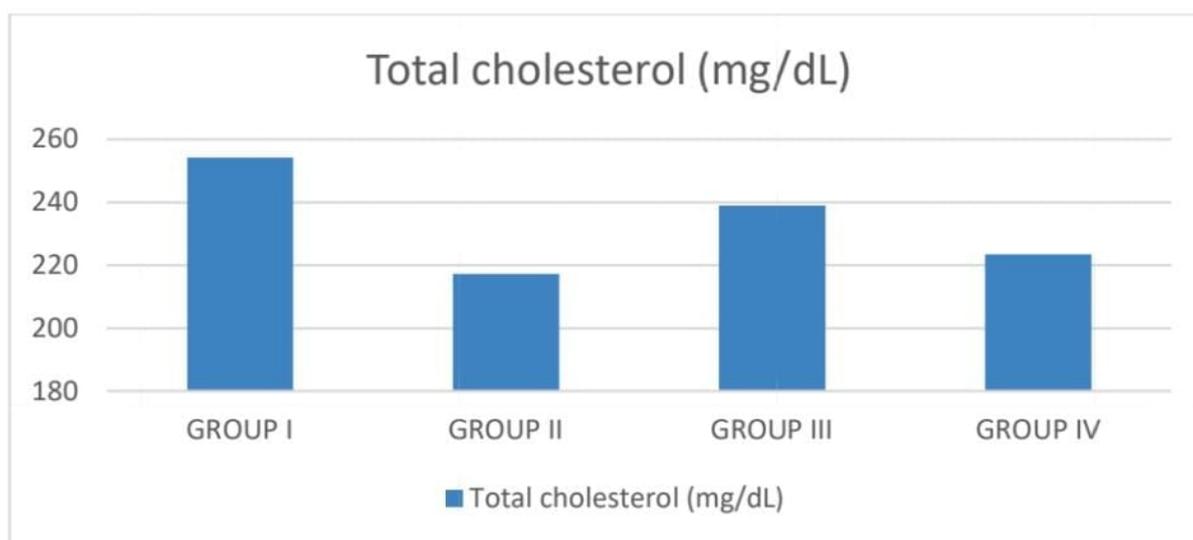
**Impact of the ethanolic extract of Rhizome of Costus speciosus on total cholesterol levels (mg/dL).**

The mean values of total cholesterol level in the vehicle control group were compared to those in the groups treated with Lovastatin and ethanolic extract of Costus speciosus rhizome. Table 5.2 and Fig 2 displayed the results.

**Table 5.2: Influence of ethanolic extract of Rhizome of Costus speciosus on Total cholesterol (mg/dL).**

GROUPS	Total cholesterol (mg/dL)
GROUP I (VEHICLE CONTROL)	253.90 ± 3.38*
GROUP II (LOVASTATIN)	218.31 ± 9.81**
GROUP III (Ethanolic extract Of Costus speciosus rhizome 100 mg/kg)	238.99 ± 6.20
GROUP IV (Ethanolic extract of Costus speciosus rhizome 200 mg/kg)	224.10 ± 9.34**

Values are expressed as mean ± SD (n=6). Values comparison were made between Group I Vs Group II, III, IV (\*\*\*\*p



**Fig 2: Impact of ethanolic extract of Rhizome of Costous specious on Total cholesterol (mg/dL).**

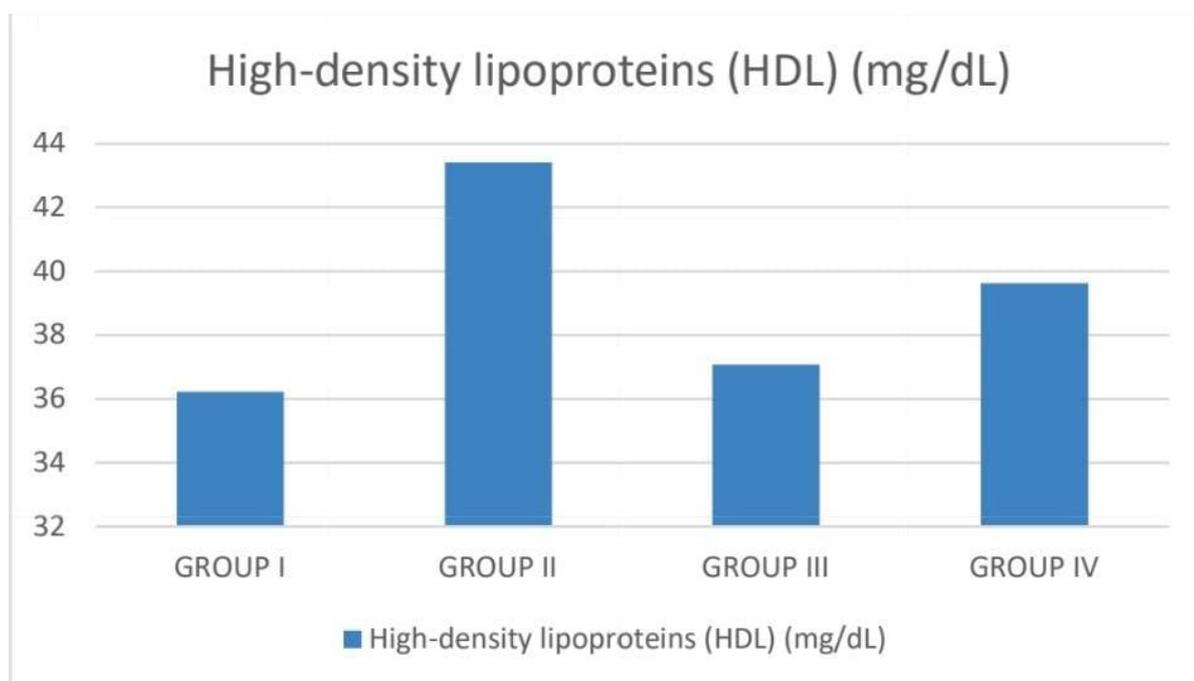
### **Impact of ethanolic extract of Rhizome of Costous specious on High-density lipoproteins (HDL)**

The mean High-density lipoproteins level values in vehicle control group were compared with Lovastatin and ethanolic extract of rhizome of Costous specious treated groups. . The results were represented in Table 3 and Fig 3.

**Table 5.3: Effect of ethanolic extract of Rhizome of Costous specious on High-density lipoproteins (HDL) (mg/dL).**

<b>GROUPS</b>	<b>High-density lipoproteins (HDL) (mg/dL)</b>
GROUP I (VEHICLE CONTROL)	36.24 ± 2.56*
GROUP II (LOVASTATIN)	43.49 ± 1.38
GROUP III (Ethanolic extract Of costus specious rhizome 100 mg/kg)	38.01± 2.70
GROUP IV (Ethanolic extract of costus specious rhizome 200 mg/kg)	38.90± 1.00

Values are expressed as mean ± SD (n=6). Values comparison were made between Group I Vs Group II, III, IV (\*\*\*\*p



**Fig 5: Impact of ethanolic extract of Rhizome of Costous specious on High-density lipoproteins (HDL) (mg/dL).**

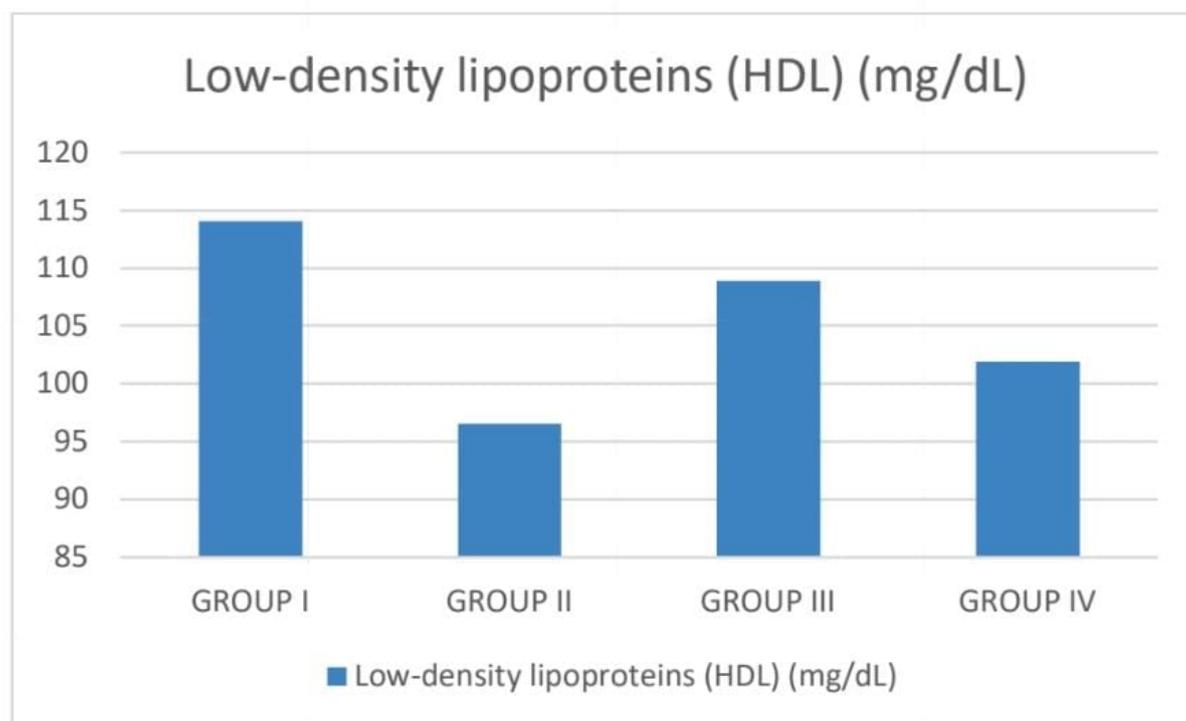
#### **Impact of ethanolic extract of Rhizome of Costous specious on Low-density lipoproteins (LDL)**

The mean Low-density lipoproteins level values in vehicle control group were compared with Lovastatin and ethanolic extract of extract of rhizome of Costus specious treated groups. . The results were represented in Table 5.4 and Fig 4.

**Table 5.4: Effect of ethanolic extract of Rhizome of Costus specious on Low-density lipoproteins (LDL)**

GROUPS	Low-density lipoproteins (LDL) (mg/dL)
GROUP I (VEHICLE CONTROL)	114.10 ± 7.30*
GROUP II (LOVASTATIN)	96.52 ± 10.90
GROUP III (Ethanolic extract Of Costus specious rhizome 100 mg/kg)	108.92 ± 8.09
GROUP IV (Ethanolic extract of Costus specious rhizome 200 mg/kg)	101.90 ± 6.10

Values are expressed as mean ± SD (n=6). Values comparison were made between Group I Vs Group II, III, IV (\*\*\*\*p



**Fig 4: Impact of ethanolic extract of Rhizome of Costus speciosus on Low-density lipoproteins (LDL) (mg/dL).**

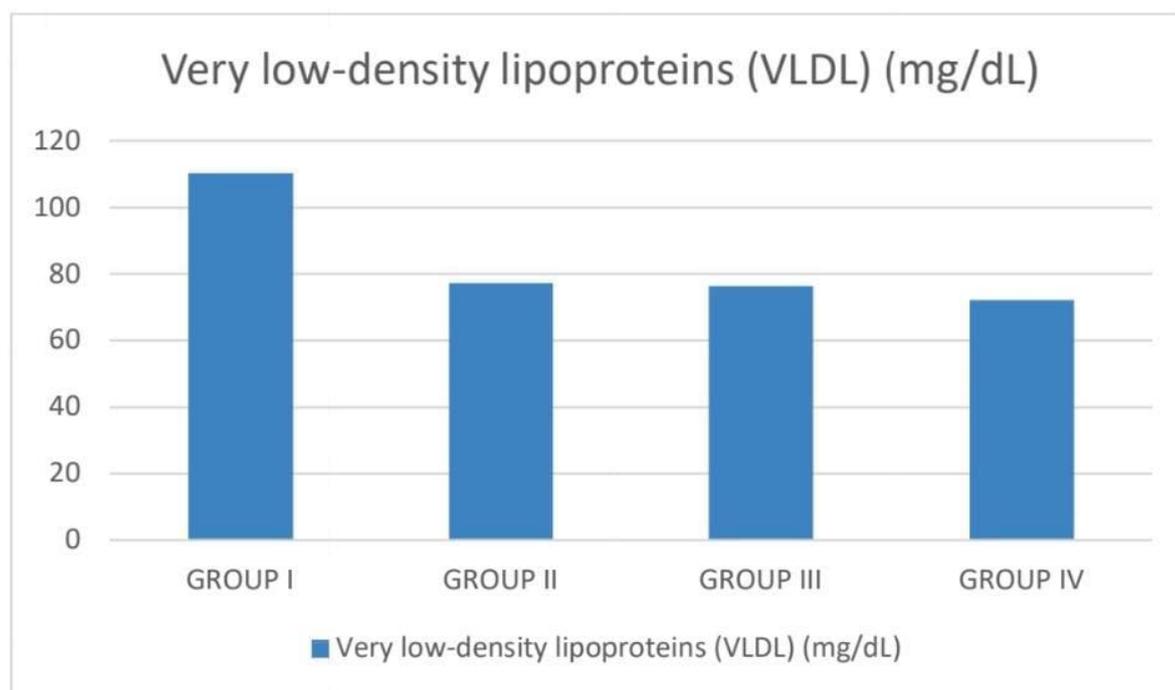
#### **Impact of ethanolic extract of Rhizome of Costus speciosus on Very low-density lipoproteins (VLDL)**

The mean Very low-density lipoproteins level values in vehicle control group were compared with Atorvastatin and ethanolic extract of rhizome of Costus speciosus treated groups. The results were represented in Table 5.5 and Fig 5.

**Table 5.5: Effect of ethanolic extract of Rhizome of Costus speciosus on Very low-density lipoproteins (VLDL) (mg/dL).**

<b>GROUPS</b>	<b>Very Low-density lipoproteins (LDL) (mg/dL)</b>
GROUP I (VEHICLE CONTROL)	110.40 ± 9.42**
GROUP II (LOVASTATIN)	77.36 ± 2.36**
GROUP III (Ethanolic extract Of Costus speciosus rhizome 100 mg/kg)	76.40 ± 0.49**
GROUP IV (Ethanolic extract of Costus speciosus rhizome 200 mg/kg)	72.20 ± 0.50**

Values are expressed as mean ± SD (n=6). Values comparison were made between Group I Vs Group II, III, IV (\*\*\*\*p



**Fig 5: Effect of ethanolic extract of Rhizome of *Costus speciosus* on Very low-density lipoproteins (VLDL) (mg/dL).**

## CONCLUSION

In summary, the results of this investigation show that *Costus speciosus* possesses considerable antihyperlipidemic action in hyperlipidaemic rats caused by a high-fat diet (HFD). Treatment with expensive *speciosus* extract resulted in a significant decrease in serum lipid levels, particularly total cholesterol, triglycerides, and LDL-C, as well as an elevation in HDL-C levels. The plant appears to have positive effects on controlling lipid metabolism and enhancing cardiovascular health, according to these findings. The findings show that *Costus speciosus* is a potential natural therapeutic agent for the treatment of dyslipidaemia and associated metabolic diseases. However, additional research, such as clinical trials and thorough mechanistic analyses, is required to completely understand the plant's pharmacological potential and prove its clinical efficacy and safety.

1. AIM-HIGH Investigators, Boden WE, Probstfield JL, et al. Niacin in patients with low HDL cholesterol levels receiving intensive statin therapy. *N Engl J Med* 2011; 365:2255– 2267.
2. Goodman, Gilman. Eds. *The pharmacological basis of therapeutics*. Macmillan Publishing Company, New York; 1970.
3. Smelt AH. Triglycerides and gallstone formation. *Clin Chim Acta* 2010;411:1625-31.
4. Sundaram M, Yao Z. Recent progress in understanding protein and lipid factors affecting hepatic VLDL assembly and secretion. *Nutr Metab* 2010;27:35.
5. Salim FA, Diab HD, Hmedan AK, Dhidah HNE, Baayo RE, Hussain S. A study of anti-bacterial, anti-fungal activities of ethanolic and aqueous extracts of *Costus speciosus*. *The Pharmaceut.& Chem. J.* 2019; 6(1):11–18

6. Ridker PM, Genest J, Boekholdt SM, Libby P, Gotto AM, Nordestgaard BG, *et al.* HDL cholesterol and residual risk of first cardiovascular events after treatment with potent statin therapy: an analysis from the JUPITER trial. *Lancet* 2010;376:333-9.
7. Danesh J, Collins R, Thijss V. Lipoprotein (a) and stroke: a meta-analysis of observational studies. *Stroke* 2007;38:1959-66.
8. Sharpe PC, Young IS, Evans AE. Effect of moderate alcohol consumption on lp (a) lipoprotein concentrations. The reduction is supported by other studies. *Br Med J* 1998;316:1675.
9. FREDRICKSON DONALDS. An international classification of hyperlipidemias and hyperlipoproteinemia's. *Annals of Internal Medicine*. 1971;75(3):471.doi:10.7326/0003-4819-75-3-471
- 10.Eliza J, Daisy P, Ignacimuthu S. Antioxidant activity of costunolide and eremanthin isolated from *Costusspeciosus* (Koen ex. Retz) Sm. *Chemico-Biological Interactions*. 2010; 188(3): 467–472.
11. S.Hasan, M.Qari, "DNA - RAPD Fingerprinting and cytogenetic screening of Genotoxic and Astringenotoxic effects of Aqueous Extract of *Costus speciosus* koen" *JKAU;Sci*,22 (1),pp.133-152,2010.
12. Rani AS, Sulakshana G, Patnaik S. *Costus speciosus*, an antidiabetic plant–review. *FS J Pharm Res* 2012;1:52-3.
- 13.Nair SVG, Hettihewa M, Rupasinghe HPV. Apoptotic and inhibitory effects on cell proliferation of hepatocellular carcinoma HepG2 cells by methanol leaf extract of *Costusspeciosus*. *BioMed Res. Inter*. 2014:1–10.
14. Stone and C. Benjamin, *The flora of Guam, Micronesia*, 6, pp. 1-659, 1970.
15. S. Srivastava, P. Singh, G. Mishra, K. K. Jha, R. L. Khosa, "*Costusspeciosus* (Keukand): A review," *Der Pharmacia Sinica*, 2 (1), pp. 118-128, 2011.
- 16.Rajasekharan. S, Pushpangadan. P and Biju, S.D,1996 .*Folk Medicines of Kerala - A Study on Native Traditional Folk Healing Art and its Practitioners* in Jain, S.K. (ed) Deep Publications, New Delhi India pp167-172.
17. S. Srivastava, P. Singh, K. K. Jha, G. Mishra, S. Srivastava, R. L. Khosa, "Anthelmintic activity of aerial parts of *Costus speciosus*," *International Journal of Green Pharmacy*, 5, pp. 325-328, 2011.