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UNLOCKING THE LIPID-LOWERING POWER OF *PIMPINELLA ANISUM*: A NATURAL THERAPEUTIC APPROACH

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ABSTRACT

The purpose of this study was to assess the antihyperlipidimic properties of *Pimpinella anisum* L. aqueous extract against hyperlipidemia produced by Triton-X 100 and high-fat diets (HFD). The animals in both experimental models were split up into five groups of six. Chronic Acute hyperlipidemia was brought on by a single intraperitoneal injection of Triton-X 100 for seven days, and hyperlipidemia was brought on by feeding HFD once daily for 28 days. Using histopathological analysis to support the findings, the degree of protection against hyperlipidemia was assessed by measuring the levels of various lipid profiles, including triglycerides (TG), total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), and very low density lipoprotein (VLDL). Preventive *P. anisum* medication (1/2 gm/kg) dramatically decreased hyperlipidemia by raising HDL and lowering blood LDL, VLDL, TG, and TC. The histological alterations in the liver in both hyperlipidemia experimental animals corroborated the findings.

KEYWORDS: Antihyperlipidemia, *Pimpinella anisum* L., High fat diet, Triton X- 100, Atorvastatin, TC, TG, LDL, HDL, VLDL.

INTRODUCTION

As a homeostatic regulator, a precursor of bile salts, sex hormones, and corticosteroids, and an essential component in preserving the integrity of cell walls, cholesterol is necessary for life.[1] In addition to its structural function in preserving fluidity and stability, cholesterol (CL) is crucial for the regulation of cell function. In addition to its many biological functions, cholesterol is necessary for maintaining cellular balance. It is necessary for the stiffness and fluidity of cellular membranes, helps produce steroids and vitamin D, and is a precursor to bile acids.[2]

Increases in one or more plasma lipids, including triglycerides (TG), cholesterol, cholesterol ester, phospholipids, and plasma lipoproteins, including very-low-density lipoproteins (VLDL-C) and low-density lipoproteins (LDL-C), along with decreased levels of high-density lipoproteins (HDL-C), are indicative of hyperlipidemia. A rise in plasma lipid levels is the primary risk factor for CVS disease.[3] Numerous illnesses are associated with an increased risk of hyperlipidemia. Modifiable risk factors include obesity, smoking, physical inactivity, and diets high in saturated and trans fats.[4] One serious lifestyle condition that has an adverse effect on people's health is hyperlipidemia. Among other cardiovascular issues, it causes angina pectoris, myocardial infarction (MI), hypertension, atherosclerosis, and congestive heart failure (CHF).[5]

According to conventional definitions, hyperlipidemia is a condition where the concentration of Blood lipoproteins that carry cholesterol or triglycerides above a certain normal level.[6] About 80% of the cholesterol in the body is produced by the liver; the remainder is obtained from foods including meat, fish, and eggs.[7]

High blood pressure is caused by cholesterol and many other lipids clumping together inside the arteries, restricting them and preventing blood flow. A buildup of cholesterol can result in blood clotting, a heart attack if it breaks down and moves via the bloodstream to the heart, and a brain injury if it moves to the brain stroke.[8] An increase in oxidative stress linked to hyperlipidemia causes a notable production of oxygen free radicals, which can cause oxidative modifications in low-density lipoproteins. These changes are crucial for the development and advancement of atherosclerosis and other cardiovascular disorders.[9] Additional problems brought on by hyperlipidemia include the oxidation of free fatty acids, which produces ketone bodies, and the concealment of insulin resistance in the muscles and liver, which culminates in the course of patients' diabetis.[10] Health care professionals are concerned about hyperlipidemia due to the proven correlation between

lipid concentrations and the risk of cardiovascular disease (CVD), which is the leading cause of death in the US.[11] One-third of all deaths globally are attributed to CVDs, which are expected to overtake all other causes of mortality and disability globally by 2020.[12]

The lipid-lowering drugs that are most frequently utilized are bile acid sequestrants, fibrates, and statins. These artificial substances have positive effects in addition to lowering cholesterol, but they can also have undesirable side effects include myopathy, rhabdomyolysis, and an elevated risk of gallstones.[13] Therefore, it is necessary to create novel lipid-lowering medications with a high therapeutic value and little or no side effects. the drawbacks of the popularity of both conventional and alternative therapies. Epidemiological findings in numerous societies demonstrate that alternative therapies, the use of medicinal plants, proper diet, and fruit consumption all effectively lessen the symptoms of hyperlipidemia.[14]

Natural products have been around since the beginning of time. Nowadays, traditional medical systems and certain of its methods are generally accepted globally. To assess to decide on herbal medications, a careful and practical approach is now required. Therefore, pharmacologists should be interested in learning about traditional healers' treatments and identifying the active ingredients for new medication development.[15]

The Umbelliferae family includes Pimpinella anisum L. (P.anisum), one of the first known medicinal herbs. It is an annual grassy plant with white blossoms and tiny green to yellow seeds that grows over the Eastern Mediterranean Region, West Asia, the Middle East, Mexico, Egypt, and Spain.[16] The main reason P. anisum is grown is for its fruits, or aniseeds, which are picked in August and September. Because aniseeds contain 1.5–5% essential oil, they are used as a flavoring, digestive, carminative, and to ease gastrointestinal spasms. nursing mothers who Babies that eat aniseed have less gastrointestinal problems and drink more milk.[17] Beneficial fatty acids like palmitic acid and oleic acid, which may help decrease cholesterol levels, are abundant in aniseed.[18]

There is no scientific evidence that P.anisum seeds have antihyperlipidemic action in an animal trial to date. As a result, the goal of this study is to show that an aqueous extract of P.anisum seeds has antihyperlipidemic activity in rats.

Epidemiology

Hyperlipidaemia is one of the most important risk factors for cardiovascular disease.

Atherosclerosis: Atherosclerosis is a condition in which fat, cholesterol, and calcium build up in the linings of the arteries. Fibrous plaques occur as a result of this deposition. A plaque is usually made up of three parts: 1) an atheroma, which is a fatty, soft, yellowish nodular mass in the core of a bigger plaque made up of macrophages, which are immune cells; 2) a layer of cholesterol crystals; and 3) a calcified outer layer. The most common cause of cardiovascular disease is atherosclerosis.[19]

Coronary Artery Disease (CAD): The major cause of coronary artery disease, atherosclerosis, is characterised by the accumulation of excess lipid and the formation of fibrous plaques within the artery wall, resulting in the narrowing of the arteries that supply blood to the myocardium, limiting blood flow and insufficient oxygen to meet the heart's needs.

Myocardial Infarction (MI): MI is a condition in which blood and oxygen supplies are partially or fully blocked in one or more cardiac arteries, resulting in heart cell damage or death. It's possible that the obstruction is caused by a ruptured atherosclerotic plaque.[20]

Angina Pectoris: Angina is a sign of a cardiac issue rather than a disease. Chest pain, discomfort, or squeezing pressure are all symptoms. Angina is caused by a decrease or complete loss of blood supply to a portion of the heart muscle. When there is a partial or total occlusion of the coronary arteries, poor blood circulation is usually the result of CHD.[21]

Ischemic stroke: Stroke is the fourth-largest cause of death in the United States. Strokes are usually caused by a blood clot blocking an artery or a piece of atherosclerotic block-breaking loose in a tiny channel within the brain. Much clinical research has shown that lowering low-density lipoprotein and total cholesterol by 15% reduces the risk of having a first stroke.[22]

Pimpinella anisum l.

One of the first oldest medicinal plants Pimpinella anisum L., a member of the Umbelliferae family. It is an annual grassy plant that grows in Mexico, Egypt, the Middle East, West Asia, and Spain. It has little green to yellow seeds, white flowers, and a height of 30 to 50 cm.[23]

Taxonomy

Domain : Eukaryota
Kingdom : Plantae
Phylum : Spermatophyta
Subphylum : Angiospermae
Class : Dicotyledonae
Order: : Apiales
Family : Apiaceae
Genus : Pimpinella
Species: Pimpinella anisum

Phytochemical Constituents

Anise seeds composed of 8-11 mass % of lipids rich in fatty acids, such as palmitic and oleic acids, as well as about 4 mass % of carbohydrates and 18 mass % of

protein, aniseed contains 1.5-6.0 mass % of volatile oil that is predominantly composed of trans-anethole.69 Other investigations have shown that the main components of anise seed essential oil include eugenol trans-anethole, methyl chavicol, anisaldehyde, estragole, coumarins, scopeletin, umbelliferone, estrols, terpene hydrocarbons, polyenes, and polyacetylenes.

The seed extract is rich in flavonoids, phenolic acids and essential oils such as anethole all of which may contribute to lipid lowering activity through antioxidant and anti-inflammatory mechanism.[24]

Experimental Studies[25,26]

1. High fat diet (HFD)-induce hyperlipidemic model

The high-fat diet induced hyperlipedemia model stimulates the dietary causes of human dyslipidemia and metabolic syndrome. It involves feeding animals a diet enriched with cholesterol, saturated fats, or both over a prolonged period typically ranging from 4 to 16 weeks.

Mechanism

A high-fat diet elevates the levels of circulating triglycerides, total cholesterol, LDL-C and reduces HDL-C by:

- Increasing lipid absorption in the intestine
- Promoting hepatic lipogenesis
- Reducing lipid clearance due to decreased lipoprotein lipase activity.

2. Triton X-100 induced Hyperlipidemic Model (acute model)

Triton X 100 (isooctylphenoxypolethoxyethanol) is a nn-ionic surfactant widely used to induce acute hyperlipidemia in rodents. A single intraperiotoneal injection of Triton X 100 leads to a rapid rise in blood lipid levels within 24-72 hours.

Mechanism

Triton X-100 induces hyperlipidemia by.

- Inhibiting lipoprotein lipase (LPL) which delays the clearance of circulating lipoproteins
- Blocking the uptake of lipoproteins by hepatic receptors
- Enhancing the hepatic synthesis of triglycerides and cholesterol.

Comparative Summary

Parameters	HFD-Induced model	Triton X-100 model
Type	Chronic	Acute
Induction time	weeks	24-72 hours
Mimics human condition	Closely	Partially
Suitability for long-term studies	High	Low
Lipid profile changes	Gradual,sustained	Rapid, transient.
Cost and ease	Moderate to high	Low

Statistical Analysis

Treatments	Serum TG	Serum TC	Serum HDL-C	Serum LDL-C	Serum VLDL-C
Normal	62.6±3.42	64.8±0.6	44.55±0.3	60.06±2.1	12.80±1.4
Diseased	106.2±1.27***	177.9±0.18***	20.25±1.27***	97.70±1.7***	32.92±1.9***
Atorvastatin (10mg/kg)	79.9±1.33$^{\#\#\#}$	75.06±1.21$^{\#\#\#}$	41.95±2.8$^{\#\#\#}$	66.65±2.9$^{\#\#\#}$	19.01±0.14$^{\#\#\#}$
Anise extract (1000mg/kg)	72.15±1.80$^{\#\#\#}$	70.18±0.14$^{\#\#\#}$	27.15±0.14$^{\#\#\#}$	76.45±0.10$^{\#\#\#}$	14.42±2.3$^{\#\#\#}$
Anise extract (2000mg/kg)	70.53±2.30$^{\#\#\#}$	68.08±1.23$^{\#\#\#}$	27.15±0.14$^{\#\#\#}$	76.45±0.10$^{\#\#\#}$	14±3.2$^{\#\#\#}$

Results are expressed as mean ± SE. Statistical significance was assessed using One-way Analysis of variance (ANOVA) followed by Tukey-Karmer multiple comparison tests.

Effects of Pimpinella anisum L., on different lipid parameters: (High fat diet induced hyperlipidemia)

All values are expressed as mean ± SEM of six observations. *p<0.05, **p<0.01, ***pp<0.001 when compared to normal #p<0.05, ###p<0.01, ###p<0.001, when compared to diseased group.

Effects of Pimpinella anisum L.,on different lipid parameter (triton X-100 induced hyperlipedemia)

Treatments	Serum TG	Serum TC	Serum HDL-C	Serum LDL-C	Serum VLDL-C
Normal	50.40±1.2	57.90±1.6	45±1.4	58.62±1.3	10.07±0.2
Diseased	86.23±1.9***	142.16±2***	23.35±1.6***	150.02±1.6***	17.15±0.5***
Atorvastatin (10mg/kg)	70.30±2.3$^{\#\#\#}$	75.28±1.2$^{\#\#\#}$	43.16±1.9$^{\#\#\#}$	76.16±1.9$^{\#\#\#}$	14.07±1.2$^{\#\#\#}$
Anise extract (1000mg/kg)	60.16±2.5$^{\#\#\#}$	65.15±1.8$^{\#\#\#}$	29.15±2.4$^{\#\#\#}$	71.23±1.3$^{\#\#\#}$	12.04±1.4$^{\#\#\#}$
Anise extract (2000mg/kg)	59.10±1.4$^{\#\#\#}$	64.23±2.3$^{\#\#\#}$	28.15±2.5$^{\#\#\#}$	70.22±1.7$^{\#\#\#}$	11.72±1.7$^{\#\#\#}$

All values are expressed as mean ± SEM of six observations. *p<0.05, **p<0.01, ***pp<0.001 when compared to normal #p<0.05, ###p<0.01, ###p<0.001, when compared to diseased group.

CONCLUSION

The findings of the present study revealed that extract of AE 1000 & 2000mg/kg p.o. showed antihyperlipidemic activity against high fat induced diet and Triton X-100 induced hyperlipidemia. There were decrease in the level of serum total cholesterol, triglycerides, LDL, VLDL and increase in the level of good cholesterol carrier HDL in the animals treated with PE extract in both high fat induced and triton x-100 model.

Antihyperlipidemic activity PE may be due to the presence of chemical constituents such as alkaloids, flavonoids, saponins, tannins & Cardiac glycosides and Major constituent like trans anethol. Further mechanistic studies as well as clinical trials are mandatory to prove the efficacy of the plant extract and essential oil as a treatment for Antihyperlipidemic in human subjects.

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