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Bhuvaneswari R
Department of Botany, Sri Saradha College for Women, Perambalur, Tamil Nadu, India

Sasikumar K
PG and Research Department of Botany, Periyar E.V.R. College, Trichy-23, Tamil Nadu, India

Ramanathan R
PG and Research Department of Botany, Government Arts College, Ariyalur, Tamil Nadu, India

Dhandapani R
PG and Research Department of Botany, Government Arts College, Ariyalur, Tamil Nadu, India

Correspondence
Bhuvaneswari R
Department of Botany, Sri Saradha College for Women, Perambalur, Tamil Nadu, India

Evaluation of antihyperlipidemic activity of *Cucumis pubescens* Willd. On atherogenic diet induced hyperlipidemia in rats

Bhuvaneswari R, Sasikumar K, Ramanathan R and Dhandapani R

Abstract
In atherogenic diet induced hyperlipidemic model the rat reciving treatment with aqueous, ethanol ans chloroform extracts of fruits of *Cucumis pubescens* Willd. Showed significant reduction in total cholesterol, triglycerides, LDL, VLDL and elevation in high density lipoprotein cholesterol. The ethanol extract at 400mg/kg. b. wt concentration is an excellent lipid lowering agent.

Keywords: *Cucumis pubescens,* Atherogenic diet, total cholesterol, triglycerides, LDL, VLDL, HDL

Introduction
The World Health Organization (WHO) has recently defined traditional medicine (including herbal drug) as comprising therapeutic practices that have been in existence, often for hundreds of years, before the development and spread of modern medicine and are still in use today [1]. Traditional medicine is the synthesis of therapeutic experience of generations of practicing physicians of indigenous systems of medicine. The traditional preparations comprise medicinal plants, minerals, organic matter etc. Herbal drugs constitute only those traditional medicines which primarily use medicinal plant preparations for therapy. The earliest recorded evidence of their use in Indian, Chinese, Egyptian, Greek, Roman and Syrian texts dates back to about 5000 years. The classical Indian texts include Rigveda, Atherveda, Charak Samhita and Sushruta Samhita. The herbal medicines / traditional medicaments have, therefore, been derived from rich traditions of ancient civilizations and scientific heritage.
Herbal medicines are being used by about 80 per cent of the world population primarily in the developing countries for primary health care. They have stood the test of time for their safety, efficacy, cultural acceptability and lesser side effects [2]. Elevation of plasma lipoprotein concentration is called Hyperlipidemia. The plasmalipids of chemical significance are cholesterol (CH) and triglycerides (TG). The clinical sequal of hyperlipidemia are acute pancreatitis, a very serious and may be even fatal condition, and atherosclerosis manifesting in coronary artery disease or cerebrovascular accidents. Hyperlipidemia must be prevented and treated to safeguard against these life-threatening conditions.
Hyperlipidemia is a human disorder due to the increase of triglycerides and lipoproteins in the blood plasma. It is invited by men and women through smoking, obesity, alcohol abuse and diabetes mellitus [3].
Cucumis pubescens Willd. is an annual, prostrate, spreading, stem creeping, angular [4] *C. pubescens* is not cultivated and it grows between other crops as weeds. It can be found between the sorghum and sesame fields. It grows on arid and poor grounds. The species occur throughout drier parts of India. It has hairy stem, yellow flowers and the fruit skin is very variable in colour; yellow, striped green and brown [5, 6]. The plant leaves contains meloside A (6C-diglucosylapigenin), meloside L (6C-diglucosylluteolin) and caffeoyl esters; six carotenes were isolated, three of which identified as α-carotene (182%), β-carotene (94.83%) and γ-carotene (2.30%) [7, 8, 9]. The unripe fruit is bitter, sour; may cause skin eruptions and strangury. The ripe fruit is sweet. The fruit is of different kinds; sweet, acid, sour; tonic laxative, galactagogue, diuretic, diaphoretic; strengthens the heart, the brain and the body in general; cures ophthalmia, urinary discharges [10, 11]. The unripe fruit is cut into small pieces and put in water boiled, filtered and 150 ml of this water is recommended by traditional medicine men to be consumed for hyperlipidemia. The available modern medical treatments induce many side effects.

Hence, the modern physicians recommend dietary, exercise and drugs therapy to control hyperlipidemia. Since, the herbal therapy is neglected by the modern physicians, the present investigation has been taken-up to find out *C. pubescens* Willd plant which are capable of reducing this plasmalipoprotein (cholesterol) concentration in the blood (Hyperlipidemia) and save the humanity from the coronary heart disease.

Materials and Methods

Materials

Cucumis pubescens Willd. is the materials of the present investigation. Fresh unripe fruit of *C. pubescens* was collected from the plant available in Villamuthur village, Perambalur district, Tamil Nadu, India.

Chemicals and reagents

Standard cholesterol kit was obtained from Randox Kits Pvt., Mumbai. Lovastatin a standard anti-hyperlipidemic agent was purchased from Aventis Pharma Ltd., Goa. All other chemicals used were of analytical grade and purchased locally. Distilled water was used for all biochemical assays.

Preparation of powder

Fruit of *C. pubescens* was collected and shade-dried for four days, sun-dried for a day and then stored in black polythene bags. Fruits were powdered in pulverizer as and when required, sieved, labeled and stored in PET bottles [12].

Preparation of plants extracts

Aqueous, Ethanol and Chloroform extracts of fruits were prepared following standard procedures [13]. The powder (500 g) was extracted sequentially with 2.5 litres of water, 2.5 litres of 70 per cent ethanol and 2.5 litres of 60 per cent chloroform in a soxhlet apparatus at 65 °C until the powder became exchausted totally. The resulting extracts were filtered, concentrated and dried in Vacuo. The extracts were stored for use in subsequent experiments.

Pharmacological studies

Animals

Wistar albino adult male rats (150-200 g) randomly bred in the animal house of Periyar Pharmacy College for Girls, Trichirappalli, Tamil Nadu, India were used. Rats were housed in standard polypropylene cages (six animals per cage), maintained under standard laboratory conditions (i.e. 12:12 h light and dark cycle; at an ambient temperature of 25 ± 5°C; 35-60 per cent of relative humidity). Animals were used for the study after prior scrutinization and approval from Institutional Animal Ethical Committee (No.PPCG-IAEC-64/2011-2012). Lovastatin was used as references standard drug. The composition of atherogenic diet used during the study was as given in Table 1.

Group I : Normal diet
Group II : Atherogenic diet containing 1% cholesterol
Group III : Atherogenic diet + Aqueous extract of *C. pubescens* (400 mg/kg/day)
Group IV : Atherogenic diet + Ethanol extract of *C. pubescens* (400 mg/kg/day)
Group V : Atherogenic diet + Chloroform extract of *C. pubescens* (400 mg/kg/day)
Group VI : Atherogenic diet + Lovastatin (5 mg/kg/day)

Table 1: Composition of normal and atherogenic diet

S. No.	Composition	Normal diet (%)	Atherogenic diet (%)
1.	Protein (Milk powder)	12	10
2.	Carbohydrates (Wheat flour)	71	61
3.	Sugar	05	05
4.	Fat (Butter)	05	16
5.	Salts	04	04
6.	Vitamins	01	02
7.	Fibers	02	01
8.	Cholesterol	-	01
	Total weight	100 g	100 g

In order to induce hyperlipidemia, the method reported by Bopanna *et al.* [14] and Dhandapani [15] were followed. The animals were divided into 6 groups of 6 rats each and they received the following diets with or without treatment for 45 days orally.

Test groups were administered aqueous, ethanol and chloroform extracts at a dose of 400 mg/kg/body wt. and lovastatin (5 mg/kg/body wt.) respectively by oral route. At the end of the treatment the rats were fasted overnight, blood was drawn from retro orbital plexus. Serum was separated and stored in refrigerator until assay.

Measurement of serum lipid profile

Total Cholesterol (TC) [16], Total Triglyceride (TG) [17], and Total High Density Lipoprotein (HDL) [18] were estimated by using standard kits of Randox, Mumbai.

Calculation of LDL and VLDL

Low Density Lipoprotein (LDL) and Very Low Density Lipoprotein (VLDL) were calculated by Friedewald's formula [19]. VLDL cholesterol = Triglycerides/5 and LDL cholesterol = Total cholesterol – (VLDL + HDL cholesterol).

Calculation of atheorgenic index

The atherogenic index calculated by using the following formula.

$$\text{Atherogenic index} = \frac{\text{Total serum cholesterol}}{\text{Total serum HDL cholesterol}}$$

Statistical analysis

Data were statistically analysed using one-way ANOVA and expressed as mean ± S.E.M. followed by Dunnett's t-test using computerized Graph pad instate version 3.05, Graph pad software, U.S.A.

Results and Discussion

The results reveal that feeding of atherogenic diet increased serum total cholesterol, triglyceride, LDL and VLDL and decreased serum HDL-cholesterol level when compared to normal group (Group I) at over a period of 45 days (Group II). Administration of 400 mg/kg per day of aqueous, ethanol and chloroform extract of *C. pubescens* showed statistically significant ($P < 0.05$ and $P < 0.01$) decrease in total cholesterol, triglyceride, LDL and VLDL level which was similar to the standard drug of Lovastatin as compared to hyperlipidemic rats (Table-2). An increase of HDL-cholesterol level was also observed. Plant extracts and Lovastatin treated animals showed decrease in the atherogenic index and increased percentage of protecting (Table-3).

Hyperlipidemia is a human disorder due to the increase of

triglycerides and lipoproteins in the blood plasma. It is invited by people through fatty diet, smoking, alcohol abuse and obesity. Indian life style is on the cholesterol path. The WHO estimates that the number of death caused by heart attacks and strokes may increase to 70 lakhs by 2020. Hyperlipidemia is a condition which can be found to be associated with over-weight and obesity. Overweight and obesity are the main risk factors in diseases such as hypertension, non-insulin dependent diabetes mellitus, gallbladder and other types of cancer [20]. It has been established that "Western diets", known for their high fat, high cholesterol, excess energy and low fiber contents, increase serum cholesterol and other lipid levels[21]. It has been reported that complications and diseases associated with hyperlipidemia cause almost 12 million death each year all over the world [22] The major risk due to hyperlipidemia related to atherosclerosis and one of the initial events in this process is the accumulation of cells containing excess lipids within the arterial wall [23].

The consumption of synthetic drugs leads to hyperuricemia, diarrhoea, nausea, myositis, gastric irritation, flushing, dry skin and abnormal liver function [24]. The available modern drugs and treatments for hyperlipidemia are costly and also show many side-effects. Is there are alternative to this? The present investigation was undertaken to find out a safe, cheap, natural and herbal alternative to treat this "top-killer" human disorder.

The present study was initiated to evaluate the hypolipidemic activity of *C. pubescens* in atherogenic diet induced hyperlipidemic rats.

Table 2: Effect of treatment for 45 days with aqueous, ethanol and chloroform extracts of *Cucumis pubescens* Willd. on plasma lipid profile of normal and atherogenic diet induced hyperlipidemic rats (Values expressed as mg/100 ml are mean ± SD of 6 animals)

S. No.	Groups	Total cholesterol	Triglyceride	HDL	VLDL	LDL
1.	Group I (Normal)	159.2 ± 13.38*	50.65 ± 1.07**	49.41 ± 1.84**	10.13 ± 0.42**	59.66 ± 1.09**
2.	Group II (Control) (Atherogenic diet only)	242.04 ± 16.41	180.47 ± 9.81	45.81 ± 1.46	36.07 ± 2.58	160.16 ± 10.48
3.	Group III (Atherogenic diet + Aqueous extract 400 mg/kg)	134.26 ± 12.65**	72.19 ± 2.39**	68.34 ± 2.14**	14.44 ± 1.26**	51.49 ± 8.19**
4.	Group IV (Atherogenic diet + Ethanol extract 400 mg/kg)	138.41 ± 11.54**	80.27 ± 4.36**	72.64 ± 2.18**	16.05 ± 1.88**	45.57 ± 7.09**
5.	Group V (Atherogenic diet + Chloroform extract 400 mg/kg)	143.28 ± 14.82*	85.34 ± 3.18*	66.29 ± 2.10*	17.06 ± 2.34*	59.93 ± 9.43*
6.	Group VI (Atherogenic diet + Lovastatin (5 mg/kg)	130.4 ± 11.92**	69.84 ± 0.73**	88.31 ± 2.46**	13.96 ± 0.29**	28.13 ± 1.28**

Statistical significance in comparison to group – III, IV, V with group II *P<0.05-significant, **P<0.01 – highly significant.

Table 3: Atherogenic index in various groups

S. No.	Groups	Atherogenic index	Protection* (%)
1.	Group I (Normal)	3.222	-
2.	Group II (Control) (Atherogenic diet only)	5.283	-
3.	Group III (Atherogenic diet + Aqueous extract of *C.* pubescens 400 mg/kg)	1.964	62.82
4.	Group IV (Atherogenic diet + Ethanol extract of *C. pubescens* 400 mg/kg)	1.905	63.94
5.	Group V (Atherogenic diet + Chloroform extract of *C. pubescens* 400 mg/kg)	2.610	50.59
6.	Group VI (Atherogenic diet + Lovastatin (5 mg/kg)	1.476	72.06

$$*\text{Protection (\%)} = \frac{\text{Atherogenic index of control} - \text{Atherogenic index treated group}}{\text{Atherogenic index of control}} \times 100$$

Conclusion

It can be concluded from the present data that the levels of total cholesterol, triglyceride, LDL and VLDL which are actually raised in atherogenic diet, can be lowered significantly with the extracts of *C. pubescens*. *Cucumis pubescens* can be utilized for providing dietary management in the prevention of atherosclerosis in hyperlipidemic patients.

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