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EFFECT OF *GARCINIA CAMBOGIA* EXTRACT ON LIPIDS AND LIPOPROTEIN COMPOSITION IN DEXAMETHASONE ADMINISTERED RATS

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Abstract : Dexamethasone (10 mg/kg body weight/day, s.c.) administered rats were treated with or without *Garcinia cambogia* fruit extract (1 g/kg body weight/day, orally) for 8 days. The administration of dexamethasone resulted in marked increase in the levels of triglycerides and cholesterol and free acids in both plasma and liver. The level of phospholipids increased in the plasma but decreased significantly in liver tissue after dexamethasone administration as compared to those in normal rats. The activities of lecithin cholesterol acyl transferase and hepatic lipoprotein lipase were lowered significantly after dexamethasone *per se* administration. The levels of HDL-triglycerides and HDL-cholesterol remained unchanged, while the LDL and VLDL increased significantly in dexamethasone administered rats. The lipid levels were maintained at near normalcy when co-treated with *Garcinia cambogia* extract in dexamethasone administered rats. This study reveals the undesirable changes in lipid profile on dexamethasone administration and the hypolipidemic property of *Garcinia cambogia* extract.

Key words : dexamethasone, *Garcinia cambogia*, lipids, lipoproteins

INTRODUCTION

Glucocorticoid excess is known to evoke plasma lipid elevation but the pattern of changes appears to vary in several species (1). The synthesis of triacylgcerols in liver is stimulated by injection of glucocorticoids in rats and consequently may lead to the production of a fatty liver (2). The accumulation of triglycerides could lead to increased secretion of very low density lipoprotein (VLDL). Increase in VLDL secretion have been reported when dexamethasone, a corticosteroid analogue is injected for several days in rats (3).

Kaur et al (2) reported that dexamethasone administration (10 mg/kg body wt) increases triglycerides level, inducing imbalance in lipid metabolism leading to hyperlipidemia. The study on the levels of plasma lipids, liver tissue lipids and plasma lipoproteins along with the activities of lecithin cholesterol acyl transferase (LCAT)

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and lipoprotein lipase will reveal the toxicity of dexamethasone on lipids and lipoprotein composition.

Rind of the fruits of *Garcinia cambogia* (Gaertn.) Desr. (Clusiaceae) is reportedly useful in the treatment of dyspepsia, hyperdipsia, diarrhoea, dysentery, inflammations, ulcers, and haemorrhoids (4, 5). *Garcinia cambogia* fruit extract containing the principle organic acid, (-)-erythro-L_s-hydroxycitric acid, is a powerful antilipogenic agent (6). The present study aims to determine the lipid lowering efficacy of *Garcinia cambogia* extract on dexamethasone induced changes in lipid metabolism.

METHODS

Chemicals

Dexamethasone sodium phosphate (Decdan, 4 mg per ml I.P.) was purchased from Merind Ltd., Bombay, India. *Garcinia cambogia* fruit extract was obtained from Siris herbex, Vijayawada, India. All other chemicals used were of analytical grade.

Animals

Male albino rats weight 175–200 g were purchased from Fedrick Institute of Plant Protection and Toxicology (FIPPAT), Padappai, Chennai. The animals were housed in plastic bottom cages and allowed free access to standard laboratory chow (Hindustan Lever Foods, Bangalore, India) and water.

Grouping

Group I - Normal control (n = 6)

Group II - Rats given dexamethasone (10 mg/kg body weight, subcutaneously) for 8 days (n = 6).

Group III - Normal rats given *Garcinia cambogia* fruit extract (1 g/kg body weight/day, orally) for 8 days (n = 6).

Group IV - Rats given dexamethasone (10 mg/kg body weight, subcutaneously) co-treated with *Garcinia cambogia* fruit extract (1 g/kg body weight/day, orally) for 8 days (n = 6).

Experimental procedures

Experimental animals were housed in individual cages and were fed with rat pellets. The pellets were weighed, before and after feeding the rat in individual cages. The difference in weight was taken as the measure of food intake.

After the experimental period the overnight fasted experimental rats were weighed and sacrificed by cervical dislocation. The plasma separated from heparinized blood samples was used for various estimations and the weight of the liver was noted.

Plasma Lecithin cholesterol acyl transferase (LCAT) was assayed by the method of Hitz et al (7). Plasma lipoptoteins were separated by a dual precipitation method (8). Total cholesterol (9), free cholesterol (10), ester cholesterol, phospholipids (11, 12) triglycerides (13) and free fatty acids (14) were determined in the plasma. Liver was removed to ice cold containers and a portion of the tissue was

used for lipid extraction (15). Total cholesterol (9), phospholipids (11, 12) triglycerides (13), and the activity of lipoprotein lipase (16) were determined in the liver. Protein was estimated by the method of Lowry et al (17).

Statistical analysis

Students paired and unpaired 't' test and Kruskal-Wallis test were used to assess statistical significance.

RESULTS

Growth and organ weight

After 8 days of treatment, animals in dexamethasone treated group, *Garcinia cambogia* treated group and co-treated group (*Garcinia cambogia* + Dexamethasone) show decrease (55 ± 2.4, 21 ± 1.5, 58 ± 2.3 respectively) in body weight. Food intake was also reduced from 16 g to 8, 13 and 7.5 g/rat/day, respectively in the above groups. The weight of livers were found to be increased in dexamethasone treated rats (3.36 ± 0.26/ 100 g body weight) as compared to those in control group rats (2.62 ± 0.18/100 g body rats weight), *Garcinia cambogia* treated group rats (2.51 ± 0.15) and co-treated group rats (2.74 ± 0.12/100 g body weight).

Lipid and lipoprotein composition

In plasma, significant increases in phospholipids, cholesterol, trigycerides and free fatty acids (FFA) was observed in dexamethasone injected rats (Table I), along with a high level of free cholesterol and low activity of LCAT. The total lipids, triglycerides and cholesterol contents increased in liver (Table II) of dexamethasone treated group, the major effects observed was on hepatic triglycerides which increased from 2.8 to 19.4 mg/g tissue while the phospholipid level decreased significantly (P<0.01). The activity of

TABLE I : Levels of total cholesterol free cholesterol, ester cholesterol, triglycerides, phospholipids, free fatty acids and activity of LCAT in plasma of control and experimental groups[a].

Parameters[b]	*I* *Normal control group (n=6)*	*II* *Dexamethasone treated group (n=6)*	*III* *Garcinia cambogia treated group (n=6)*	*IV* *Dexamethasone + Garcinia cambogia group* (n=6)
Total cholesterol[†]	91.7± 4.9	126.0±5.4[3y]	80.2± 4.1[2]	98.5 ± 4.6[4δ]
Free cholesterol[†]	24.2± 2.6	39.6±2.1[3y]	21.3± 3.2[1]	28.8 ± 2.0[4α]
Ester cholesterol[†]	67.5± 4.3	86.4±4.8[3y]	58.9± 4.6[2]	69.7 ± 3.9[4α]
Triglycerides[†]	78.3± 4.1	101.2±6.7[3y]	69.3± 4.5[2]	82.0 ± 5.3[4δ]
Phospholipids[†]	103.6± 6.2	126.5±7.1[3y]	94.4± 5.6[2]	108.7 ± 6.5[4δ]
Free fatty acid[†]	18.5± 1.5	32.1±1.9[3y]	15.2± 1.3[2]	21.4 ± 1.6[4δ]
LCAT	67.2± 3.8	43.5±4.2[3y]	64.1± 3.9[NS]	60.6 ± 3.4[4δ]

[a]Values are expressed as mean ± SD. [b†]Values are expressed as mg/dl plasma.
[1]P<0.05; [2]P<0.01; [3]P<0.001 as compared to group I; y-0.05 as compared to group I. [4]P<0.001 as compared to group II; δ = 0.05; α-0.10 as compared to group II.
LCAT - nmole cholesterol esterified/hr/ml
NS - Non-significant.

TABLE II : Levels of total lipids, cholesterol, triglycerides, phospholipids, free fatty acids and activity of lipoprotein lipase in the liver of control and experimental groups[a].

Parameters[b]	*I Normal control group (n=6)*	*II Dexamethasone treated group (n=6)*	*III Garcinia cambogia treated group (n=6)*	*IV Dexamethasone + Garcinia cambogia group (n=6)*
Total lipids[†]	62.3± 4.3	78.7±5.2[3y]	56.4± 4.5[1]	67.7 ± 4.8[4δ]
Cholesterol[†]	4.18± 0.46	6.06±1.07[3y]	3.61± 0.32[1]	4.85 ± 0.96[4α]
Triglycerides[†]	3.8± 0.35	12.4±3.16[3y]	3.3± 0.41[1]	4.2 ± 0.71[4δ]
Phospholipids[†]	34.8± 2.5	29.1±2.8[2]	32.6± 2.1[NS]	27.8 ± 1.9[NS]
Free fatty acid[†]	9.5± 0.83	14.8±1.42[3y]	8.2± 0.67[1]	11.4 ± 0.91[4δ]
LPL	5.16± 0.37	3.02±0.26[3y]	5.48± 0.41[NS]	4.63 ± 0.32[4α]

[a]Values are expressed as mean ± SD. [b†]Values are expressed as mg/g tissue.
[1]P<0.05; [2]P<0.01; [3]P<0.001 as compared to group I; y-0.05 as compared to group I . [4]P<0.001 as compared to group II; δ = 0.05; α-0.10 as compared to group II.
LPL - µmole of glycerol liberated/min/g protein.
NS - Non-significant.

TABLE III : Levels of HDL, LDL, VLDL - Cholesterol and triglycerides, lipoprotein fraction in the plasma of control and experimental groups[a]

Parameters[b]	*I Normal control group (n=6)*	*II Dexamethasone treated group (n=6)*	*III Garcinia cambogia treated group (n=6)*	*IV Dexamethasone +Garcinia cambogia group (n=6)*
HDL - Cholesterol	36.40± 2.36	34.2±3.92[NS]	33.7± 2.84[NS]	31.6 ± 3.12[NS]
HDL -Triglycerides	28.7± 2.31	31.5±3.90[NS]	26.8± 2.10[NS]	29.2 ± 2.68[NS]
LDL - Cholesterol	30.3± 3.28	46.5±4.73[2y]	25.1± 3.04[1]	34.6 ± 3.20[4α]
LDL - Triglycerides	17.4± 1.41	30.3±2.90[2y]	15.2± 1.15[1]	18.1 ± 1.26[4δ]
VLDL - Cholesterol	18.5± 1.8	43.7±2.1[2y]	15.9± 1.6[1]	21.6 ± 1.97[4δ]
VLDL - Triglycerides	15.2± 2.71	24.6±2.36[2y]	12.1± 2.54[NS]	18.5 ± 2.68[3α]

[a]Values are expressed as mean ± SD. [b]Values are expressed as mg/dl plasma.
[1]P<0.05; [2]P<0.001; as compared to group I; y-0.05 as compared to group I . [3]P<0.01; [4]P<0.001 as compared to group II; δ = 0.05; α-0.10 as compared to group II.
NS - Non-significant.

hepatic lipoprotein lipase was observed to be decreased after dexamethasone administration (group II). In plasma, LDL and VLDL triglycerides, cholesterol increased in concentration (Table III) significantly (P<0.001) in dexamethasone injected rats (group II), but HDL concentration showed no significant changes. *Garcinia cambogia* treated group showed significant (P<0.01) reduction in the levels of various lipid levels (group III) in the plasma, and marginal reduction in the liver. Co-treatment with *Garcinia cambogia* (group IV) significantly decreased the levels of lipids both in plasma and liver tissue, and the activity of LCAT and lipoprotein lipase (LPL) (Tables I and II) was also maintained near normalcy, thereby reducing the elevation in plasma lipoproteins (Table III).

DISCUSSION

On administering cortisone the development of fatty liver has been reported (2). The increase in liver weights could be attributed to a rapid mobilization of depot fat under the influence of glucocorticoids rendering more fatty acids available for deposition in the form of triglycerides (3). The enormous increase in triglycerides from 2.8 to 19.4 mg/g tissue in liver of dexamethasone treated rats may be due to the enhancement of the activities of the key enzymes of fatty acid synthesis (1).

A significant increase in the level of triglycerides, cholesterol and phospholipids is generally observed in the plasma of dexamethasone administered rats (1). The observed increase in triglycerides and cholesterol may be due to the increase in plasma VLDL. Cotreatment with *Garcinia cambogia* extract reduced serum triglyceride levels, hepatic lipogenesis (18) and depressed the cholesterol synthesis through its activity as a potent inhibitor of ATP-citrate lyase (19).

Dexamethasone administered rats have shown an increase in free cholesterol along with the decrease in the activity of LCAT, while rats on cotreatment with *Garcinia cambogia* have maintained near normal level of plasma free cholesterol along with near normalcy in LCAT activity. The low level of lipoprotein lipase activity in the liver may be responsible for low degradation of lipoprotein, triglycerides and cholesterol. The hyperlipidemic effect of dexamethasone was minimized by co-treatment with *Garcinia cambogia* fruit extract (group IV).

The corticoid treatment is known to increase the secretion of VLDL by liver, and in addition corticoids may also stimulate VLDL formation by the intestine (1), moreover the activity of hepatic lipoprotein lipase has been shown to be depressed in rats after administering glucocorticoids (20) which will inhibit the removal of VLDL from plasma and contribute to an increase in the level of plasma VLDL. Hepatic lipoprotein lipase selectively hydrolyses the VLDL - TG forming partial glycerides and free fatty acids (21). The low level of liver LPL activity could have been responsible for the high VLDL - TG level (1) in dexamethasone administered rats. Cotreatment with *Garcinia cambogia* extract maintained the activity of LPL of near normalcy thereby preventing a rise of VLDL and LDL levels in the plasma.

Garcinia cambogia which contain the principle organic acid (-)-erythro-L_s-hydroxycitric acid is an effective antilipogenic agent (22) since :

a. it is a potent competitive inhibitor of enzyme ATP-citrate lyase (23), thereby reduces acetyl CoA production,

b. it inhibits hepatic fatty acid and cholesterol synthesis and reduces circulating triglycerides and cholesterol levels.

c. it converts the excess lipids in blood to glycogen (through gluconeogenesis) which is stored in the liver (6), and

d. it alters the activities of lipid metabolising LCAT and LPL.

The accumulation of lipids in liver and hyperlipidemia of dexamethasone administered rats might be responsible for functional disorders. *Garcinia cambogia* has

been proved to be successful in preventing fat accumulation both *in vitro* and *in vivo* (25, 26). The present study suggests that *Garcinia cambogia* on cotreatment with dexamethasone reduced the significant alterations in the lipid level therapy preventing the risk factors associated with hyperlipidemia.

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