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HYPOLIPIDEMIC ACTIVITY OF *ALOE VERA* IN HYPERLIPIDEMIC RATS

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ABSTRACT: The hypolipidemic activity of *Aloe vera* (Family**:** Liliaceae) extract has been studied in two models of hyperlipidemia in rats. In an acute model, hyperlipidemia was induced by injecting a single dose of triton WR-1339 (400mg/kg, b.w.) intraperitoneally in rats. Feeding with *Aloe vera* extract at the dose of 500 mg/ kg, b.w. exerted a significant lipid-lowering effect as assessed by the reversal of plasma levels of total cholesterol (TC), phospholipids (PL), triglyceride (TG) and reactivation of post-heparin lipolytic activity (PHLA). In the chronic model, hyperlipidemia was induced by feeding with cholesterol-rich- HFD in rats. The treatment with seeds extracts of *Aloe vera* (500 mg/ kg b.w) simultaneously for 15 days also caused lowering of lipid levels in plasma and liver following reactivation of plasma post-heparin lipolytic activity and hepatic lipoprotein lipase activity in animals. The hypolipidemic activity of *Aloe vera* was compared with a standard drug guggulipid (200 mg/ kg, b.w.) in both models.

INTRODUCTION: Aloes are members of the Liliaceae family and are mostly succulent with a whorl of elongated, pointed leaves [1]. Taxonomists now refer to Aloe barb and enosis as *A. vera*. The central bulk of the leaf contains colorless mucilaginous pulp, made up of large, thin-walled mesophyll cells containing the *A. vera* gel itself.

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Despite its extensive use as a folk remedy over a long period, the biochemical details of its action as physiological/Path physiological functions have not been systematically investigated.

The National Health Interview Survey revealed that out of 10 adults in the United States age 18 and older used a form of complementary and alternative medicine (CAM) in 2007. *Aloe vera* use has been reported in 8.5-13.8% of predominantly Hispanic populations in the Southern United State. *Aloe vera* in used just as frequently outside the United States by 10.8%, 10.3% and 7.6 % of adults in Australia, Italy, and Jamaica, respectively, according to Surveys.

It is often used in ointments, Creams, and lotions intended for wound healing or skin protection. The International Aloe Science Council (IASC) describes three components of the plant that are used: leaf Juice (whole leaf as the Starting point), inner leaf juice (from the inner gel fillet), and aloe latex (Yellow-brown sap between the inner parenchymal tissues). Good Scientific evidence exists for beneficial effects of topical *Aloe vera* in genital herpes, psoriasis vulgaris, and seborrheic dermatitis. Monographs from Health Canada, the German Commissions, and the World Health Organization recognize the use of oral *Aloe vera* as a laxative. In an evaluation of children with diabetes mellitus (type-1) from Turkey and Germany, *Aloe vera* was one of the most commonly consumed herbal medicines used by 12.9% and 7.3% of the patients' respectively [1].

MATERIAL AND METHODS:

Preparation of *Aloe vera* Extract: *Aloe vera* were collected from a local area of Lucknow and identified taxonomically by Department of Pharmacology, Era's Lucknow Medical College Lucknow. A voucher specimen (AV-005/10) was also submitted. Seeds were crushed and dried under shade. The powder (500g) was extracted with 95 % ethanol in a Soxhlet extractor for 72 h, the extract was concentrated to dryness under reduced pressure and controlled temperature (50-60°C), yielding 23g of reddish brown solid (crude extract). This was stored in a refrigerator and used to investigate hypolipidemic activity in rats. Triton WR 1339, deoxycholic acid, cholesterol, and heparin were procured from Sigma Chemical Company, St. Louis, MO, USA. Guggulipid, a potent lipid-lowering agent from the gum resin of *Commephora mukul* (guggul) developed in Central Drug Research Institute, Lucknow, was used as a standard drug [2].

Preparation of Cholesterol Rich- High-Fat Diet: Deoxycholic acid (5g) was mixed thoroughly with 700g of powdered rat chow diet supplied by Ashirvad Industries, Chandigarh, India. Simultaneously cholesterol (5g) was dissolved in 300g warm coconut oil. This oil solution of cholesterol was added slowly into the powdered mixture to obtain a homogeneous soft cake. This cholesterol-rich -high-fat diet (HFD) was molded in the shape of the pellet of about 3g each [3].

Animals: *In-vivo* experiments were conducted as per guidelines provided by the Animal Ethics Committee of Central Drug Research Institute, Lucknow, India. Male adult rats of Charles Foster strain (200-225g) bred in the animal house of the Institute were used. The animals were housed in polypropylene cages and kept in uniform hygienic conditions, temperature 25-26 °C, relative humidity 50-60% and 12/12 h light/dark cycle (light from 8:00 am to 8:00 pm) and provided with standard rat pellet diet and water *ad libitum*.

Triton and Cholesterol Rich- HFD Induced Hyperlipidemia: The rats were divided into four groups having six animals in each as follows: control, hyperlipidemic, hyperlipidemic treated with *Aloe vera* or guggulipid. In the acute experiment to induce hyperlipidemia, triton WR-1339 was administered (400 mg/ kg b.w., p.o.) by intraperitoneal injection. *Aloe vera* extract and guggulipid were macerated with aqueous gum acacia (1 % w/v) suspension and fed orally at the doses of 500 and 200 mg/kg, b.w., respectively, simultaneously with triton. Control animals received the same amount of vehicle. The diet was withdrawn, and blood from fasted rats was collected after 18 h.

Animals were anesthetized with thiopentone solution (50 mg/ kg b.w., i.p.), prepared in normal saline. Heparin (10mg/ml) in normal saline was prepared and injected to each rat (1mg/kg, b.w.) through the tail vein. After 15 min, blood was withdrawn from retro-orbital plexus using glass capillary in EDTA coated tubes. In the chronic experiment, hyperlipidemia was produced by feeding with cholesterol-rich-HFD for 15 days. Drugs were administered orally once daily at the same doses as above, simultaneously, with cholesterol-rich-HFD in the drug-treated groups. Control animals, kept over normal rat pellet diet, received the same amount of vehicle.

At the end of the experiment, rats were fasted overnight and anesthetized. Blood was withdrawn just after 15 min of heparin treatment. After that, animals were sacrificed, the liver was excised promptly, washed with cold 0.15 M KCl and kept at –40 °C till analyses. Blood was centrifuged and plasma was taken.

Biochemical analysis of plasma and Liver: Plasma Post heparin lipolytic activity (PHLA) was assayed in plasma spectrophotometrically using intralipid as artificial substrate[4]. Plasma was diluted with normal saline in a ratio of 1:3 and used for the analysis of total cholesterol (TC), phospholipids (PL) and triglyceride (TG) using standard enzymatic kits supplied by Merck India Ltd. Mumbai India [5, 6, 7]. The liver was homogenized (10% w/v) in cold 100mM phosphate buffer pH 7.2 and used for the assay of lipoprotein lipase (LPL) activity[4]. The lipid extract of each homogenate prepared in a mixture of $CHCl_3$: CH_3OH (2:1, v/v) was used for estimation of TC, PL, and TG. Plasma and tissue were also estimated for protein content [8].

Statistical Analysis: One way analysis of variance (ANOVA) was performed by comparison of values for hyperlipidemic groups with control, hyperlipidemic and drug-treated groups with hyperlipidemic All hypothesis testing were two-tailed. P<0.05 was considered statistically significant, and results were expressed as mean ± SD of six rats. The graph pad INSTAT 3.0 software carried out statistically analysis [9].

RESULTS AND DISCUSSION:

Effect of *Aloe vera* Extract in Triton Induced Hyperlipidemia: The data in **Table 1** shows that acute administration of triton WR-1339 in rats caused marked increase in their plasma levels of TC (168%), PL (187%) and TG (176%) following inhibition of PHLA by 31%. Treatment with *Aloe vera* extract at the dose of 500mg/kg, b.w., caused a decrease in these levels of TC, PL and TG by 28, 25 and 26% respectively, simultaneously with reactivation of PHLA by 22%. However, lipid-lowering action of guggulipid even at a lower dose of 200mg/kg b.w. was comparatively higher (33-40%) to that of *Aloe vera* extract.

TABLE 1: EFFECT OF *ALOE VERA* EXTRACT AND GUGGULIPID ON PLASMA-LIPIDS IN TRITON INDUCED HYPERLIPIDEMIA IN RATS

Groups	Total Cholesterol (mg/dl)	Phospholipids (mg/dl)	Triglyceride (mg/dl)	Post heparin lipolytic activity (nmol FFA released/h/L)
Control	90.52±6.11	84.46±3.33	90.66±8.69	16.89 ± 0.95
Triton treated	234.60***±12.09 (+168)	235.89***±12.09 (+186)	250.57***±24.86 (+176)	11.56** ± 1.34 (-31)
Triton + *Aloe vera* (500mg/kg, b.w.)	169.87**±6.14 (-28)	177.89**±8.69 (-25)	185.88**±12.80 (-26)	14.11* ± 0.70 (+22)
Triton + Guggulipid (200mg/kg, b.w.)	153.13***±8.65 (-39)	159.14***±7.85 (-33)	149.14***±8.23 (-40)	14.36* ± 0.68 (+25)

Values are expressed as mean ± SD. Triton treated group as compared with control, triton and drug-treated with triton. Values in parenthesis indicate percent change. *P<0.05; **P<0.01; ***P<0.001.

Effect of *Aloe vera* Extract in Cholesterol-Rich-HFD Induced Hyperlipidemia: In this model of hyperlipidemia **Table 2**, feeding with cholesterol-rich- HFD in rats caused a significant increase in their plasma levels of TC (135%), PL (72%) and TG (119%) following inhibition of PHLA by 32%. Treatment with *Aloe vera* extract for 15 days, reversed these plasma levels of TC, PL, and TG by 25, 21 and 31%, respectively, simultaneously with reactivation of PHLA by 21%. The hypolipidemic action of *Aloe vera* at the dose of 500 mg/kg, b.w., was comparable to that of guggulipid at the dose of 200 mg/kg b.w.

TABLE 2: EFFECT OF *ALOE VERA* EXTRACT AND GUGGULIPID ON PLASMA-LIPIDS IN CHOLESTEROL RICH-HFD INDUCED HYPERLIPIDEMIA IN RATS

Groups	Total Cholesterol (mg/dl)	Phospholipids (mg/dl)	Triglyceride (mg/dl)	Post heparin lipolytic activity (nmol FFA released/h/L)
Control	88.59±6.98	80.62±4.29	114.80±11.30	19.31±1.30
Cholesterol rich- HFD treated	208.18***±22.10 (+135)	138.27***±24.86 (+72)	251.35***±24.59 (+120)	13.11**±1.18 (-33)
Cholesterol rich -HFD + *Aloe vera* (500mg/kg, b.w.)	155.36**±11.13 (-25)	108.86*±6.78 (-21)	172.88**±6.49 (-31)	15.88*±1.78 (+21)
Cholesterol rich- HFD+ Guggulipid (200 mg/kg, b.w.)	153.39**±8.83 (-28)	100.30**±8.77 (-28)	169.92**±6.09 (-32)	16.33 * ± 1.64 (-25)

Values are expressed as mean ± SD. Cholesterol-rich-HFD treated group is compared with control, cholesterol-rich-HFD, and drug-treated groups with cholesterol-rich-HFD. Values in parenthesis indicate percent change. *P<0.05; **P<0.01; ***P<0.001.

Effect of *Aloe vera* Extract in Cholesterol-Rich-HFD Induced Steosis in Liver: Feeding with cholesterol-rich- HFD in rats also caused accumulation of TC (53%), PL (72%) and TG (57%) following diminution of LPL activity by 37% in their liver **Table 3**. However, treatment with *Aloe vera* extract exerted a decrease in these levels of TC, PL and TG by 26, 22 and 29%, respectively, following reactivation of LPL activity (26%) in hyperlipidemic animals. Guggulipid was more effective hypolipidemic than *Aloe vera*, as it could decrease the level of lipids by 26 to 40%, following reactivation of LPL activity (29%) in the liver of hyperlipidemic rats.

TABLE 3: EFFECT OF *ALOE VERA* EXTRACT AND GUGGULIPID ON LIVER LIPID IN CHOLESTEROL RICH-HFD INDUCED HYPERLIPIDEMIA IN RATS

Groups	Total Cholesterol (mg/dl)	Phospholipids (mg/dl)	Triglyceride (mg/dl)	Post heparin lipolytic activity (nmol FFA released/h/L)
Control	6.75±0.30	22.43±2.71	4.54±0.38	79.85±4.82
Cholesterol rich- HFD	10.33***±0.62	38.58***±5.33	8.56***±1.02	50.26***±2.72
treated	(+53)	(+72)	(+87)	(-37)
Cholesterol rich- HFD + *Aloe Vera* (500mg/kg, b.w.)	7.67**±0.62	29.40**±3.60	5.22***±0.74	63.09*±3.75
	(-26)	(-24)	(-39)	(+25)
Cholesterol rich-HFD + Guggulipid (200mg/kg, b.w.)	7.36**±0.90	28.47**±5.04	5.11***±0.62	64.99**±4.66
	(-29)	(-26)	(-40)	(-30)

Values are expressed as mean ± SD. Cholesterol-rich- HFD treated group is compared with control, cholesterol-rich-HFD, and drug-treated groups with cholesterol-rich-HFD. Values in parenthesis indicate percent change. *P<0.05; **P<0.01; ***P<0.001.

Triton WR-1339 acts as a surfactant and suppresses the action of lipases to block the uptake of lipoproteins from circulation by extrahepatic tissues, resulting in increased blood lipid concentration [10]. The lipid-lowering effect caused by feeding with *Aloe vera* extract, as in the case of guggulipid, may be due to early clearance of lipids from circulation in triton model and it may be due to reactivation of lipolytic enzymes as evidenced by increased plasma PHLA [11]. We have successfully used this model for the evaluation of the lipid-lowering activity of some natural products [12, 13]. The present investigation with cholesterol-rich–HFD fed hyperlipidemic animals showed that *Aloe vera* extract could stimulate PHLA and hepatic LPL activity, both of which play a key role in lipid catabolism and their utilization in body [14]. This situation imposed by feeding with the test sample may be responsible for the decrease in the level of plasma and liver lipids in this model. We have reported that hypolipidemic action of guggulsterone, the active principle of guggulipid, is mediated through activation of PHLA, LPL, and lecithin cholesterol acyltransferase activities, inhibition of hepatic cholesterol biosynthesis, and increased fecal bile acid excretion [13]. The same mechanisms may also interplay to cause the hypolipidemic effect of *Aloe vera* extract.

CONCLUSION: In the present study, we have tested crude extract of *Aloe vera* which, however, upon research and development, may produce a more potent lipid-lowering natural product or a pure compound like guggulipid/ guggulsterone from *Commephora mukul*. Further, work on drug metabolism and to assess the biological activity *in-vivo* and *in-vitro* of *Aloe vera* and its fraction is in progress to substantiate the present findings.

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CONFLICT OF INTEREST: Nil

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