ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACEUTICAL SCIENCES

Published by JK Welfare & Pharmascope Foundation Journal Home Page: www.ijrps.com

Pharmacological screening of anti-diabetic and antihyperlipidemic activity of aqueous extracts of leaves of *Aloe barbadensis*

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Article History:

Received on: 20 Jul 2020
Revised on: 18 Aug 2020
Accepted on: 23 Sep 2020

Keywords:

Aloe barbadensis, Diabetes Mellitus, Oral Hypoglycemic Agent, Glucose Tolerance, Antilipidemic, Alloxan, Glibenclamide

ABSTRACT

The present study was to estimate the anti-diabetic and antihyperlipidemic activity of aqueous extract of leaves of plant *Aloe barbadensis.I*n alloxan-induced diabetes in rats, the research examined six groups of six male wister rats every to value the hypoglycaemic effect of the barbadensis (ALEC) exposed to hostile to diabetic action in rodents where alloxan monohydrates were utilized as a portion of 120.00 mg/kg in intraperitoneal portion as a diabetogenic specialist to an acquainted diabetic with test rodents. In sub intense, treatment, bunch blood glucose levels are seen on 14.00th, 21.00th and 30.00th-day present treatment compare on typical control in diabetic control checked expanded blood glucose level was watched, with dosages of 100.00, 250.00 and 500.00 mg/kg b.w. A portion of 500.00 mg/kg b.w/day was seen as having the most significant activity. Glibenclamide was applied as a standard drug, and the outcome was compared about it. In the anti-hyperlipidemic activity, serum cholesterol levels were recorded at aqueous extracts of 100.00, 250.00 and 500.00 mg/kg, on 30.00th-day post-treatment. Serum cholesterol levels were ordinary benchmark groups was 107.70±01.21 mg/dl diabetic control 178.50±01.04 mg/dl and standard medications treatment bunches was 111.30±02.40 mg/dl and ALEC treatment bunches were 171.20±01.03 mg/dl, 145.80±02.92 mg/dl and 118.80±03.86 mg/dl for 100.00, 250.00 and 500.00 mg/kg separately. The results show that the aqueous extract of *Aloe barbadensis* has significant and continuous oral hypoglycaemic activity, equivalent to the hypoglycaemic result of glibenclamide, a sulfonylurea derivative and hyperlipidemic activity. Extracts also confirmed antihyperlipidaemic possible of the plant extract is establish to be comparable with that of the standard.

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ISSN: 0975-7538

DOI: https://doi.org/10.26452/ijrps.v11iSPL4.4265

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INTRODUCTION

Diabetes Mellitus (D.M.) is a major metabolic disorder considered by chronic hyperglycemia as an outcome of a relative or entire lack of insulin or the actions of insulin (Tripathi and Srivastava, 2006). The state affects the metabolism of carbohydrates, protein, fat, water and electrolytes leading to structural variations in a range of cells especially those of the vascular system, consequently leading to long-term problems of diabetes (Blaak *et al.*, 2012). Diabetes is the most public of the endocrine complaints. It is appraised that there are presently 285 mil-

lion people worldwide, and this number is usually to rise to 438 million by the year 2030 (Shaw *et al.*, 2010). India has the peak number of patients with known diabetes worldwide, with a spread of 11.6%. Most of these cases will be type 2 diabetes, which is highly related to an inactive lifestyle and high calorie-nutrition and obesity (Verma, 2012). On the foundation of the aetiology, type 1 may be due to immunological devastation of pancreatic β cells causing in insulin deficiency. Its pathogenesis includes environmental activates that may stimulate autoimmune mechanisms in genetically susceptible persons, leading to progressive loss of pancreatic islet β cells (Aathira, 2014). Various of the severe belongings of this disease can be controlled by insulin replacement treatment, but there are long-term adverse effects on blood vessels, nerves and other organ systems. Type 2 D.M. is connected with both reduced insulin secretion and insulin resistance. Type 2 D.M. is a more predominant form of the disease and shared in individuals over 40 years of age. It is often connected with obesity and hereditary disposition.

Diabetes generally impacts or upsets a more significant part of the basic body framework as a result of irregularity of blood glucose level in the body (American Diabetes Association, 2009). Metabolic unsettling influence related to a high danger of retinopathy cardiovascular aggravation full-scale vascular turmoil thickening of carotid oxidative pressure other related with endothelial brokenness (Wadker *et al.*, 2008). Pathogenesis basic being developed of diabetes is, for the most part, connected with beta cells of the pancreas. Because of the absence of insulin carbohydrates are not used appropriately in the body, or insulin resistance happens (Wilcox, 2005).

Hyperlipidemia is a condition when significant abnormal levels of lipids, i.e. greasy substance, are found in the blood. This condition is additionally called hypercholesterolemia or hyperlipoproteinemia (Amit *et al.*, 2011). The human body is mind-boggling hardware and for keeping up homeostasis of different organ and organ framework. Potential medicines for lipid issue incorporate dietary changes, decrease in weight, regular exercise, discontinuance of smoking, drugs and standard lipid screenings (Kotas and Medzhitov, 2015).

More than 1200 plants species are world wild use in diabetes phytotherapy and experimental studies support the hypoglycaemic activity of a large number of these plants. In addition to the correction of blood glucose levels, several hypoglycaemic plants are potential in ameliorating lipid metabolism abnormalities of diabetes mellitus. Thus, the study of plant hypoglycaemic activities of aqueous and alcoholic extract may give a new pharmacological approach in the treatment of diabetes mellitus (Patel *et al.*, 2012).

Numerous plants had potent hypolipidemic property because of the quality of Flavonoids, and Phenolic mixes just as certain glycosides were accounted for to have against the hyperlipidemic property. Aloe vera (A. barbadensis), enduring succulent xerophyte, having a place with a group of Liliaceae. The Sanskrit name of Aloe vera, i.e., Kumari truly signifies 'young lady'. Aloin is broadly used to direct menstrual stream. According to Ayurveda, it conciliates Apana Vata, which controls the monthly cycle (Tiwari and Upadhayay, 2018). It has hostile to uncontrollable property that diminishes menstrual inconvenience. It has been asserted that A. vera plant can fix gastric ulcers or secure against its arrangement in two creatures and people. Be that as it may, it was additionally indicated that aloe gel couldn't forestall ethanol-initiated gastric injuries in rodents, hostile to ulcer exercises of A. vera has been ascribed to few potential components including its calming properties, recuperating impacts, bodily fluid stimulatory impacts and guideline of gastric emissions (Suvitayavat *et al.*, 2004). Hepatoprotective activity was likewise ascribed to protecting utilizing proteins of the liver through cell reinforcement movement (Chandan *et al.*, 2007). The phytochemical screening of fluid concentrate of A. vera plant has uncovered nearness of alkaloids, anthraquinones, phenols, saponins, sugars, starch, glucose, amino acids, proteins, cell reinforcements and cancer prevention agent chemicals demonstrating nearness of pharmacologically significant phytochemicals.

Aloe vera has additionally been appeared to have anti-diabetic and hypoglycemic properties (Okyar *et al.*, 2001). Oral organization of Aloe vera may be valuable subordinate for bringing down blood glucose in diabetic patients just as for diminishing blood lipid levels in patients with hyperlipidemia.

MATERIALS AND METHODS

Plant material

The leaves of Aloe were collected around the regional area. The leaves were dried under shade, subjected to the soxhlet extraction procedure. The dried leaves extracts were freshly re-dissolved in normal saline and given to animals.

Animals

Male Wistar Rodents of each sex weighing 150-200g

were used for Alloxan-induced anti-diabetic activity. All rats fasted for 72 hours before the experiments. Each experimental group consisted of five animals housed in separate cages.

Experimental design

In the experiment, the rodents were divided into 6 groups of 6 rodents each. Group I – Normal control rodents; Group II – Alloxan treated control rodents (120.00 mg/kg b.wt); Group III – Alloxan + standard medication Glibenclamide (10.00 mg/kg b.wt); Group IV – alloxan + aq.extract of A. barbadensis (100.00 mg/kg b.wt); Group V–alloxan +aq. extract of A. barbadensis (250.00 mg/kg b.wt); Group VI-Alloxan + aq. extract of A. barbadensis (500.00 mg/kg b.wt) (Jain and Arya, 2011).

Induction of diabetes

Type II diabetes was initiated to pale skinned person rodents by solitary intraperitoneal (i.p) infusion of alloxan monohydrate (120.00 mg/kg b.wt) in typical clean saline (00.90%). The diabetic state was resolved following 3.00 days of allocation by high blood glucose level and loss of body weight. Toward the finish of the tenth day for intense treatment and 30th day's sub intense treatment, blood glucose level was evaluated by one touch glucometer and rodents were relinquished under chloroform sedation (Sancheti *et al.*, 2011).

Determination of blood glucose levels

Acute treatment was performed for 10.00 days. Furthermore, adorable sub treatment was done at 01 months. Toward the finish of 30^{th} day's treatment, blood glucose level was assessed by one touch glucometer and rodents were yielded under chloroform sedation. Blood was gathered and centrifuged at 3000.00 rpm for 20.00 minutes to isolate serum. The liver was expelled and washed with super cold typical saline (00.90 %) to evacuate the blood. Around 1.00 g of liver tissue was homogenized utilizing 00.10 M Tris – HCl cushion at pH 04.70, and the supernatant was isolated. Serum and supernatant were utilized to break down biological parameters inside 01 day of penance. Above strategy are followed for sub intense treatment gathering. For sub intense gathering blood tests were gathered on 30th day of treatment.

Statistical analysis

Blood glucose levels for each group were expressed in mg/dl as mean $\pm$ SEM. The data were statistically analyzed using ANOVA with multiply comparisons versus the control group.

RESULTS AND DISCUSSION

Phytochemical Study.

In Preliminary phytochemical examination of fluid leaves, a concentrate of A. barbadensis showed positive subjective test for tannins, phenols, flavonoids quercetin and starches. Tests for proteins are negative, and saponin additionally discovered missing in aqueous extract and isolation was finished by HPTCL.

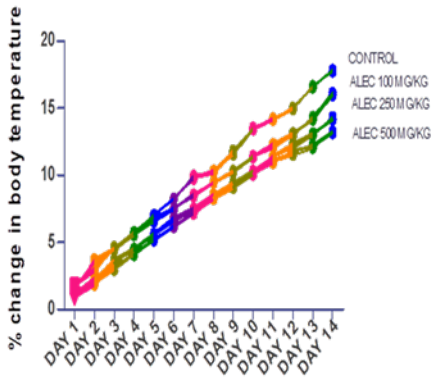
Acute Toxicity studies

In current examination creatures utilized were permitted to get to ordinary nourishment and water admission. Tangible movement, engine action, refluxes and skeletal muscle action was likewise ordinary in all examination creatures. There is no significant impact on body weight watched. All rodents were ordinary all through examination and no mortality observed following 14.00 day of the test period (Graph 1).

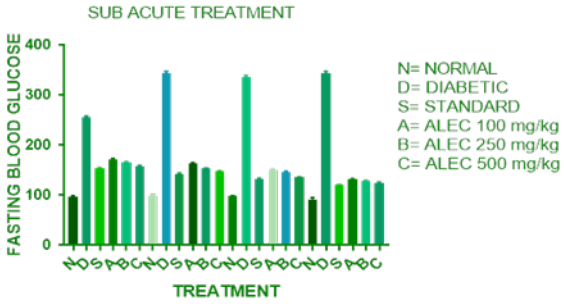
Anti-diabetic Studies

Alloxan (120.00 mg/kg b.w) was found to initiate diabetes in rodents as prove by expanded glucose levelling in blood and studied for ten days and thirty-days treatment, respectively. In alloxan-induced diabetic models Revealed portion subordinate anti-diabetic potential in rodents with dosages of 100.00, 250.00 and 500.00 mg/kg b.w. A portion of 500.00 mg/kg b.w/day was seen as having the most significant activity, and the impact was seen equivalent to levels of blood glucose with standard anti-diabetic medicate glibenclamide, significantly turned around a decline in body weight found in diabetes. Glibenclamide, utilized as standard anti-diabetic tranquillize, was seen as progressively powerful as it essentially diminished blood glucose levels while it had a non-huge impact on different parameters (West E, 1996). We were looking at both outcomes we presume that the most significant impact was found in sub intense treatment bunches at portion 500.00 mg/kg.

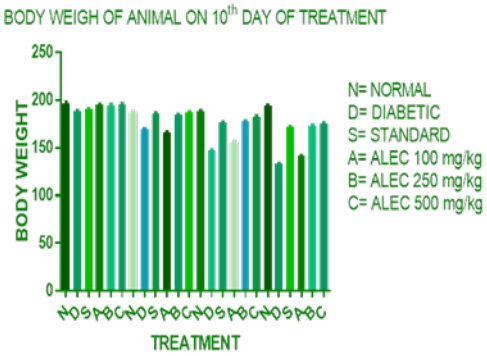
Aqueous extracts of A. barbadensis (ALEC) was exposed to hostile to diabetic action in rodents where alloxan monohydrates were utilized as a portion of 120.00 mg/kg in intraperitoneal portion as a diabetogenic specialist to an acquainted diabetic with test rodents. In intense sub treatment, bunch blood glucose levels are seen on 14.00th, 21.00th, and 30.00th-day present treatment compare on typical control in diabetic control checked expanded blood glucose levels was watched. ALEC portion of 100.00 mg/kg caused a decrease in blood glucose level; however, outcomes were found measurably non-significant. The fluid leaves concentrate



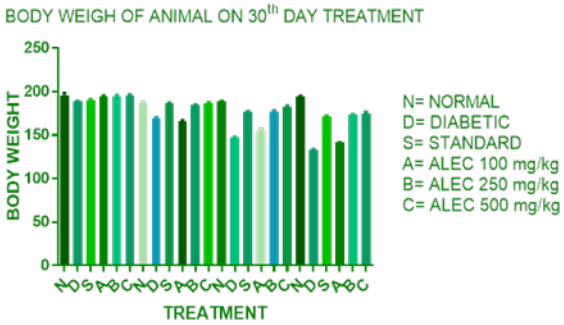
Graph: 1- Effect of aqueous leaf extract of A. barbadensis (ALEC) on percentage body weight rise in repeated 14.00 days oral toxicity study



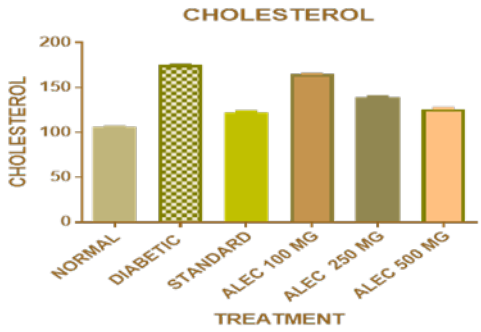
Graph: 2a- Effect of ALEC on fasting blood glucose level on sub-acute alloxan treatment group



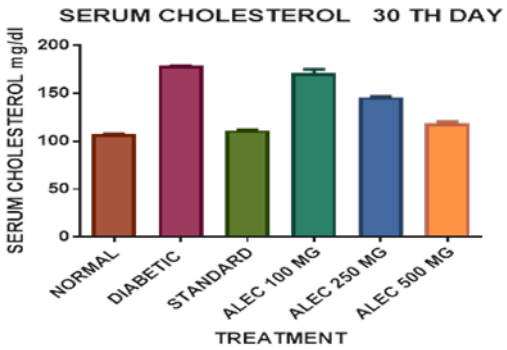
Graph: 2b- Effect of ALEC on body weight in the acute alloxan treatment group



Graph: 2c- Effect of ALEC on body weight in sub-acute alloxan treatment group



Graph: 3a- Effect of ALEC on cholesterol



Graph: 3b- Effect of ALEC on cholesterol

Graph 1: Effect of ALEC

of A. barbadensis at portion 250.00 mg/kg cause decrease in blood glucose level; however, contrast with 500.00 mg/kg 250.00 was less yet both are noteworthy. On 14.00th 21.00th and 30.00th-day post-treatment with ALEC produce portion reliance against hyperglycemic action. A portion of 100.00 mg/kg was found non-importance contrast and reference standard medications are glibenclamide. Anti-diabetic action was discovered portion subordinate 500.00 mg/kg was watched progressively noteworthy (Graph 1 - 2a, 2b & 2c).

Anti Hyperlipidemic Activity

The current investigation additionally confirmed the antihyperlipidemic activity of A. barbadensis, at portion 100.00 mg/kg of p.o to hyperlipidemia to the animal group brought about diminished of all-out cholesterol, triglyceride, LDL cholesterol, VLDL cholesterol with treated with 250.00 mg/kg of ALEC treatment huge decrease in all-out cholesterol, triglyceride, LDL cholesterol VLDL cholesterol and atherogenic list. With 500.00 mg/kg/p.o organizations of fluid leaves concentrated of A. barbaden-

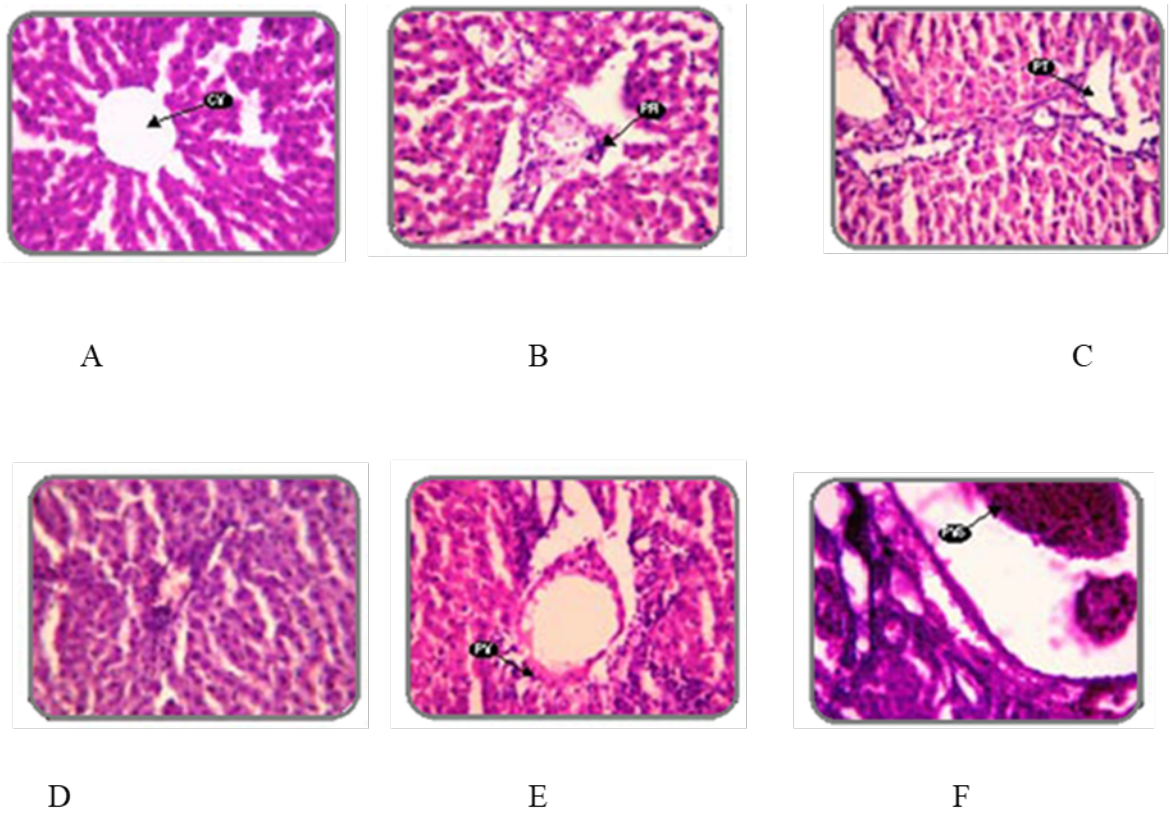


Figure 1: Histopathology of the liver in an alloxan-induced diabetic animal after treatment with ALEC of different dose

sis treatment increasingly huge decrease in complete cholesterol triglycerides LDL cholesterol VLDL cholesterol atherogenic list and faecal cholesterol discharge and expanded in HDL cholesterol was portion needy and successful (West *et al.*, 1996). ALEC at a portion of 100.00, 250.00 and 500.00 mg/kg, on 30.00th-day post-treatment. Serum cholesterol levels of all gatherings are recorded. Serum cholesterol levels were ordinary benchmark groups was 107.70±01.21 mg/dl diabetic control 178.50±01.04 mg/dl and standard medications treatment bunches was 111.30±02.40 mg/dl and ALEC treatment bunches were 171.20±01.03 mg/dl, 145.80±02.92 mg/dl and 118.80±03.86 mg/dl for 100.00, 250.00 and 500.00 mg/kg separately. From this information, we watched stamped expanded in serum cholesterol level in diabetic control contrast with ordinary control rodent (Graph 1 - 3a & 3b).

Histopathology

Aqueous extracts of leaves of A. barbadensis when regulated (100.00, 250.00 and 500.00 mg/kg b.w) to rodents demonstrated islet structure with hardly any inflammatory cells at a portion of 100.00 mg/kg b.w while at portion level of 500.00 mg/kg b.w indicated not many fiery cells in the islet of the pancreas. From histopathology, it affirmed that change of tissue treated with high fat kicked bucket are recouped by utilized of wet leaves concentrate of A. barbadensis. As same as simvastatin. Simvastatin utilized as standard medications (Figure 1). Histopathological Changes in the Liver of Control and Experimental rats. A. Group I - Normal liver showing CV with radiating cords of hepatocytes; B. Group II – treated with alloxan Diabetic liver shows periportal fatty infiltration (PFI) with focal fat necrosis; C. Group III treated with ALEC 100mg/kg - Shows normal portal tract (P.T.); D. Group IV Portal track showing normal features; E. Group V - Congested and edematous P.V. with mild haemorrhage; F. Group VI - Portal vein shows haemorrhage in a lumen in PVS. Kidney sections of diabetic rat showed tubular damage, proteinuria and haemorrhage. Haemorrhage is seen within Bowman's space due to glomerular damage (diabetic control). In aqueous leaves extract of A. barbadensis (250.00 and 500.00 mg/kg body weight) treated diabetic kidney, damaged capillary loops with an increase in the thickness of wall, glomeruli and tubules without proteinuria and haemorrhage. Group V and VI did altered structure of the kidney, which are deformed in the alloxan-induced diabetic group when compared with group I.

Aqueous extracts of leaves of A. barbadensis was

assessed for treatment of anti-diabetic and hostile to hyperlipidemic action in alloxan incited diabetic, and SZT initiated people with diabetes in rodents. Extraction and starter phytochemical investigations of A. barbadensis uncovered nearness of Flavonoids, glycosides alkaloids, Carbohydrate, and Tannins. In comparison, saponin and proteins give negative outcomes. The acute oral poisonous quality investigation was performed to discover test portion as indicated by OECD 425 rules, and wet leaves concentrate of A. barbadensis was seen as protected at a portion of 2000mg/kg body weight. Alloxan (120.00mg/kg, i.p) and streptozotocin (50.00mg/kg i.p) were utilized to actuate diabetic in pale-skinned person rodents. Glibenclamide (10.00mg/kg, i.p) was utilized as standard. Various physical parameters and biochemical parameter relating to these exercises, for example, fasting blood glucose and standard conventions estimated lipid profile. Blood tests were gathered through the tail vein of mildly anaesthetized animals for a week by week investigation of fasting blood glucose. Aqui-check glucometer was utilized to gauge blood glucose, though, for estimation of different parameters, the blood test was gathered from retro-orbital plexus. Glucose take-up by separated rodent hemidiaphragm. All these perceptions bolster discoveries that aqueous extracts of leaves of A. barbadensis had the option to offer critical insurance in treatment gatherings while glibenclamide utilized as standard medications. In all animals gatherings of alloxan initiated diabetic Mellitus has been examined. A high-fat eating regimen actuated antihyperlipidemic. Right now, a portion of 4.00 mg/kg was utilized as standard medications. Aqueous leaves extracts of A. barbadensis treatment further decreased in all cholesterol triglycerides LDL cholesterol VLDL cholesterol atherogenic record and faecal cholesterol discharge. They expanded in HDL cholesterol was portion reliant and successful.

CONCLUSIONS

The results indicate that the test compound aqueous extract of *Aloe barbadensis* has significant and sustained oral hypoglycemic activity, comparable with the hypoglycemic effect of glibenclamide, a sulfonylurea derivative. The anti-diabetic effect may be due to increased insulin secretion. Plant species also produced significant hyperlipidemic activity. By utilizing the vast reserves of phytotherapy, we can reduce the economic burden, especially in poor & developing countries.

Funding Support

The authors declare that they have no funding support for this study.

Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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