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Research Article

ANTI-DIABETIC AND HYPOLIPIDEMIC ACTIVITY OF FRUITS OF *PYRUS COMMUNIS* L. IN HYPERGLYCEMIC RATS

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ABSTRACT

Objective: To evaluate the hypoglycemic and hypolipidemic effect of ethyl acetate (EAEPC) and ethanolic (EEPC) extracts from fruits of *Pyrus communis* by dexamethasone-induced diabetic rats.

Methods: The different groups of animals were induced for diabetes with dexamethasone (10 mg/kg bw- sc) once daily for 11 days except normal control. The extracts 200mg/kg and glibenclamide 5mg/kg was administered to treat the diabetic rats once daily for 11 days.

Results: The treated groups showed significant ($p<0.01$) anti-diabetic and hypolipidemic activity as compared to diabetic control. The extracts show beneficial effects on blood glucose like as standard. It also reduces the elevated biochemical parameters such as triglycerides (TGL), low density lipoprotein (LDL), very low density lipoprotein (VLDL), and total cholesterol (TC), increased the reduced level of high density lipoprotein (HDL) and maintains body weight.

Conclusion: The both extracts could serve as good oral hypoglycemic agents and seems to be promising for the development of phytomedicines for diabetes mellitus and its complications.

Keywords: Anti-diabetic, Hypolipidemic, *Pyrus communis*, Dexamethasone and Glibenclamide.

INTRODUCTION

According to WHO, the prevalence of diabetes is likely to increase by 35% by the year of 2025 currently there are over 150 million diabetics worldwide and this is likely to increase to 300 million or more. Statistical projection about India suggests that the number of diabetics will rise from 15 million in 1995 to 79.4 million by 2025, making it the country with the highest number of diabetics in the world [1,2]. Diabetes is a serious metabolic disorder with micro and macrovascular complication that results in significant morbidity and mortality [3]. Chronic hyperglycemia during diabetes causes glycation of body proteins that in turn leads to secondary complications affecting eyes, kidneys, nerves and arteries [4]. Modern medicines like Biguanides, Sulphonylureas and Thiozolidinediones are available for the treatment of diabetes. But they also have undesired effects associated with their uses [5]. Alternative medicines particularly herbal medicines are available for the treatment of diabetes. Common advantages of herbal medicines are effectiveness, safety, affordability and acceptability [6]. Medicinal plants and their products have been used in the Indian traditional system of medicine and have shown experimental or clinical anti-diabetic activity [7, 8]. Medicinal Plants are a rich source of natural products. Medicinal plants and their products have been widely used for treatment of diabetic populace all around the world with less known scientific basis of their functioning [9, 10]. Hence, natural products from medicinal plants need to be investigated by scientific methods for their anti-diabetic activity. The Pear (*Pyrus communis* L.) is among the most economically important fruit tree crops of the temperate zones [11]. It belongs to family Rosaceae. It also called Common Pear- in English, in Hindi – Babbugoshaa, in Sanskrit – Amritphala and tamil-perikkai. Ancient Greek poet Homer described Pears as one of the 'gifts of God'. This prehistoric fruit has been under cultivation both in Europe and Asia for long times, also known as European Pear [12] Sand pear (Japanese and Chinese species) has been domesticated as edible fruit and cultivated in Asia for more than 3000 years [13].It has astringent, sedative activity and act as febrifuge. Its leaves and bark can be used in wound healing. Leaves, buds, and bark of the tree are domestic remedies among the Arabs on account of their astringent action [14]. Pear is a rich source of Vitamin C, ascorbic acid and it is an antioxidant. It acts against reactive Oxygen species [15, 16]. Arbutin is commonly used in urinary therapeutics and as a human skin whitening agent. It decreases melanin in the skin. In the past, the presence of arbutin in Pear has been correlated with biochemical processes that operate as defence mechanism against bacterial invasion. Therefore acts as antibacterial too. The flowers of common pear are used in folk medicine as components of analgesic and spasmolytic drugs [17]. Its fruits are good source of pectin, help in maintaining desirable acid balance in the body. As per literature review the *Pyrus communis* is medicinal important plant and it has number of active constituent which will used for number of disease like diabetic etc but most of them not scientifically documented. So the present study, we reported hypoglycemic and hypolipidemic potentials of *Pyrus communis* in dexamethasone induced diabetic rat model.

MATERIALS AND METHODS

Preparation of extracts

The collected fruits were shade dried completely. The dried fruit was then coarsely powdered and was sieved (sieve # 60) to get uniform powdered. The powdered materials were defatted with Petroleum ether by maceration for 48 hours. The marc was dried and successive extracted with solvent ethyl acetate and 80% ethanol by maceration. Final compound was concentrated by vacuum drying. The traces of the solvents were removed by keeping the dried extracts in to desiccators.

Preliminary phytochemical screening

The different extracts of fruits of *pyrus communis* was screened for the presence of various phytoconstituents like alkaloids, flavonoids, saponin, tannin, glycosides [18].

Experimental Animals

All the experiments were carried out using Swiss Albino mice (25-30 g) and Wister rats (150-200g). The animals were placed at random and allocated to treatment groups in polypropylene cages with paddy husk as bedding. Animals were housed at a temperature of 24 ± 2^0C and relative humidity of 30–70%. A 12:12 light: day cycle was followed. All animals were allowed free access to water and fed. Ethical clearance was obtained from Institutional Animal Ethical Committee (IAEC) of Sri Krishna Chaithanya college of Pharmacy, Madanapalle, Andhra Pradesh. No: SKCP/IAEC/PGCOL/12-13/02.

Acute oral toxicity studies

The acute toxicity study was carried out with various extracts of *Pyrus communis* as per OECD 423 Guidelines. Mortality in each group within 24 h was recorded. The animals were observed for a further 14 days for any signs for delayed toxicity.

Oral glucose tolerance test [19]

Fasted rats were divided into five groups of six rats in each. Group I served as control, received 1% v/v tween 80 and Group II received only glucose. Group III received standard drug glibenclamide as an aqueous suspension at a dose of 5mg/kg b. wt. Groups IV & V received the different extracts at a dose of 200 mg/kg b. wt. as a fine tween 80 suspension. After 30 min of extract administration, the rats of all groups were orally treated with 2 g/kg of glucose except Group I. Blood samples were collected from the rat tail vein just prior to glucose administration and at 30, 90 and 120 min after glucose loading. Blood glucose level was measured immediately by using digital glucometer (one touch select, Johnson & Johnson, USA).

Dexamethasone induced diabetic model [20]

In the experiment a total of 30 overnight fasted rats were used. The 24 rats were rendered diabetic by dexamethasone (10mg/kg, s.c.) once daily for 11 days. The animals divided into five groups of six rats each. Group I normal control received 1% v/v tween 80, Group II served as Diabetic control, Group III received 5 mg/kg of Glibenclamide, Group IV & V treated with 200 mg/kg of ethyl acetate and ethanolic extracts of *Pyrus communis* respectively. Treatment was continued for 11 consecutive days along with dexamethasone except normal control. The blood samples were collected from the retro orbital of each rat under mild ether anesthesia on 11th day and serum separated by centrifugation of blood at 4000 rpm for 10mins. Blood was subjected to glucose measurement on 0,3,6,9 and 11th day. The biochemical parameter such as TGL, HDL, LDL, VLDL and TC was estimated by a semi auto analyzer in serum. Urine glucose level was estimated on 11th day by Benedict's test.

Statistical Analysis

One-way analysis of variance (ANOVA) followed by Dunnett's method of multiple comparisons was employed using Graphpad Instat 3.0 software. $p<0.01$& $p<0.05$ was considered to be statistically significant.

RESULT

Preliminary phytochemical screening

The preliminary phytochemical analysis of extracts of *Pyrus communis* shows presence of alkaloids, flavonoids, glycosides, tannin and carbohydrate. (Table 1)

Table No 1: It shows- (Preliminary phytochemical screening of the ethyl acetate and ethanolic extract of fruits of *Pyrus communis* L.)

Extracts	Steroids	Alkaloids	Glycosides	Flavonoid	Tannin	Phenolic compound	carbohydrate
Ethyl acetate	-	-	-	+	+	+	+
Ethanol	+	+	+	+	+	+	+

Where + =present, - =absent

Acute toxicity

The ethyl acetate and ethanol extracts of *Pyrus communis* had good margin of safety and did not shown any lethal effects on the animals up to the doses of 2000mg/kg. Hence the LD50 of both extracts of *Pyrus communis* was considered as 2000mg/kg. Studies were carried out with 1/10 of the LD50 as effective dose 200mg/kg.

Body weight and urine glucose level

The table 2 shows the body weight of the normal and treated groups significantly differ from diabetic control on 11th day. In the same way urine glucose level of normal and treated groups also significantly differ from diabetic control on 11th day shown in Table 3.

Table 2: It shows - (effect of *Pyrus communis* L. on body Weight)

Groups	Treatment	Body weight 0th day	11th day
I	Normal control	166.66±3.07	212.5±3.59**
II	Diabetic control	171.66±2.47	158.83±2.24
III	glibenclamide (5mg/kg)	173.33±3.07	205.83±3.00**
IV	Ethyl acetate +Dexamethasone	170.83±2.38	197.16±2.77**
V	Ethanol + Dexamethasone	174.16±3.74	196.66±3.07**

The values are mean±SEM, n=6 when compared with diabetic control
**p<0.01

Table 3: It shows - (Effect of fruits of *Pyrus communis* on urine sugar level in Dexamethasone induced diabetic rats.)

Groups	Treatment	Urine sugar on 11th day
I	Normal control	-
II	Diabetic control	+++
III	Standard treated glibenclamide (5mg/kg)	+
IV	Ethyl acetate 200 mg/kg +Dexamethasone	+
V	Ethanol 200 mg/kg+ Dexamethasone	+

(Trace = +, significant= +++, Nil = -)

Glucose tolerance test

The effects of extracts of *Pyrus communis* (200 mg/kg) on glucose tolerance test are shown in Figure 1. The administration of *Pyrus communis* improved the glucose tolerance in the fasted normal rats. At 30 min after glucose administration the peak value of blood glucose level increased rapidly and then subsequently decreased at 90 and 120 minutes. Extracts showed significant hypoglycemic ($P < 0.01$) effect after 90 minutes of treatment.

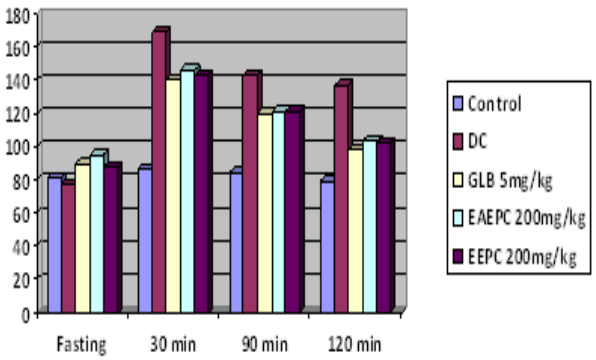

Figure 1: It shows – (Effects of Pyrus communis extracts on oral glucose tolerance in rats)

Blood glucose level

The standard Glibenclamide (5mg/kg), ethyl acetate and ethanol extracts (200 mg/kg) treated groups revealed significant decrease in blood glucose level from 3rd day to 11th day (Table 4). Thus, the extracts was found to be more significant ($p<0.01$) as standard drug in lowering blood glucose level compare to diabetic control.

Table 4: It shows – (Effect of ethyl acetate and ethanol extracts of *Pyrus communis* on blood glucose level in dexamethasone induced hyperglycemic rats)

Groups	Treatment	Blood glucose level in mg/dl				
		0th day	3st day	6th day	9th day	11th day
I	Normal control	94.66±4.88**	89.33±4.07**	80.16±2.57**	101.7±4.11**	86.5±4.61**
II	Diabetic control	206.83±5.26	288.16±4.98	333.33±3.27	356.33±2.84	381.33±3.46
III	Glibenclamide	212.16±2.27	178.5±4.00**	156.33±2.06**	144.3±2.51**	123.3±2.72**
IV	EAEPC +Dexamethasone	207.33±3.21	175.5±3.73**	164.66±1.45**	146.7±2.59**	126.66±2.62**
V	EEPC + Dexamethasone	203.83±1.99	176.66±2.72**	167.5±2.90**	153.5±3.04**	128.16±2.37**

The values are mean±SEM, n=6 when compared with diabetic control **p<0.01

Biochemical parameters

Table 5 shows *Pyrus communis* have significantly reversed the diabetes-induced hyperlipidemia Compared to diabetic control. A significant reduction of total cholesterol level, LDL, TGL and VLDL were observed in treated groups compare to control. However HDL level increased with extracts and GLB group respectively.

Table 5: It shows – (Effect of ethyl acetate and ethanol extracts of *Pyrus communis* on biochemical parameters in dexamethasone induced hyperglycemic rats)

Groups	Groups	TG (mg/dl)	TC (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
I	Normal control	129.47±3.13**	152.06±4.55**	26.08±2.80**	31.36±2.28**	23.62±2.24**
II	Diabetic control	248.79±5.25	217.44±4.91	14.01±1.05	60.78±3.38	69.13±4.25
III	glibenclamide (5mg/kg)	139.50±3.00**	149.28±3.33**	30.92±2.93**	30.43±2.36**	25.52±2.32**
IV	Ethyl acetate +Dexamethasone	144.18±4.93**	153±2.88**	25.53±2.14**	32.43±2.15**	27.44±2.62**
V	Ethanol + Dexamethasone	141.82±1.00**	152.77±4.83**	24.65±2.69*	35.18±3.81**	27.70±2.83**

The values are mean±SEM, n=6 when compared with diabetic control **p<0.01& *p<0.05.

DISCUSSION

Glucocorticoids are widely used therapeutic tools, particularly in treatment for anti-inflammatory and immunomodulatory purposes. Side effects of glucocorticoid treatment include steroid diabetes [21,22]. Glucocorticoid-induced hyperglycemia is partially due to increased hepatic glucose production and insulin resistance of peripheral tissues. Moreover, glucocorticoids are known to inhibit insulin secretion [23, 24]. The underlying mechanism involves increased α_2- adrenoceptor signaling [25], increased Potassium channel activity [26] and impaired glucose metabolism [27, 28]. Although reduced insulin secretion during glucocorticoid treatment can be overcome by blocking adrenoceptor signaling or by inhibition of potassium channel, compelling evidence suggests that the proper functioning of β-cells also depends on cell survival [29]. Accordingly, a reduction of β-cell mass in long-standing glucocorticoid therapy may contribute to the consecutive development of steroid diabetes. In the present study, diabetic rats had lower body weight, high blood sugar levels as compared to normal rats. However, orally administered ethyl acetate and ethanol extracts of *Pyrus communis* significantly decreased the blood glucose level. This could be due to potentiation of the insulin effect of plasma by increasing the pancreatic secretion of insulin from existing β-cells of islets of Langerhans or its release from bound insulin. Extracts at 200mg/kg dose resulted in a significant fall in blood glucose level, 120 min after a single dose of treatment in glucose loaded rats. The extracts were effective in depressing the peak value of blood sugar at 90 min after glucose loading. The extract producing its hypoglycemic activity by a mechanism independent from the insulin secretion, it may be by inhibition of endogenous glucose production or by the inhibition of intestinal glucose absorption or the consistent antidiabetic effect of ethyl acetate and ethanol extracts of *Pyrus communis* in dexamethasone induced rats may also be due to enhanced glucose utilization by peripheral tissues.

Lipid abnormalities accompanying with atherosclerosis is the major cause of cardiovascular disease in diabetes. Therefore ideal treatment of diabetes, in addition to glycemic control, should have a favorable effect on lipid profiles. High level of TC and LDL are major coronary risk factors. Hence, measurements of biochemical parameters are necessary to prevent cardiac complications in diabetes condition. In this study reveals fruit of *Pyrus communis* not only lowered TC, TG, LDL, VLDL levels but also increased level of cardioprotective lipid HDL. Therefore, *Pyrus communis* has potential role to prevent formation of atherosclerosis and coronary heart disease. Several authors reported those secondary metabolites, such as saponins, flavonoids, phenolic compounds, and triterpenoids have anti-hyperglycemic and hypolipidemic activity [30-32]. The phytochemical screening of *Pyrus communis* revealed the presence of flavonoids, steroids, alkaloids, carbohydrates, tannins and other polyphenolic compounds. Hence, the antidiabetic and hypolipidemic activity of ethyl acetate and ethanol extracts is probably due to the presence of several bioactive anti-diabetic principles and their synergistic properties.

CONCLUSION

The present study demonstrated that fruit of *Pyrus communis* could be useful in management of diabetes associated with abnormalities in lipid profiles. Further study need to be isolate, identify the active compounds, develop a formulation and find out the possible mechanism of actions.

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CONFLICT OF INTEREST STATEMENT

The authors report no conflict of interest.

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