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Research Article

Phytochemical investigation and evaluation of antihyperglycemic activity of *Praecitrullus fistulosus* fruits

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Abstract

Diabetes mellitus [antihyperglycemic] is the endocrine metabolic disorder characterized by raised glucose level in the sanguine liquid of body i.e. blood serum due to disturbance of carbohydrate metabolism. In Diabetes mellitus extent of glucose is maintained by well know endocrine pancreatic secreted hormone fuel called insulin which help in metabolizing the glucose level by muscular utilization and other organ pathological activity. When the levels of insulin fall below the body desire it can to hyperglycemic condition. Antihyperglycemic therapeutic plant has an ability to restore abnormal pancreatic condition by increase of insulin, enhancement of body carbohydrate utilization. There are more than 400 reported plant species used an antihyperglycemic and antihyperlipidemic. *Praecitrullus fistulosus* is reported to contain polyphenols, flavonoids, ascorbic acid, tannin, alkaloid, saponin, phytosterol, diterpines, thiamin, and carotene that possess antidiabetic, antioxidative and anthelmintic activity. On investigation and understanding the cause of diabetes mellitus, had opened the large view for the treatment. Phytomedicine has considerably taken the prominent position for the treatment of many metabolic disorders. Biochemical studies concluded that *Praecitrullus fistulosus* extract shows alteration in blood glucose level and also *Praecitrullus fistulosus* improved the lipid profile and showed positive aspect on different parameter in diabetic control rats and it was noted that *Praecitrullus fistulosus* drug extract was effective and helped in controlling the BG level in Albino Wistar Rat *Praecitrullus fistulosus* is reported to contain polyphenols, flavonoids, ascorbic acid, tannin, alkaloid, saponin, Phytosterol, diterpines, thiamin, and carotene that possess antidiabetic, antioxidative properties. The aim of research is to evaluate and investigate the anti-hyperglycemic activity of *Praecitrullus fistulosus* fruit extract on Streptozotocin (STZ)-Nicotinamide induced diabetic rat.

Keywords: Antihyperglycemic, *Praecitrullus fistulosus,* Phytochemicals, Phytomedicine

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder that has emerged as one of the main alarms to human health in the 21st century[1]. It is characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or both. DM may be suspected or recognized clinically by the onset of one or more of the characteristic symptoms such as polyuria, polydipsia, polyphagia and unusual weight loss. Under normal physiological conditions, the blood glucose levels are controlled by insulin which lowers the blood glucose level by facilitating the entry of glucose in to the cells for energy production[2]. About 80% of people with diabetes are in developing countries, of which India and China share the larger contribution. The pathogenesis, progress and the possibility of diabetes management by oral antidiabetic medications have stimulated great interest in recent decades. Numerous therapies designed for the treatment of DM have proven to be fairly effective, but none is ideal due to undesirable side effects and diminution after prolonged use. Management of diabetes without any side effects is still a challenge to the medical system. This leads to increasing demand for an antidiabetic medicinal plant which has comparatively less side effects. According to the recommendation of the WHO expert committee on Diabetes mellitus, an investigation of hypoglycaemic agents of plant origin used in traditional medicine has become more important. In the series of medicinal plants that lacks scientific scrutiny is *Praecitrullus fistulosus,* which belongs to the family *Cucurbitaceae.* It is commonly known as Tinda and the other vernacular names include Indian roung guord, apple gourd, and Indian Baby pumpkin[3]. It is one of the excellent plants gifted by nature having the composition of essential

constituents that are required for normal and good human health[4]. It has been cultivated in Asia since ancient times and has been considered as an under exploited crop in the western world[5]. The tender fruits are picked at the immature stage and cooked as a cooked vegetable. Though, the plant has morphological features similar to watermelon both have different monoploid chromosome number and pollen morphology. The plant prefers sandy soils where its roots can penetrate easily and grown in dry season. The fruits are ready to harvest in 13-15 weeks from sowing, depending on the temperature and other growing conditions. The tender fruits are green in colour and have a diameter of 10-12cm and the seeds are still soft. Up to 6 fruits of about 500g each can be harvested per plant. The fruit is a type of berry called a pepo by Gerald Carr**.** The fruit is approximately spherical, and 10–12 cm in diameter[6]. Fruit is about the size of a small turnip, depressed at each end, hispid when young afterwards glabrous[7]. The fruit is a berry that has a fleshy fruit with several seeds each with hard coat (Joseph),smooth(wealth of India), black in which all parts of the pericarp are pulpy or fleshy except the exocarp which is often skin-light. They are green coloured, apple-sized fruits, spherical in shape and 50 to 60 grams in weight. Plants are vigorous, productive and begin to bear fruits in 70 days[8]. *Praecitrullus fistulosus* possess a wide range of pharmacological properties such as a antioxidant activity (fruits), antimicrobial activity (seeds) [9, 10]. The leaves are cooked as vegetable and taken for blood pressure[8].

Figure 1: *Praecitrullus fistulosus*[9]

MATERIAL AND METHODS

Source of plant

The fruit of *Praecitrullus fistulosus* was picked from fresh farmland from area of Prayagraj, Uttar Pradesh, India in the month of March and April. It further authenticated from Botanical Survey of India, Prayagraj by botanical scientist with the voucher Accession No. 0406210002307. Further plant material was collected and dried under hot sunlight after being sliced or chopped finely .Then dried fruit is coarsely powdered for extraction.

Drug, chemicals and instruments

Streptozotocin (STZ) and nicotinamide was purchased from Central Drug House Private Limited New Delhi. Standard drug metformin was taken from IRM Pvt. Ltd Ahmedabad. Absolute ethanol was purchased from Mxrady Lab Solution Pvt. Ltd New Delhi. HCL, KOH, Iodine, NaoH, Cuso4, Fehling solution A &B Potassium permagnate, n-Hexane, Formic acid, Acetic Acid,KMNO4, Picric acid, Biuret reagent, Formaldehyde, Millions reagent, purchased from Fizmerk India Chemicals. Blood Glucose Monitoring System was used from (Dr Morepen BG 03 Morepen Laboratories).

Preparation of plant material extract

Fruit of plant *Pracecitrullus fistulosus* were primarily air dried under the sunlight after being washed thoroughly with water and control required condition .After air dry fruits were cut into small pieces and dried again to remove complete moisture. Finally air dried and chopped materials were coarsely crushed. Powdered fruit were macerated with petroleum ether to draw out excessive fatty material. After removal of fatty substance powdered drug were packaged for ethanolic hot soxhlet extraction (temp 40-50^{0}C) which remained in continuous operation for 6 days. Alcoholic extract were filtered and evaporated in water bath at 45^{0}C to obtain a semisolid featured material and kept in air tight container[11].

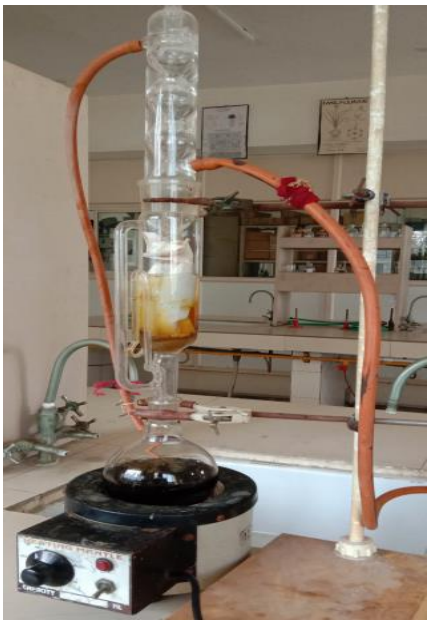


Figure 2: Hot soxhlet extraction

Physiochemical parameter of analysis

To evaluate the quality of the drug for the formulation WHO has set up the certain physical and chemical parameter guidelines.

Foreign matter

Weighed quantity of drug spread over the sieve no 250 to remove admixture, then weight sorted portion and determine the %w/w.

Loss of drying

1.5g of powered drug weighed along the weight of empty china dish. Dry the dry to remove the moisture. Further measure the weight of china dish .Continue this process until two consecutive weighing donot differs by more than 0.5mg.

Ash value

Used to determine the quality and purity of a crude drug.

Total ash value determination

Weigh and ignite 2gm of powdered drug after taking the weight of empty silica crucible along the weight with the sample. Continue igniting to become carbonless. Cool, weigh and calculate by such below.

Wt. of the empty dish = x

Wt. of the sample taken = y

Wt. of the dish + Ash =z

Wt of the ash = (z-x)g

Total ash value of the sample = 100(z-x)/y.

Acid insoluble ash value

Steps are processed as per total ash value determination. Here ashes being washed using 25 ml dilute HCL. Filter by use of ashless filter paper. Ignite, cool and weigh.

%Acid Insoluble ash value = 100*a (wt of residue)/ y (air dried drug).

Water soluble ash value

Determination is similar to acid insoluble ash using instead 25ml of water is used.

Extractive value

4g of coarsely powdered drug transferred into 100 ml graduated flask with the solvent (for Water soluble extractive value use water as solvent and for Alcohol extractive value 90%enthnaol is used as solvent. Keep this flask for overnight. Filter and transfer the 25 ml of filtrate to a weighed porcelain dish. Evaporate to dryness. Then calculate.

Fluorescence analysis

Powdered drug evenly spread over glass slide with addition of chemical and viewed under apparatus Ultra violet chamber exposing at 254nm and 366nm. Evaluation is done by predicting the colors.

Phytochemical analysis

A variety of phytoconstituents, including alkaloids, carbohydrates, glycosides, phytosterols, saponins, tannins, proteins, amino acids, and flavonoids were qualitatively analysed in the fruits extracts of *Praecitrullus fistulosus*[12,13].

Thin layer chromatography

TLC frequently used chromatography techniques, were the stationery phase coated into glass slide and made to run by mobile phase. Retention factor is calculated by the ration of mobile and stationary phase solution. Small quantity of extract of plant material Pracecitrullus fistulosus dissolved in solvent. Silica gel slurry prepared and evenly spread over the glass slide with the thickness of layer 0.21mm - 0.22. The coated glass slide dried in hot air oven and allowed to cool. Different Mobile phase prepared according to polarities and elution for saturating the phytoconstituents present in proper ration e.g Toluene: Ethyl acetate: Formic acid, Benzene: pyridine: formic acid) etc.

HPTLC determination

It is most modern technique separation method. It is much utilized for chemical analysis of the compound purity, uniformity accuracy. It can handle several samples at one time. Different RP2, RP8 and RP18 plates are used for selection of non-polar substances. Samples are dissolved in solvent which are used for quantitative determination of the compounds solvent like Ammonia: Methanol: Chloroform (1:10:90), Ethyl acetate: Methanol (1:1) etc.

Pharmacological evaluation

Animals

Wistar albino rat (male) of weight mostly lies between 160-210gm was purchased from Animal House of Central Drug Research Institute Lucknow**.** Animals were kept in well cleaned polypropylene cages under standard temperature condition room by maintaining the light and dark cycle. Animals pellet feed were given Experiment on Animal was approved by IAEC department for conduction the experimental procedure with it proper protocol (Reg.No.UIP/IAEC/Nov-2020/14).

Toxicological studies

Toxic study is the relevant concern that deals with the severe effect of biological active substances on survival organism before the use as drug during clinical trial basis. Different OCED principles like 401,423 and 425 applied for toxicity studies. It can be categorized into 3 types, acute, sub acute and chronic.

Acute toxicity studies

Lone dose in much quantity is administered to see immediate toxic effect. It helps to determine the LD_{50}which is known as lethal dose and can be defined as the dose of the test sample that is lethal for 50% of the animal in the group dosed.

Procedure

- Oral extract formulation is prepared and administered to animal by mean of oral gavage. The dose of the extract was determined under OCED 423 guidelines.
- Animal should be fasted without food before 24 hours of experiment but water is administered.
- Six experimental animals taken to move the toxicity further.
- The initial and final dose administered for toxicity study which is of 5, 50, 300 and 2000 mg/kg. These are dosed in steps wise days taking 14 days in each dose.

Sub-acute toxicity studies

Same dose repeatedly administered in sub lethal amount for the time of 15 to 20days. It is used in the determining the biochemical parameters of tissues.

Chronic toxicity studies

Different concentration of dose is administered for period of longer duration i.e for 90 days. It is useful in the prospect of carcinogenic nature of the drug. OCED 425 Annex 2d of Oral acute toxicity method applied to estimate the toxic nature of ethanolic extract of *Praecitrullus fistulosus* fruit[14].

Extract dose preparation

- Suspension of *Pracecitrullus fistulosus* fruit extract was prepared by dissolving in water.
- Dose of the extract was given by 200mg/kg and 400mg/kg of body weight.

Induction of diabetes

Non–insulin dependent diabetes was induced in 24 hours overnight albino Wistar male rat by Streptozotocin (STZ) and Nicotinamide. STZ (60mg/kg b.w) was freshly prepared at pH 4.5.

Nicotinamide (120mg/kg) which is prepared in normal physiological saline solution was administered just after 15mints of STZ. All administration was delivered intraperitoneal. The blood glucose level is measured in 2days after injection. Rats with fasting glucose level greater than 200mg/dl considered hyperglycemic .Then the animal were divided into 5 groups[15].

Experimental design and procedure

The rats were divided into 5 groups consisting of 6 animals in each group. The detailed of group are as follows -:

GROUP 1 - Normal Control Group

GROUP 2 - Diabetic control group treated with normal saline.

GROUP 3- Diabetic control group treated with PFextract200mg/kg b.w.

GROUP 4 - Diabetic control group treated with PF extract 400mg/kg b.w

GROUP 5- Diabetic rats treated with standard drug Metformin (100mg/kg) body weight

Antihyperglycemic activity

Antihyperglycemic activity of experimental animals carried out after induction of diabetes. Before induction Wistar male rat fasted overnight and their blood glucose level measured. When Streptozotocin (STZ)-Nicotinamide administered intraperitoneal then B.G level found to be raised after 48 hours of administration. Animals whose BG level is more than 200mg/dl said to be diabetic. In normal condition the BG level remains at 97mg/dl. PF extract preparation done to evaluate the antidiabetic activity. Dose administered at 200mg/kg b.w and 400mg/kg.b.w. This oral administration continued for 21 days .BG level of animals measured in 0, 7th, 14th, 21st days. The level of the Blood glucose considerable declined which indicate the effectiveness of *Praecitrullus fistulosus* plant extract[16].

Biochemical parameters

Lipid profile

Triglycerides have complex form which is called as lipoprotein which increases during intake of high lipid dietary food and modulate the body to come in the state of hyperlipidemia. Onset of hyperlipidemia altered the hepatic secretions which elevate the VLDL and their clearances are inhibited. Retardation in clearance of VLDL led to the production of small dense particles LDL. Rise of LDL level in blood glucose inversely retards the proportion of HDL level. Enrichment of lipolytic products in the body cholesteryl ester protein hydrolysed triglycerdies and phospholipid by hepatic enzymes. The HDL is multifactorial associated with type 2 diabestes and insulin resistance.

- At the end of 21 days of experimental activities blood sample was collected in blood collecting tube by the method of retro-orbital sinus after giving ether anesthesia.
- Blood serum was centrifuged for 10 mints keeping at 300rpm.
- Collection of serum was done in small tubules.
- Serum sample send to Blood Testing Pathology for further investigation of lipid profile parameter which include HDL, VLDL, LDL, Triglycerides and total cholesterol level.

Histopathological study

The animal which was used for conducting experiment were sacrificed and their organ such pancreas, kidney, liver were isolated. These dissected organs kept in formalin solution. Under well-equipped hygiene condition histopathology were performed.

Statistical analysis

Data were evaluated by the mean of applying Newmans Keul method ANOVA.

RESULT AND DISCUSSION

Physiochemical parameters

Result of physiochemical parameter of powdered *Praecitrullus fistulosus* fruit.

Table 1: Physiochemical parameters analysis of coarse powder of *Praecitrullus fistulosus*

S. No	Parameters	%w/w
1.	Foreign Matter	5.9%
2.	Loss on Drying	1.4%
3.	Total Ash Value	6.5%
4.	Acid Insoluble Ash Value	1%
5.	Water Soluble Ash Value	1.6%
6.	Water soluble extractive value	12.75%
7.	Alcohol soluble extractive soluble	6.4%

The alcoholic extract involves the various parameter such as unwanted substance or impurities and its extractive value along this it includes various pharmacological and physiochemical parameter. The presence of various bioactive constituent and compound such as amino acid, amygdaline, alkaloids, carbohydrates, flavonoids, phenolic, and steroids give us mindful ideas for the valuable and inherent treatment of miscellaneous disease.

Fluorescence analysis

Table 2: Result of fluorescence of coarse powder of *Praecitrullus fistulosus* fruit

S.No	Reagent	UV light (254nm)	UV light (366nm)	Visible light
1.	50% H_2SO_4	Brown	Light pale green	Dark brown
2.	Conc. HCL	Greenish brown	Black	Brown
3.	Methanol	Green	Bright Green	Dark Brown
4.	Picric Acid	Dark Green	Fade Brown	Greenish Brown
5.	Sodium hydroxide	Algae Green	Pale green	Dark Brown
6.	Iodine	Dark green	Fade yellow	Fade brown

Fluorescence analysis done to evaluate the transparency of the crude powdered drug. Introductory or precursory and phytochemical test arbitrate the presence of carbohydrate, alkaloids, proteins, amino acid, flavonoids, amygdalins and many more.

Phytochemical analysis

The result of phytochemical analysis of crude powder extract.

Table 3: Screening of *Praecitrullus fistulosus* fruits extract

S. No	Phytoconstituents	Interferences
1.	Alkaloids	+
2.	Saponins	+
3.	Tannins	+
4.	Glycosides	+
5.	Phenols	+
6.	Diterpenes	-
7.	Phytosterol	+
8.	Triterpenoids	-
9.	Flavonoids	+

Qualitative analysis of *Praecitrullus fistulosus* fruits extract found to contain many phytoconstituents like alkaloids, saponins, tannins, phytosterol. It has been reported by research that presence of above compound possesses anti-hyperglycemic and antioxidant activity.

Thin layer chromatography analysis

Different Mobile phase was prepared to check the efficiency of presence of different constituent present in the sample by use of different solvent system. Rf values after spotting the sample on stationery phase are calculated under UV light. The solvent system used are Toluene: Ethyl acetate: Formic acid (3.6:1.2: 0.5), Water: Ethanol: Diethyl ether (0.5:3.5:6.0), n-butanol: acetic acid: formic acid (12:3:5). The Rf value found to 0.25.

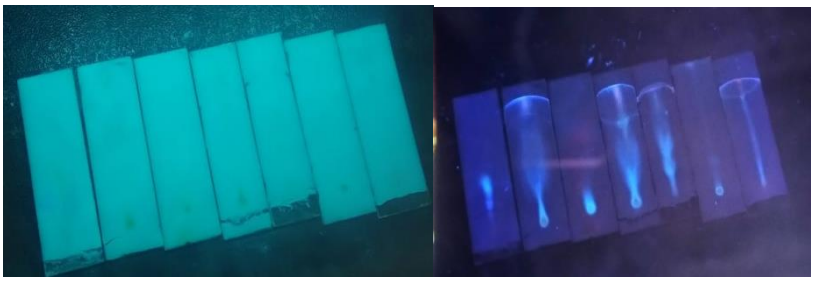


Figure 3: TLC of *Praecitrullus fistulosus* extracts showing various spots under UV light

HPTLC analysis

Graph obtained during HPTLC analysis shows the no. of peaks, maximum % Rf value, maximum Rf value, area and total% of area mentioned. *Praecitrullus fistulosus* shows 09 peaks in the range of 100-1000 nm range (spectra). In *Praecitrullus fistulosus* the maximum % area 68.80**%** was surrounding by peak NO**.** 1 **(**RF value 0.04). This procedure may useful in providing relevant information's good qualitative analysis and determination of the formulation containing *Praecitrullus fistulosus* fruit extract.

Table 4: HPTLC analysis of ethanolic extract of *Praecitrullus fistulosus* fruits

Peak	Max. Rf	Max%
1.	0.04	60.87
2.	0.15	22.38
3.	0.32	7.92
4.	0.50	7.13
5.	0.79	1.70

HPTLC of *Praecitrullus fistulosus* extract gives a number of peaks with density at 254 nm. Most important Rf valuesare**0.04, 0.15, 0.32, 0.50, 0.79.**

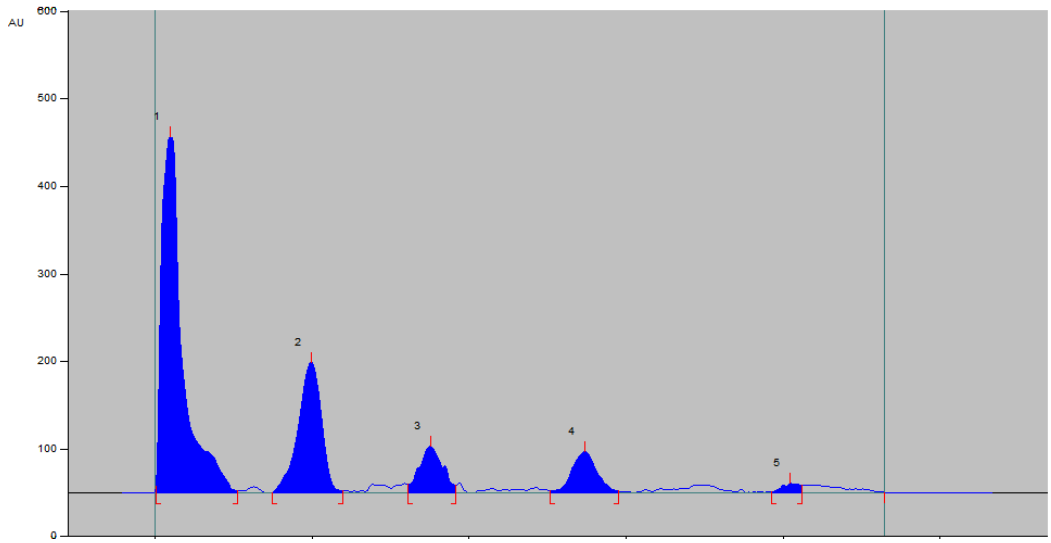


Figure 4: HPTLC spectra of ethanolic extract of PF.

Pharmacological evaluation

Determination of acute oral toxicity study

In oral acute toxicity study, different amount of dose was taken (i.e.; 10,100, 500 and 1000mg/kg) of body weight for determining the toxicity. During experimental study and procedure, it was evaluated that different doses PF drug extract showed no sign of mortality. Toxicity has been recorded. It clearly assumed that the extract of plant is safe to be use.

Anti-hyperglycemic activity

Table 5: Effect of ethanolic extract of *Praecitrullus fistulosus* extract on BG level in Streptozotocin (STZ) – Nicotinamide induced experimental animals.

Group	Treatment (dose)	0 day (mg/dl)	7th day (mg/dl)	14th day (mg/dl)	21st day (mg/dl)
1	Normal Control	102±2.3	99.6±3.5	98.6±2.8	98.1±2.5
2	Diabetic Control	248.8±3.3h	257.8±6h	239.8±8.2h	225.8±5.1h
3	PF(200mg/kg)	240.8±4.5	196.6±8	158.5±5.3sss	111±9.5sss
4	PF(400mg/kg	227.1±15	162.3±1	142.6±20.5sss	105.8±6sss
5	Metformin treated (100mg/kg)	241.8±3.5	201.8±4.0	162.6±4.2sss	101.8±4.3sss

The data represent the mean ± standard deviation for six animals per group, [sss]Indicates statistical significance, compared to the diabetic control group (p<0.001), [h]Indicates statistical significance, compared to the normal group (p<0.001). On Streptozotocin (STZ)-Nicotinamide administration it raised the blood glucose level significantly due to beta cells cytotoxicity as it destroys beta cell of pancreas which inhibit the insulin function which affect the oxidative mechanism of the body. The *Praecitrullus fistulosus* extract showed anti-hyperglycemic activity as reduces the blood glucose level in experimental animals. As *Praecitrullus fistulosus* extract are rich in antioxidant which interfere in oxidative mechanism. Excessively high levels of free radicals cause damage cellular proteins, membrane lipids and nucleic acids, and eventually cell death. The superoxide anion radicals undergo dismutation to form hydrogen peroxide, which if not degraded by catalase or glutathione peroxidase, and in the presence of transition metals, can lead to production of extremely reactive hydroxyl radicals. Antioxidants include lipoic acid, mixed carotenoids, coenzyme Q10, several bioflavonoids, antioxidant minerals (copper, zinc, manganese, and selenium), and the cofactors (folic acid, vitaminsB1, B2, B6, B12). They work in synergy with each other and against different types of free radicals and intake of this generation of free radicals. Oral administration of crude extract at a dose of 200mg/kg and 400mg/kg leads to fall in blood glucose from 0 day to 21st day is recorded from 240.8 ± 4.5 to 105.8±4.6 mg/dl (p<0.001) and 227.1±15.7 -101.8 ± 6.6 mg/dl (p<0.001) respectively. Whereas the diabetic rat treated with Metformin use as standard drug at a dose of 100mg/kg the result from 241.8±3.5 to 101.8±4.9 mg/dl.

Biochemical parameters

Lipid profile

Table 6: The effect of orally administered of ethanolic extract of *Praecitrullus fistulosus* 200mg/kg and 400mg/kg (Mean ± SD)

Treatment Dose	Triglycerides (mg/dL)	Total Cholesterol (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
Normal Control	79.5±3.3	63.6±17.6	19.16±2.3	100±4.53	35.16±2.31
Diabetic Control	169.6±21.04	150±50	20.16±2.3	101.16±4.53	34.16±3.06
PF(200mg/kg)	114.83±15.96	76.8±14.83[a]	47.16±7.27	66.13±3.55[aa]	28.50±5.6
PF(400mg/kg)	111.83±16.96[a]	95.50±13.6[a]	50.16±7.27	25.0±3.63[a]	29.0±8.37
Metformin (100mg/kg)	101.50±27.06	78.83±14.83[a]	38.83±10.25[aa]	33.0±10.25[a]	24.66±3.8

The above data represented the mean ± SD (standard deviation) for 6 experimental animals in each group, [a]Statistical significance compared to diabetic control group (p<0.001), [aa]Statistical significance compared to diabetic control group (p<0.001)

During experimental study various physiochemical parameters are evaluated to check the efficacy of *Praecitrullus fistulosus* extract. HDL, VLDL, Total cholesterol, Triglyceride this parameter showed significant change on the administration. All diabetic induced animal treated with extract for 21 days and their lipid profile are overseen by blood test. TC, TG, VLDL, LDL significantly found to decrease, and there is enhancement of HDL level. The values of TG, TC, VLDL, LDL from Diabetic control group are 169.6±21.04, 150±50, 101.16±4.53, 34.16±3.06 respectively whereas HDL level is 20.16±2.3 .Similarly on administration of *Praecitrullus fistulosus* extract these values recorded as decrement 111.83±16.96, 78.83±14.83, 25.0±3.63, 29.0±8.37 respectively and enhancement of HDL values 50.16±7.27 which signify the extract possess to control lipid profile of body and can be used as Antihyperglycemic agent to control blood glucose level in the body.

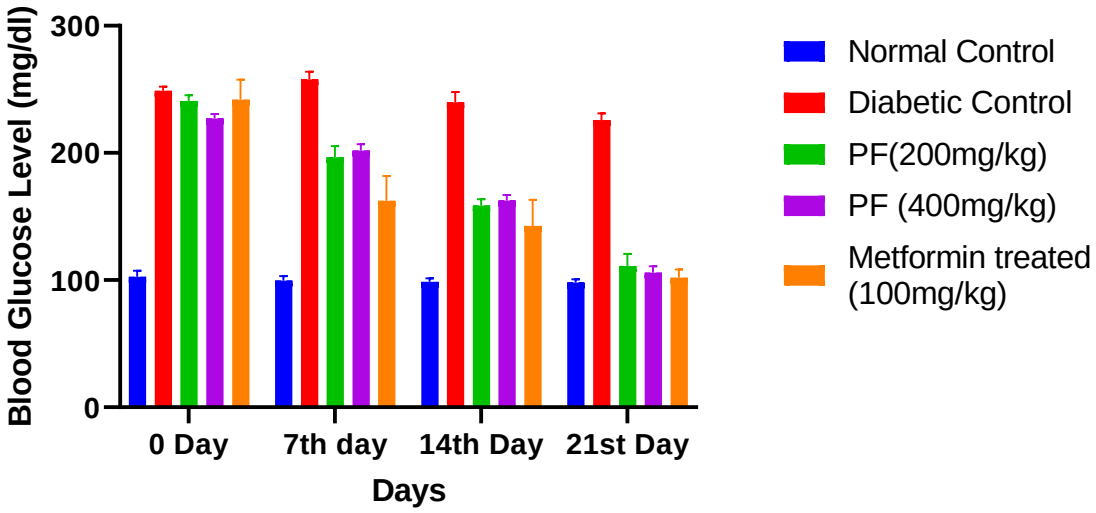


Figure 5: Represents Blood glucose level in experimental animals in Streptozotocin STZ-Nicotinamide induced diabetic animals

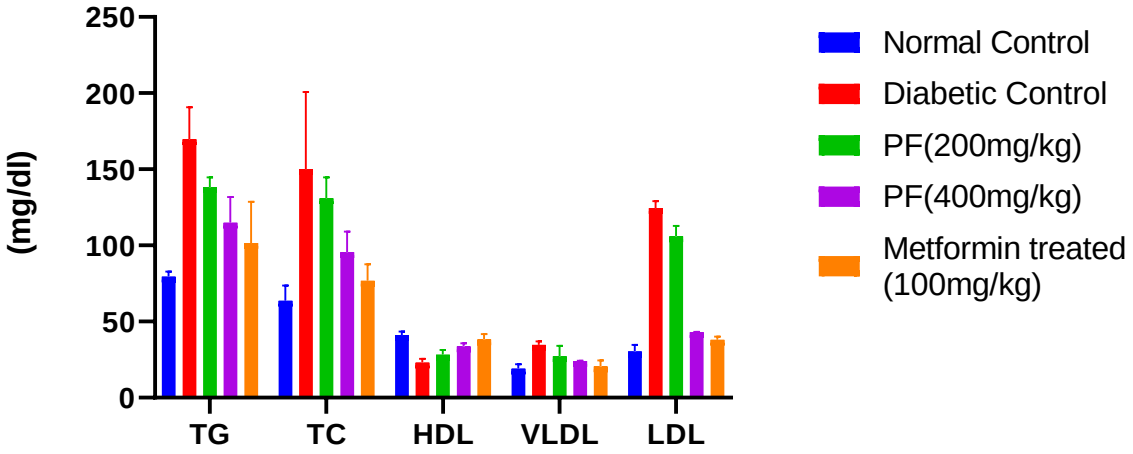
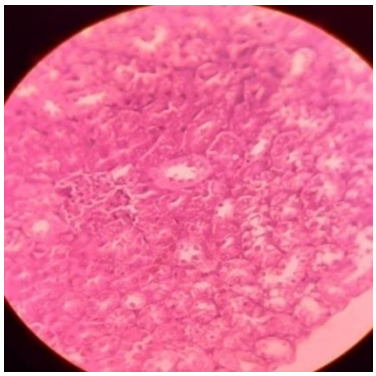


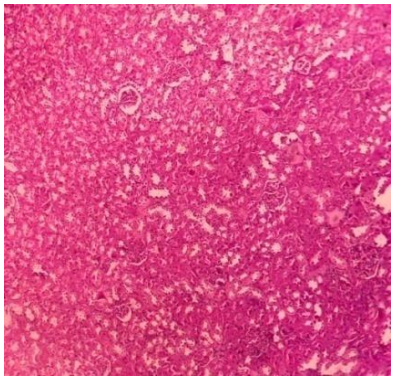
Figure 6: Graph representing lipid profile in diabetic induced animals

Histopathological study

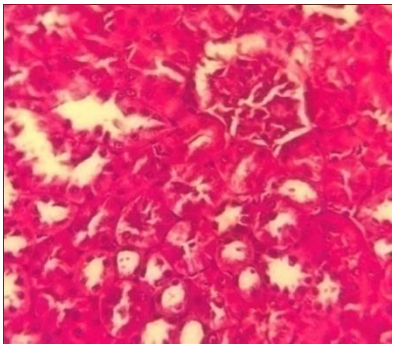
The histopathology study was done of various organs like kidney, pancreas, and liver. Respective images are depicted below.



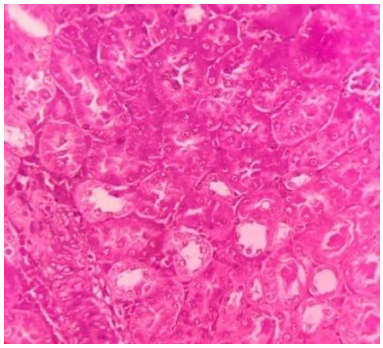
(A) Kidney Normal Control



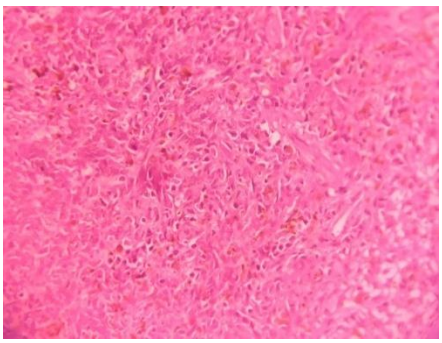
(C) Kidney Diabetic Control



(B) Kidney *Praecitrullus fistulosus* 200mg/kg



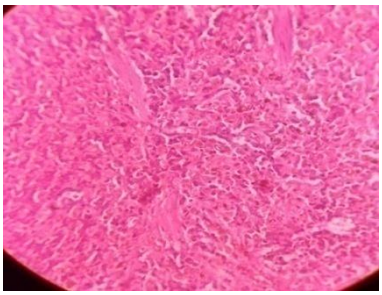
(D) Kidney *Praecitrullus fistulosus* 400mg/kg



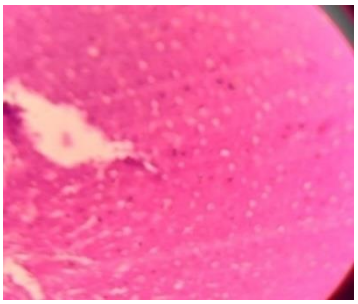
(E) Kidney Standard Metformin 100mg/kg

Figure 7: Histopathology of kidney

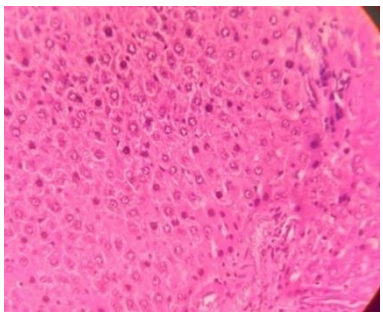
In Group 1 Glormerulli cells appears to be normal. Normal glomerulus, tubules shows cytoplasmic vasculation. Proteinous material are present .GBM is normal and there is no deposition. In Group 2 the nodules contain lipid and fibrin. Renal ischemia leading to tubular atrophy seen and intestinal fibrous which result in small contracted kidney was observed. Thickened of GBM and diffused increase of mesangial matrix with mild proleriferation of mesangial cells. Various excudative lesion and fibrin is present. In Group 3 reduced thickening of GBM and hyaline of arterioles, fibrin deposits seen. In Group 4 there is significant decrease in fibrin deposit as well as reduction of GBM. In Group 5 lesser thickening of GBM with significant reduction in proliferation of mesangial cells, fibrin caps and capsular drops. Significant decreased nodular lesion was found.



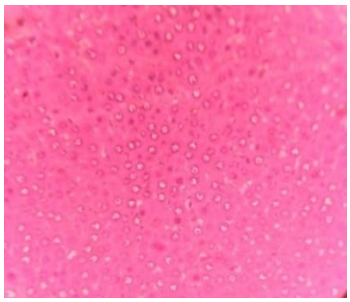
(A) Pancreas Normal control



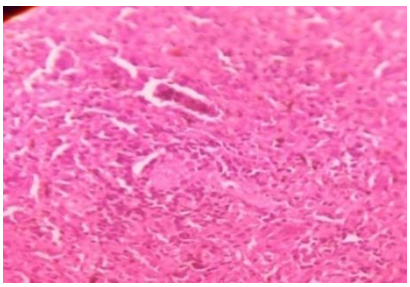
(C) Pancreas Diabetic Control



(B) Pancreas *Praecitrullus fistulosus* 200mg/kg



(D) Pancreas *Praecitrullus fistulosus* 400mg/kg



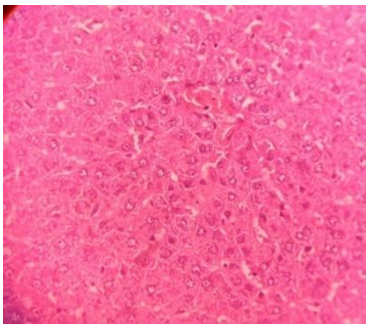
(E) Pancreas Standard Metformin 100mg/kg

Figure 8: Histopathology of pancreas

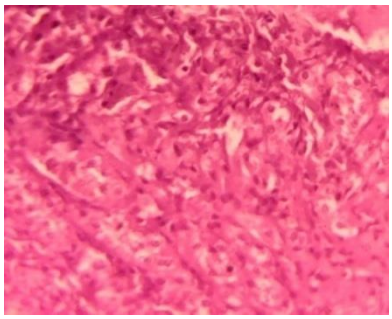
Pancreas

In Group 1 no leucocytic infiltration in the islets. Beta cell mass is normal and hyperplasia and hypertrophy is not seen. In Group 2 beta cell mass is reduced. Hyperplasia and hypertrophy of islets is seen. Deposition of amylin around the capillary of the islets. Atrophy of cell observed.

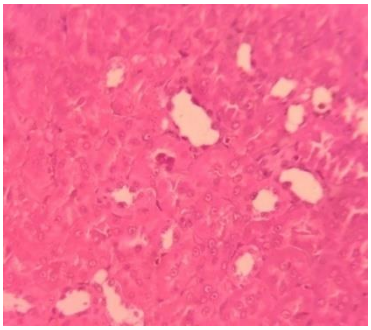
In Group 3 and group 4 significant decreases in fibrous tissue in the islet and beta cell are less inflamed reduction of amylin. No beta cell degranulation is observed. In standard group 5 there is decrease of fibrous tissue in the islets. Beta cells reduced. Decreased deposition of amylin around the capillaries of islets is seen. Reduced atrophy of islet tissue.



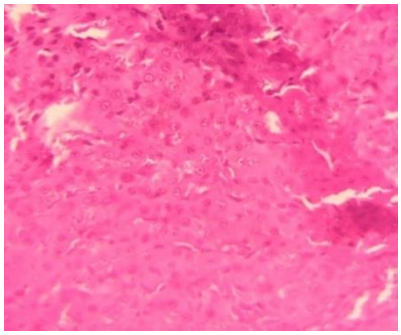
(A) **Liver Normal Control Group**



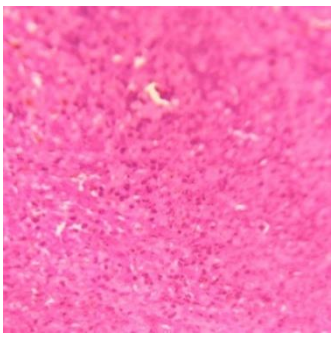
(B) Liver Diabetic Control Group



(C) Liver *Praecitrullus fistulosus* (200mg/kg



(D) Liver *Praecitrullus fistulosus* (400mg/kg)



(E) Liver Standard Metformin (100mg/kg)

Figure 9: Histopathology of liver

Liver

Inn Group 1 the histopathological examination of sectioned liver, it showed normal view of hepatocytes containing single rounded nucleus and nucleolus. Kupffer cells normal in shape. Bile duct appears to be normal classical nodules with branches of bile duct seen. In Group 2 pyramidal classical lobules were disturbed. Destruction of hepatocytes. Disarrangement of Kupffer cells observed. Significant inflammatory cells infiltration with fibroses. In Group 3 significant reduction of necrosis of hepatocytes in group of lobules were observed. In Group 4 reductions in inflammatory cells. Normal nobular architecture of liver observed. In Group 5 Hepatocytes were observed having round nucleus and nucleolus. Decreased cell infiltrations.

CONCLUSION

On investigation and understanding the cause of diabetes mellitus, had opened the large view for the treatment. Phytomedicine has considerably taken the prominent position for the treatment of many metabolic disorders. Biochemical studies concluded that *Praecitrullus fistulosus* drug extract shows alteration in blood glucose level and also *Praecitrullus fistulosus* improved the lipid profile and showed positive aspect on different parameter in diabetic control rats and it was noted that *Praecitrullus fistulosus* drug extract was effective and helped in controlling the BG level in Albino wistar rat *Praecitrullus fistulosus* is reported to contain polyphenols, flavonoids, ascorbic acid, tannin, alkaloid, saponin, phytosterol, diterpines, thiamin, and carotene that possess antidiabetic, antioxidative properties.

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