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Anti-Diabetic Activity of Piper Betel Linn in Alloxan Induced Female Wistar Rats

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ABSTRACT:

Piper betel Linn. (family Piperaceae), has a long history spanning more than two millennia, since plants are abundant sources of pharmaceuticals, many cultures worldwide employ them directly as remedies. An increase in blood glucose levels above 200 mg/dL is known as hyperglycaemia, and it is one of the early signs of diabetes mellitus. Literature study and research methods have shown hyperglycaemia can be tackled effectively by piper betel linn. Flavonoids are among the phytochemical substances found in piper betel leaves. By scavenging hydroxyl radicals that harm the pancreatic β cells, these antioxidants can maximize the synthesis of insulin. It has been demonstrated empirically that the flavonoid content of betel leaves can reduce blood glucose levels and treat diabetes mellitus. An evaluation of the anti-hyper glycaemic qualities of the piper betel leaf ethanol extract fraction was carried out. In rats with experimental diabetes produced by alloxan, the current study sought to assess the anti-diabetic potential of Piper betel leaves. When Piper betel leaf extract was given orally to diabetic rats for 25 days, the altered levels of biochemical markers like blood glucose, LDL, VLDL, cholesterol, and triglycerides were dramatically restored. Six Female Wistar rats was split up into four groups: group 1 received normal saline, group 2 received diabetic control, group 3 received a standard oral medication for diabetes, and group 4 received ethanolic extract of Piper betle. No evidence of toxicity upon autopsy was found, no enlargement of liver, kidney, spleen .in conclusion piper betel linn was more effective and safer in diabetic control Wistar rats compared to standard drug. Piper betle linn extracts demonstrated anti-diabetic and antioxidant effects in alloxan-induced diabetic Wistar rats, supporting its traditional use and potential as a therapeutic agent for managing diabetes mellitus.

KEY WORDS: Piper betle leaves, hyperglycaemia, Anti diabetic, Antioxidants, Alloxan induced diabetes, Beta cells, Toxicity studies

1. INTRODUCTION:

1.1 DIABETES MELLITUS:

Diabetes mellitus is a metabolic disorder characterized by impaired ability of the body to produce or respond to insulin. Insulin plays a crucial role in regulating glucose metabolism. Here are some key points about diabetes:

1. High Blood Sugar: Diabetes leads to sustained high blood sugar levels.
2. Types of Diabetes:
    - Type 1 Diabetes: Also known as insulin-dependent diabetes mellitus, this type results from the immune system attacking and destroying the insulin-producing cells in the pancreas. People with type 1 diabetes require insulin injections for life.
    - Type 2 Diabetes: Commonly referred to as non-insulin-dependent diabetes mellitus, this type occurs when the body's cells become resistant to insulin. Lifestyle factors, genetics, and obesity play a role in type 2 diabetes.
    - Gestational Diabetes: Occurs during pregnancy and affects blood sugar levels. It usually resolves after childbirth.
3. Symptoms of Diabetes:
    - Frequent Urination: The term "diabetes" itself comes from Greek, meaning "to pass through." Increased urination (polyuria) is a common symptom.
    - Excessive Thirst: Due to dehydration caused by frequent urination.
    - Weight Loss: Despite increased appetite, weight loss can occur.
    - Itching: Skin itching is another symptom.
    - Weakness and Fatigue: High blood sugar affects energy levels.
    - Blurred Vision: Diabetes can impact the eyes.
4. Complications:
    - Macrovascular Disease: Diabetes increases the risk of diseases affecting large blood vessels, including coronary heart disease and peripheral arterial disease.
    - Microvascular Disease: Small blood vessels can be affected, leading to retinal and renal vascular disease.
    - Neuropathy: Nerve damage can cause pain, tingling, and loss of sensation.
    - Other Conditions: Diabetes is associated with other health issues like skin infections, slow wound healing, and foot ulcers.

1.2 DISORDERS OF DIABETES:

1.2.1 TYPE 1 DIABETICE CAUSES:

Type 1 diabetes is an autoimmune condition where the immune system mistakenly attacks and destroys the insulin-producing beta cells in the pancreas. The exact cause of this autoimmune reaction is not fully understood, but genetic predisposition and environmental factors likely play a role. Type 1

diabetes, also known as juvenile diabetes or insulin-dependent diabetes, is a chronic condition where the pancreas produces little or no insulin. Insulin is a hormone that allows sugar (glucose) to enter cells and produce energy. Here are some key points about Type 1 diabetes:

Symptoms: Type 1 diabetes symptoms can appear suddenly and may include:

1. Feeling more thirsty than usual.
2. Frequent urination.
3. Bed-wetting in children who can monitor its effects and adjust the dosage as needed have never wet the bed during the night.
4. Feeling very hungry.
5. Losing weight without trying.

Causes: The exact cause of Type 1 diabetes is not fully understood. However, factors that may contribute include:

1. Genetics: A family history of Type 1 diabetes increases the risk.
2. Autoimmune Response: The body's immune system destroys the insulin-producing cells (islet cells) in the pancreas.
3. Environmental Factors: Exposure to viruses and other environmental triggers may play a role.
4. Autoimmune Origin: Type 1 diabetes results from an autoimmune response where the body's immune system mistakenly attacks and destroys the insulin-producing cells (islet cells) in the pancreas.
5. Genetic Predisposition: A family history of Type 1 diabetes increases the risk.

1.2.2 Treatment and management of Type 1 diabetes:

Although there is no cure for Type 1 diabetes, treatment focuses on managing blood sugar levels using insulin, diet, and lifestyle adjustments, requires lifelong insulin therapy, Monitoring blood sugar levels and adjusting insulin doses, Rigorous blood sugar monitoring, Carbohydrate counting and meal planning, Regular physical activity.

1.2.3 TYPES 2 DIABETICS CAUSES:

Type 2 diabetes is a chronic condition that affects how the body uses sugar (glucose) for energy. Unlike Type 1 diabetes, which often develops in childhood or adolescence, Type 2 diabetes typically occurs in adulthood, although it can manifest at any age. Here are some key points about Type 2 diabetes.

Symptoms: The symptoms of Type 2 diabetes usually develop gradually and may include:

1. Frequent urination
2. Increased thirst
3. Fatigue or tiredness
4. Sudden weight loss
5. Itching around the genitals
6. Slow healing of cuts or wounds

Causes: Type 2 diabetes occurs when the body becomes resistant to insulin or when the pancreas doesn't produce enough insulin. Factors contributing to Type 2 diabetes include:

1. Genetics: A family history of diabetes increases the risk.
2. Lifestyle: Sedentary habits, obesity, and poor dietary choices play a role.
3. Age: People above 45 years are at higher risk.
4. Prediabetes and gestational diabetes are also risk factors.

Complications: If left untreated, Type 2 diabetes can lead to serious complications, including:

1. Hyperosmolar Hyperglycaemic Non-ketotic Syndrome: A medical emergency characterized by extremely high blood glucose levels.
2. Atherosclerosis: Clogged blood vessels due to diabetes, increasing the risk of heart attacks and strokes.
3. Microvascular complications: Affecting eyes, kidneys, and nerves.
4. Macrovascular complications: Impacting the heart, brain, and blood vessels.
5. Insulin Resistance: Type 2 diabetes occurs due to insulin resistance, where the body's cells become less responsive to insulin. The pancreas compensates by producing more insulin, but over time, it may fail to keep up.
6. Lifestyle Factors: Obesity, sedentary lifestyle, poor diet, and aging contribute to Type 2 diabetes.
7. Genetics: Family history also plays a role. Usually manifests in adulthood, although it can occur at any age.
8. Gradual onset with symptoms developing over time.

1.2.4 Treatment and management of type 2 diabetes:

Initially managed through lifestyle modifications (diet, exercise, weight loss), Oral medications or injectable medications (including insulin) may be prescribed, Lifestyle changes (healthy eating, exercise), Medications to improve insulin sensitivity, Blood pressure and cholesterol management.

Others:

Increased Thirst and Urination: Excess glucose in the bloodstream leads to increased urination as the kidneys work to remove the excess sugar. This can result in dehydration, leading to increased thirst. Fatigue: Cells may not receive an adequate supply of glucose for energy production, leading to feelings of fatigue and weakness.

Blurred Vision: High blood sugar levels can cause changes in the shape of the lens of the eye, resulting in blurred vision.

Slow Wound Healing: Elevated blood sugar levels can impair the body's ability to heal wounds, increasing the risk of infections and complications.

1.3 TREATMENT:

- METFORMINE: Metformin is a widely used medication primarily prescribed for the management of type 2 diabetes mellitus. Its primary function is to lower blood sugar levels by improving the

body's response to insulin and reducing the amount of glucose produced by the liver. Here's a breakdown of its mechanism of action and uses:

Mechanism of action: Decreased Glucose Production: Metformin reduces the amount of glucose produced by the liver. It does this by inhibiting gluconeogenesis, the process by which the liver produces glucose from non-carbohydrate sources like amino acids and fats.

Enhanced Insulin Sensitivity: Metformin improves the sensitivity of body tissues, such as muscle and fat cells, to insulin. This allows these tissues to take up glucose more effectively from the bloodstream, reducing blood sugar levels.

- ALPHA-GLUCOSIDASE INHIBITORS: Such as acarbose and miglitol, which delay the absorption of carbohydrates from the digestive tract, leading to lower postprandial blood sugar levels.
- SULFONYLUREAS: Sulfonylureas stimulate the pancreas to release more insulin. Examples: Glipizide (Glucotrol), Glyburide (Dia Beta, Glynase), Glimepiride (Amaryl)
- MEGLITINIDES (GLINIDES): Meglitinides also stimulate insulin secretion from the pancreas, but they have a shorter duration of action compared to sulfonylureas. Examples: Repaglinide (Prandin), Nateglinide (Starlix) 5. Thiazolidinediones (TZDs): TZDs improve insulin sensitivity in peripheral tissues and decrease glucose production by the liver. Examples: Pioglitazone (Actos), Rosiglitazone (Avandia) [Note: Rosiglitazone is restricted in some countries due to cardiovascular risks]
- DIPEPTIDYL PEPTIDASE-4 (DPP-4) INHIBITORS: DPP-4 inhibitors help lower blood sugar levels by preventing the breakdown of incretin hormones, which stimulate insulin release and reduce glucagon secretion. Examples: Sitagliptin (Januvia), Sitagliptin (Onglyza), Linagliptin (Tradjenta)
- SGLT2 Inhibitors: These drugs work by blocking the reabsorption of glucose by the kidneys, leading to increased glucose excretion in the urine and lower blood sugar levels. Examples: Canagliflozin (Invokana),
  Dapagliflozin (Farxiga), Empagliflozin (Jardiance)
- GLP-1 Receptor Agonists: GLP-1 receptor agonists mimic the action of incretin hormones, stimulating insulin secretion, suppressing glucagon release, slowing gastric emptying, and promoting satiety. Examples:

Exenatide (Byetta, Bydureon), Liraglutide (Victoza, Saxenda), Dulaglutide (Trulicity)

2. PLANT PROFILE:

Fig.no: 1 Piper Betle linn:

2.1 MORPHOLOGICAL CHARACTERISTICS:

Piper betel Linn, commonly known as betel leaf, is a tropical evergreen vine native to South and Southeast Asia. Here's a profile and brief history of this culturally significant plant:

2.2 BOTANICAL PROFILE:

Scientific Name : Piper betel Linn

Family : Piperaceae

Description : Betel leaf is a climbing vine that can grow up to several meters in length. It has heart-shaped, glossy leaves that are typically deep green in color. The plant produces small white flowers and red berries.

Symbolism: Betel chewing has deep cultural and social symbolism in many Asian countries. It is often associated with hospitality, social gatherings, ceremonies, and religious rituals. The practice holds significant cultural value and plays a role in various rites of passage and festivities.

2.3 CHEMICAL CONSTITUENTS:

The leaf is carminative, aphrodisiac, tonic, laxative and improves appetite. Leaves contained caryophyllene, cadinene, γ-lactone, allyl catechol, p-cymene and eugenol methyl ether in varying amounts. Betel leaf (Piper betel L.) is a popular ingredient in many traditional cuisines and is Betel leaf (Piper betel L.) is a popular ingredient in many traditional cuisines, and is known for its distinctive flavours, aroma, and medicinal properties. The leaves are also used for medicinal purposes, including to treat gastrointestinal disorders, ease flatulence, and improve digestion.

2.4 USES

1. Medicinal Uses: Betel leaf has a long history of use in traditional medicine systems such as Ayurveda, Siddha, and traditional Chinese medicine (TCM). It is believed to possess various medicinal properties, including antimicrobial, anti- inflammatory, antioxidant, and digestive-stimulant effects. Betel leaf extracts and preparations have been used to treat a wide range of ailments, including respiratory conditions, digestive disorders, skin diseases, and oral health issues.

2. Culinary Uses: Betel leaves are also utilized in culinary preparations across South and Southeast Asia. They are often used as wrappers for flavouring and enclosing ingredients such as nuts, spices, and meats in dishes like "paan" or in Savory snacks and appetizers.

3. Therapeutic Uses:

3.1 Manages Diabetes: Betel leaves are rich in antioxidants that combat oxidative stress in diabetic patients. This helps reduce blood glucose levels and acts as an anti-diabetic agent.

3.2 Heals Injuries and Wounds: Betel leaves increase protein content and enhance wound contraction rate. They also reduce oxidative stress, aiding in faster healing of wounds, especially burn injuries.

3.3 Decreases Bad Cholesterol Levels: The compound eugenol found in betel leaves blocks cholesterol synthesis in the liver and absorption in the intestines.

It also aids in the breakdown of low-density lipoprotein (LDL) cholesterol, reducing the risk of heart diseases and strokes.

3.4 Prevents Asthma Attacks: Betel leaves have antihistamine and anti-inflammatory properties.

4. Traditional Use: Betel leaf has been used for centuries in South and Southeast Asian cultures for its medicinal, culinary, and social significance. It is an integral part of traditional practices such as "betel chewing" or "paan chewing," where it is combined with areca nut and slaked lime and chewed for its stimulating and digestive properties.

3. MATERIALS AND METHODS:

3.1 Collection and Authentication of plant materials:

Collect fresh betle leaves and wash it under the running water and clean the wet with cloth and kept it under shade drying under the room temperature with good ventilation avoid microbial growth. After the shade dry leaves are powdered in a grinder. And placed in a tight container.

Fig.no: 2 Shade dry of leaves after 8 days

Fig.no: 3 Shade dry of leaves after 15 days

3.2 Experimental Animals:

Female albino Wistar rats (150-180 g) were purchased from Animal house, Medchal district, The rats were housed in polypropylene cages lined with husk and kept in Animal house, Department of Biochemistry. It was renewed every 24 hrs. The rats were fed with commercial pelleted rats' chow. Medchal district, India and had free access to water. The experimental rats were maintained in a controlled environment hours (light/dark cycle) and temperature (30 ± 2°C). The experiments were designed and conducted in accordance with the ethical norms approved by Ministry of Social Justices and Empowerment, Government

of India and Institutional Animal Ethics Committee Guidelines for the investigation of experimental pain in conscious rats. The rats were acclimatized for one week before starting the experiments

3.3 Preparation of plant extract:

Weight accurately about 50g of dried betle leaves powder and tie it in a cotton cloth and place in thimble. In a round bottom flask take 250ml of ethanol and place in heating mantle and the thimble is placed on the round bottom flask, the condenser is placed on the thimble and connect the water flow. The heating is maintained at 60^0c When the temperature is increased ethanol gets evaporate from the round bottom flask then condensed and fall drop wise in the thimble on the drug. The drug gets wet, and the extract will fill the cycle and again fall into the round bottom flask. Like these approximately 15 cycles are fall. After the extraction Soxhlet apparatus are removed and the extract was taken it into the beaker and kept for heating for evaporator of ethanol. After getting the drug take it into the well closed container and kept in a normal temperature and avoid microbial growth.

Fig.5 Soxhlet extraction of betle leaves

4. EXPERIMENTAL PROCEDURE:

4.1 ALLOXAN DRUG Preparation: Weigh 37mg of alloxan in a watch glass and add 1ml of saline and then mix it properly until get dissolved properly. And take the drug in a syringe and administer into rat via intraperitoneal route. Take rat (250 gm) and divided into 3 groups such as control, test, standard. Take dissolved drug and administered into the rat peritoneal route.

4.2 Induction of experimental diabetes in rats:

Rats were induced diabetes by single intraperitoneal injection of alloxan monohydrate dissolved in sterile normal saline at a dose 120 mg/Kg, after 18 hours fasting to induce hyperglycemia.14 After 1-hour alloxan administration, the animals were fed on standard pellets and water ad libitum. Rats were supplied with 5% glucose solution for 48 hours after alloxan injection in order to prevent severe hypoglycaemia. After 1 week time for the development and aggravation of diabetes, the rats with moderate diabetes having persistent glycosuria and hyperglycaemia (Blood Glucose range of above 250

mg/dL) were considered as diabetic rats and used for the experiment. The treatment was started on the eighth day after alloxan injection, and this was considered as first day of treatment.

Fig. no: 6 Induction of diabetes to the animal

4.3 Grouping:

Group 1: Control Rats (Water and food ad libitum).

Group 2: Alloxan induced diabetic Rats.

Group 3: Diabetic Rats treated with Piper betel leaves extract (250 mg/Kg Body weight/day) in aqueous solution orally for 30 days

Group 4: Diabetic Rats treated with gliclazide (5mg/Kg body weight/day) in aqueous solution orally for 30 days.

Group	Day 0	Day 5	Day 10	Day 15	Day 20	Day 25
Group-1 Normal control	96.83+- 19.71 SEM=8.04	92.83+- 4.708 SEM=1.92	94.00± 6.38 2.60	90.83± 7.33 2.94	88.75±2.55 2.85	75.60± 2.745
Group-2 Diabetic control	319.67+- 50.409 20.579	251.17+- 41.513 16.87	172.33± 41.433 16.87	134.67± 32.445 13.246	101.69± 30.658 12.69	90.83± 30.425 12.30

Group-3 Diabetic standard (0.5mg)	347.17+- 32.45 13.25	307.17+- 16.67 6.809	262.17± 32.090 13.101	217.50± 19.460 7.945	170.25± 20.52 11.252	140.20± 19.25 10.345
Group-4 Diabetic test 1 (piper betle leaf extract 50 mg)	310.67± 50.409 20.579	251.17± 41.513 16.948	172.33 ± 41.433 16.915	134.67 ± 32.445 13.246	186.00 ± 23.332 9.525	160.75± 20.652 8.546

5. RESULTS

Table.1: Mean Blood glucose levels of all groups

Table Description:

1. The table consists of four groups labelled as “Normal Control,” “Diabetic Control,” “Diabetic Standard 0.5mg,” and “Diabetic test (Piper Betle Leaf Extract 50mg).”
2. Each group has data recorded over a period of 15 days (from “Day 0” to “Day 15”).
3. The data is presented in green and white colours.

5.1 Data Interpretation:

1. **Normal Control**:

The values for this group are around 211.67 on Day 0, decreasing slightly to 213.33 on Day 15.

The second row (without plus/minus signs) shows values around 20.14 on Day 0, decreasing to 18.36 on Day 5, and then increasing to 20.35 on Day 10.

2. **Diabetic Control:**

The initial value is 208.00 on Day 0, decreasing to 187.33 on Day 15.

The second row shows values around 11.52 on Day 0, decreasing to 10.63 on Day 5, and further to 8.73 on Day 15.

3. **Diabetic Standard 0.5mg:** The values start at 210.33 on Day 0 and decrease to 191.17 on Day 15. The second row shows values around 15.92 on Day 0, decreasing to 6.50 on Day 5, and then increasing slightly to 7.11 on Day 15.

4. **Diabetic test (Piper Betle Leaf Extract 50mg):**

The values begin at 213.21 on Day 0 and decrease to 182.10 on Day 15.

The second row shows values around 15.91 on Day 0, decreasing to 9.01 on Day 5, and further to 7.42 on Day

15.

5. SEM (Standard Error of the Mean):

Each group has an associated SEM value (Standard Error of the Mean) below the data rows. SEM provides information about the variability of the data points within each group.

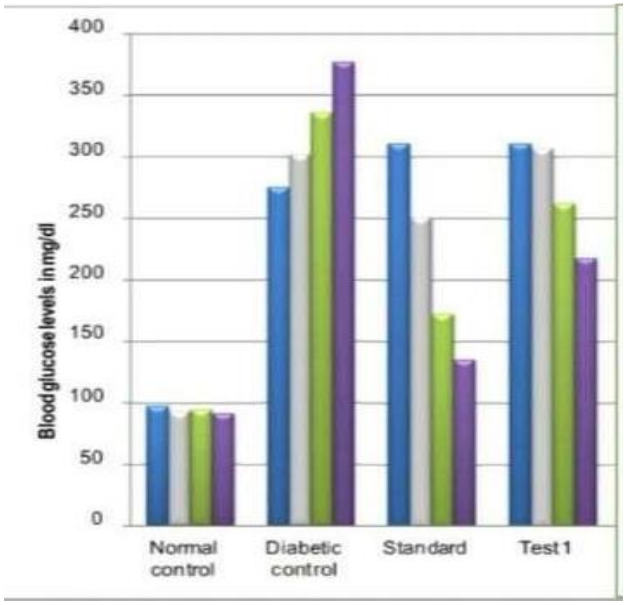
6. Conclusion:

It seems that the "Diabetic test" group (with Piper Betle Leaf Extract) shows the most significant decrease in values over the 15-day period.

Group	Day 0	Day 5	Day 10	Day 15	Day 20	Day 25
Group 1 normal control	211.67+- 20.14 SEM; 8.22	213.33-+ 18.36 7.5	211.33+- 20.35 8.31	214.33+- 17.45 7.11	210.35+- 15.55 6.75	190.45± 14.22 5.83
Group 2 Diabetic control	208.00+- 11.58 SEM;4.71	187.33+- 10.63 4.34	166.67+- 8.73 3.57	145.99+- 8.55 3.50	134.56+- 7.65 3.11	120.65+- 5.92 2.55
Group 3 Diabetic standard (0.5mg)	210.33+- 15.92 SEM;6.52	191.33+- 17.19 7.02	184.33+- 18.17 7.44	181.00+- 18.54 7.51	175.25+- 15.55 7.11	140.35+- 12.32 7.09
Group 4 Diabetic test 1 (piper betle leaf extract 50mg)	213.22+- 21.74 SEM; 3.22	199.00+- 7.14 2.94	182.66+- 10.24 4.56	166.55+- 8.45 3.45	155.44+- 7.55 3.21	150.33+- 5.32 2.04

Table.no: 2 Mean blood glucose levels of all groups

The other groups (Normal Control, Diabetic Control, and Diabetic Standard) also exhibit changes, but to a lesser extent.



Graph.no: 1 Mean blood glucose levels of all groups

Graph 1: Mean blood glucose levels of all the groups." Here's a detailed analysis: Normal Control: This group serves as the baseline for comparison. Their blood glucose levels remain consistent across all days, indicating a stable metabolic state.

Diabetic Control: Exhibits a spike in blood glucose levels from Day-0 to Day-5, likely reflecting the uncontrolled state of diabetes without intervention. The levels then stabilize, suggesting some form of homeostasis.

Standard Group: Shows a decrease in blood glucose levels over time, indicating the effectiveness of a standard treatment in managing diabetes.

Test Groups (Test1, Test2, Test3): These groups are likely receiving different experimental treatments or dosages.

Test1 and Test2: Both groups show a rise in blood glucose on Day-5, followed by a gradual decrease. This pattern may suggest a delayed response to the treatment.

Test3: Demonstrates a significant and consistent reduction in blood glucose levels starting from Day-5, hinting at a potentially more effective treatment option.

The graph provides a visual comparison of treatments over a 15-day period, with each bar representing the mean blood glucose level for a group at a specific time point. The y-axis measures the blood glucose levels in mg/dl, while the x- axis categorizes the data into the respective groups. The color-coded bars for each day allow for quick assessment of the temporal changes in glucose levels, which is crucial for evaluating the long-term efficacy of diabetes Treatments.

Fig. No: 7 observing the blood glucose levels of animal

6. DISCUSSION:

Diabetes Mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycaemia. Several distinct types of DM are caused by a complex interaction of genetics and environmental factors. The factors contributing to hyperglycaemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production. Plants have played a major role in the development of new therapeutic agents. But there is still an extensive demand for new oral anti-diabetic drugs which are cheaper and have lesser side effects. Different indigenous drugs are used in the traditional systems of medicine for the treatment of diabetes mellitus, but they lack scientific investigations for their efficacy in a laboratory setting. Betel leaves is used by many people in Asia as a medicinal plant, which can cure many diseases. Betel leaves possess activity like anti diabetic, anti-ulcer, anti platelet aggregation, respiratory depressant and anti helminthic property (Tripathi Shalini Etal). Hence the present study was carried out to evaluate the anti-hyperglycaemic effect of extracts of leaves of piper betle in streptozotocin induced diabetic rats. In the present study, 50% ethanolic extract of dried leaves piper betel was given to different groups of animals at a dose of 50, 100 and 150 mg/kg body weight (groups IV, V and VI) and the blood glucose lowering effect of these groups were compared with the diabetic control group. The observations of this study were showed that the test drug (Piper betle leaf extract) and Standard drug (glibenclamide 0.5mg/kg body weight) reduces blood glucose level from the 5th day onwards.

7. CONCLUSION:

Diabetes mellitus is becoming a health-care problem worldwide, with the raise in disease prevalence being even more worrying as it not only affects the developed world but also developing nations with fewer resources to cope with yet another major disease burden. Current therapies used for diabetics have side effects, so the current shift to the use of herbal preparations may be more effective, relatively low cost, less side effect and low toxicity. The present data indicates that Piper betel juice possesses potential as an antidiabetic action. Piper betel shows promise in potentially managing diabetes mellitus due to its reported antidiabetic, antioxidant, and anti-inflammatory properties, further research, particularly well-designed clinical trials, is needed to confirm its efficacy and safety. Existing evidence suggests potential benefits, including improved insulin sensitivity and regulation of blood glucose levels, but more robust studies are required to establish its role in diabetes management. Additionally, safety considerations, especially regarding long-term consumption and potential adverse effects, should be carefully evaluated. Overall, while Piper betel holds potential, its use in diabetic mellitus should be approached with caution until more conclusive evidence is available Piper betel is one of the famous climbers used for treating numerous diseases as mentioned above. Richest source of nutrients and phytochemical it's all parts are used as medicine for humans and animals without any toxicity or side effects. Piper betel dried leaves powder successfully showed the affirmative effects against the glucose, lipid and oxidative stress levels on rats. This leads that Piper betel can be used in curing potential pharmaceuticals for diabetics, hyperlipidaemic and oxidative stress levels as well as effect full for other parameters like haemoglobin, albumin, protein, HDL cholesterol and LDL cholesterol. It can be used in different form like incorporating in our food products; table or capsule form as well as we can take the form of powder with normal water. Piper betle juice had shown significant lowered the blood glucose levels in all groups. In addition, body weight, organ (liver, kidney, heart and pancreas) weight, food intake, water intake was also examined in all treated groups and compared against diabetic control group.

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