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EVALUATION OF ANTI-DIABETIC ACTIVITY OF ETHANOLIC EXTRACT OF *MORINDA CITRIFOLIA* ON STZ INDUCED RATS

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ABSTRACT

This study explores the protective and hypoglycemic effects of *Erythrina indica* (EEMC) on lipid profiles of serum in streptozotocin (STZ)-induced rats suffering from diabetes. Numerous plants have traditionally been used to treat diabetes, with compounds like polysaccharides, flavonoids, terpenoids, tannins, and steroids known to exert antidiabetic effects. EEMC contains these bioactive compounds, which likely contribute to its observed hypoglycemic activity. Streptozotocin administration in rats induces rapid destruction of pancreatic β-cells, impairing glucose-stimulated insulin release and causing insulin resistance, hallmark features of type II diabetes. While oral hypoglycemic agents and insulin are used to manage diabetes, there is emerging interest in herbal remedies due to the ill effects of conventional drugs. The study shows that EEMC significantly decreases level of glucose in blood ($P < 0.05$) in rats suffering from diabetes compared to controls. The potential mechanisms for its hypoglycemic effect include potentiation of pancreatic insulin secretion, enhanced glucose transport to peripheral tissues, and possibly other actions like inhibiting glucose production or stimulating gluconeogenesis in the liver and muscles. Diabetes often leads to hyperlipidemia due to decreased insulin levels and impaired lipoprotein lipase activity. The observed improvement in plasma lipid levels in EEMC-treated rats suggests its potential role in improving insulin secretion. These findings confirm that antidiabetic action of ethanolic extract of *Erythrina indica* bark, warranting further research to isolate and characterize the specific hypoglycemic compounds and understand their mechanisms of action.

KEYWORDS: *Erythrina Indica* Bark, Antidiabetic, Hypoglycemic.

1. INTRODUCTION

Diabetes is a dangerous, long-term condition which arises when our body is not able to use insulin that the pancreas generates, or when the hormone that controls blood sugar levels, insulin, is not produced in sufficient amounts. Uncontrolled diabetes frequently results in elevated blood glucose, which over time can seriously harm the heart, blood vessels, eyes, nerves as well as kidneys. Diabetes affects over 400 million individuals globally. Type 2 diabetes (formerly called as adult-onset diabetes or non-insulin-dependent), Type 1 diabetes (previously known as childhood-onset, juvenile, or insulin-dependent diabetes), gestational diabetes mellitus (GDM), a transient state which develops during pregnancy and brings a long-term danger of developing Type 2 diabetes, and Maturity Onset Diabetes of the Young (MODY) are four kinds of diabetes mellitus.

1.1 Diabetes Mellitus

"Diabetes" comes from the Greek term "Diabainein," that means "to pass through." It is typified by symptoms like hunger, thirst, and gradual weight loss, as well as an

excess of glucose in the urine and blood. By acting at multiple locations and promoting uptake of glucose into cells, hormone named insulin controls the metabolism of carbohydrates and triglycerides. Additionally, it moderates the gluconeogenic process and promotes glucokinase production. Patients with diabetes have a malfunction in the normal functioning of the insulin.

Type – 1 Type 1 diabetes is not usually linked to obesity but rather to acidosis or ketosis. Individuals suffering from Type 1 diabetes must be administered insulin. There are two subtypes of this diabetes: idiopathic and immune. Although the majority of patients receive a diagnosis before the age of 30, the immune form is the most prevalent and can impact people of any age. It is called juvenile diabetes when it develops in childhood or infancy (because of a congenital condition). Although there is a multifactorial genetic linkage and genetic predisposition, only 15–25% of individuals have a positive family record. Degeneration of β cells in pancreatic islets of Langerhans is a feature of type 1 diabetes. Viral infections, congenital conditions, and autoimmune reactions—in which the body creates antibodies against its own β cells.

Type – 2 Tissue resistance to insulin and a relative lack of insulin production are hallmarks of diabetes. It is frequently referred to as mature onset diabetes mellitus since it usually manifests after the age of 40. High-density lipoprotein (HDL) levels are normally low in type 2 diabetes, but impaired insulin action impacts fat metabolism, resulting in raised triglyceride levels and increased free fatty acid flow. Insulin levels in the blood and the β cell's structure and activity are both often normal in Type 2 diabetes. However, the disorder arises because the body's cells lack or have fewer insulin receptors, which hinders the body's ability to properly absorb glucose.

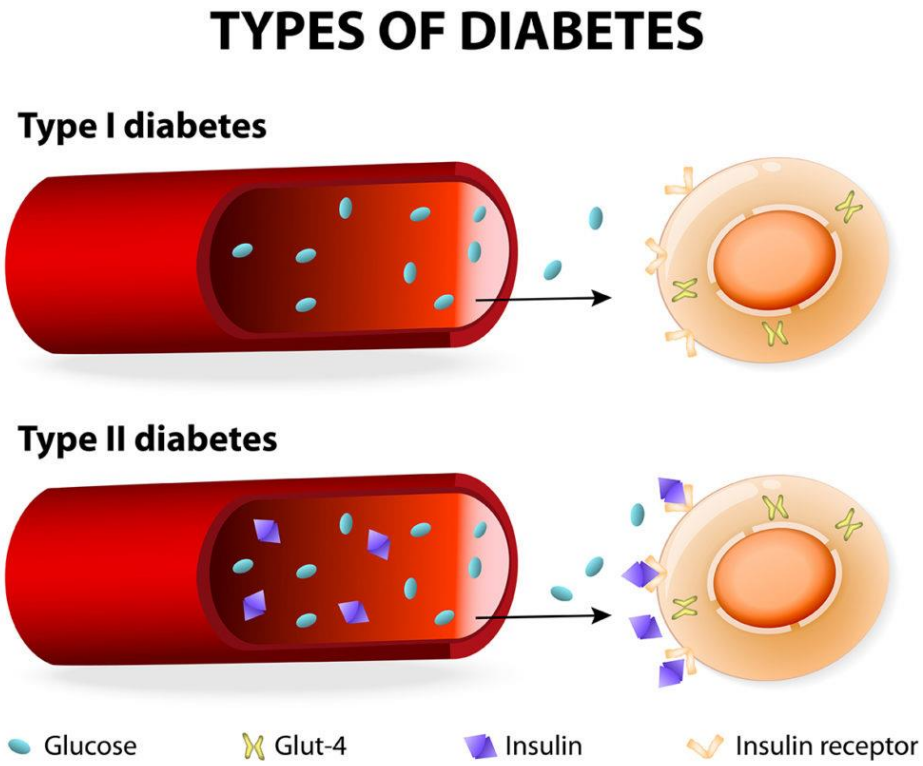

Fig. 1: Types Of Diabetes.

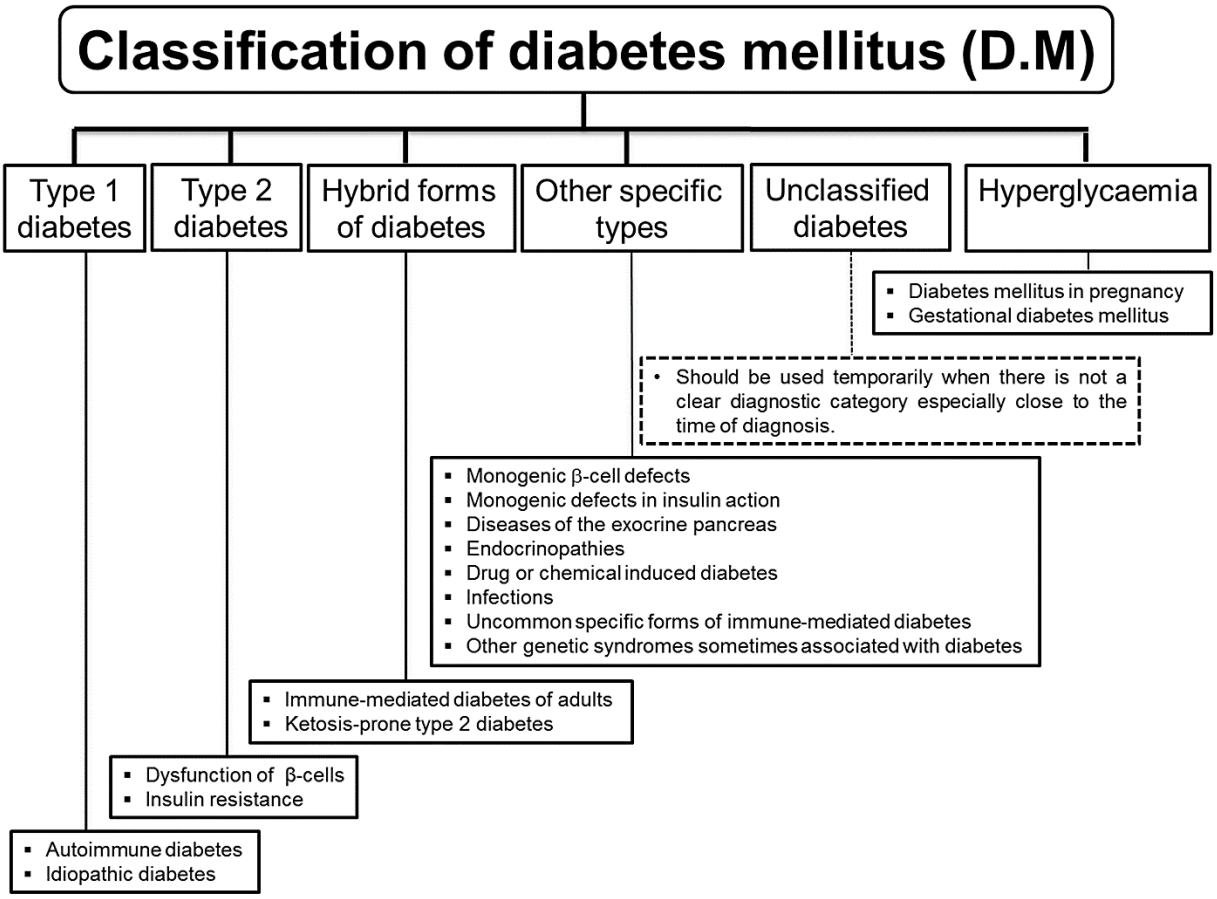

Fig. 2: Drug Classification Of Diabetes Mellitus.

2. PLANT PROFILE

2.1 General Information

- Biological Name : *Morinda citrifolia linn*
- Family : Rubiaceae
- Parts used : Leaf

2.2 Taxonomical Classification

- Kingdom : Plantae
- Order : Gentianales
- Family : Rubiaceae
- Genus : *Morinda*
- Species : *M.Citrifolia*

2.3 Vernacular Name

- Hindi : Achi
- English : Indian Mulberry
- Tamil : Nuna
- Telugu : Maddi chetty
- Kannada : Noni
- Malayalam : Manmanatti

2.4 Description

The plant, commonly known as Noni, has the scientific name *Morinda citrifolia Linn* and belongs to the Rubiaceae family. This plant is called Indian Mulberry in India and Noni in Hawaii. It is called Menkudu in Malaysia and Hair and Cheese Fruit in other parts of the western Pacific. The plant grows quickly and usually reaches a height of four to six meters. It features huge, fleshy leaves that range in shape from lanceolate to oval.

The plant's stem is straight and sturdy. The fruit is oval, fleshy, and hard when immature, becoming soft upon ripening. The usual width is 1-2 inches and length is 2-3 inches. Fruit contains numerous seeds, which can range from 200 to 300 in number. Once fully ripe, the fruit emits a foul and unpleasant odor.

2.5 Phytochemistry

Morinda citrifolia Linn is a nutrient-rich plant containing over 100 different chemical compounds that have been isolated to date. The composition of these compounds varies depending on factors such as drying and harvesting methods, the time and place of cultivation, growth conditions, and climate. The plant is often harvested for its bark, which is rich in sugars. About 35% of the stem bark is made up of water, with the remaining 10% to 15% consisting of fiber and particles that contain sugars. The stem has a sweet taste because to its almost 5% fructose and glucose content and 1% sucrose content.

Proteins make up the majority of the remaining solids; the bark's nutritional value is roughly 70% carbs, 30% fiber, and 0-5% proteins. Dietary lipids, potassium (up to 3500 ppm), salt (16-200 mg/L), and vitamin C (0.1-0.5%) are also present in the bark. Additionally, essential

micronutrients such as calcium, selenium, and iron are present in sufficient amounts to meet the daily requirements for adults. Freeze-dried juice from the stem bark also contains trace elements such as copper, cobalt, molybdenum, and manganese.

2.6 Pharmacological Action

Anti-inflammatory Action, Anti dementia Action, Analgesic Action, Anti arthritic Action, Anti hyperlipidemic Action, Anti-parasitic Action, Antibacterial Action, Antioxidant Action, Hepato protective Action.

Fig. 3: Leaf Of *Morinda citrifolia Linn.*

3. MATERIALS AND METHODS

3.1 Plant Extract Preparation

Hot continuous Soxhlet extraction method was used to extract 50 g of powdered plant material. The extraction process was conducted in a percolator for two days using 500 ml of ethanol (99.9% v/v) as the solvent. Solvent can move via extractor numerous times thanks to this continuous extraction process. After passing through the condenser, the solvent's vapors are sent back to the extractor for more extraction. The lower end of the equipment is connected to a distillation flask, while the extractor body (thimble) is connected to a side siphon tube. Standard joints are used to attach the extractor's mouth to the condenser.

Procedure: After being weighed, about 50 g of dried powdered plant material was put into a thimble for packaging. The material was wetted with (99.9% v/v) ethanol throughout the packing process, and the ethanol was poured until the siphon tube was full. To keep the round-bottom flask from bumping while the extraction was taking place, a piece of porcelain was added.

A gelatin salt reagent was added to the third component, and a solution was made for the second portion in order to identify the tannins. Tannins were detected by precipitation with the gelatin salt reagent or with both reagents. But precipitation from the salt solution by itself was regarded as a false-positive. By adding a some droplets of diluted $FeCl_3$ (1%) to the test extracts, which produced a green or black coloring, positive tests were further verified. In order to establish the tannin presence, the extract was also combined with a solution of lead acetate and watched for the white precipitate formation

3.2 Preliminary Phytochemical Analysis

To identify the plant components, the ethanolic extract of *Morinda citrifolia Linn* leaves is put through a preliminary phytochemical screening process.

- Carbohydrate Test
- Alkaloid Test
- Steroid and Sterol Test
- Glycoside Test
- Saponin Test
- Tri-terpenoid Test
- Tannin and Phenolic Compound Test
- Fixed Oil and Fatty acid Test
- Gums and Mucilage Test
- Protein and Amino acid Test

3.3 Animals

The Institutional Animal Ethics Committee gave its approval for the current study, and the protocol complied with the national CPCSEA criteria. Wistar albino rats weighing 150 and 200 grams were purchased for this investigation from Animal House, Aadhi Bhagawan College of Pharmacy in Tiruvannamalai, India.

Quarantine and Acclimatization: Separating recently arrived rats from those already housed in facility till health and perhaps microbiological status of latter are established is known as quarantine. To reduce the

possibility of introducing diseases into established animals, the recently acquired Wistar albino rats were placed in quarantine for a week. This allowed the rats to stabilize psychologically, physiologically, and nutritionally before being used.

Housing: Animals lived in a well-ventilated animal home that was kept between 55 to 60 percent relative humidity and at a consistent temperature. Rats were kept in spacious polypropylene cages with bedding made of paddy husk.

Water and Diet: The animals were kept on purified water and a typical pellet diet. With the exception of fasting, rats were provided with unlimited access to food as well as water. Twice a week, the bed's material was replaced.

Animal identification: Every animal cage utilized in the research was properly identified by labels. For proper identification, each animal in the cage had a picric acid mark applied to its head, body, or tail.

3.4 Experimental Protocol

At the start of the trial, each animal's body weight and fasting glucose levels were noted. Throughout the investigation, a one-touch glucometer was used to measure the blood glucose levels of 30 rats, who were segregated into 5 groups, each containing 6 animals.

- **Group1:** Distilled water was given to normal control rats.
- **Group2:** For 21 days, rats with STZ-induced diabetes were given distilled H_2O and used as diabetic control.
- **Group3:** For 21 days, STZ-induced diabetic rats were given the usual medication Glibenclamide (5 mg/kg BW p.o.).
- **Group4:** EEMC was given to STZ-induced diabetic animals for 21 days. (200 mg/kg BW p.o.).
- **Group5:** EEMC was given to STZ-induced diabetic animals for 21 days. (400 mg/kg BW p.o.).

Each rat's body weight was recorded on days 7, 14, and 21 of the treatment, as well as before to the induction of diabetes (day 4). During the study period, blood glucose levels were assessed using the tail tip cutting method on days 1, 7, 14, and 21.

3.5 Pharmacological Evaluation

3.5.1 In-vivo Anti-diabetic Evaluation

Diabetic Wistar rats were used to test the antidiabetic properties of *Morinda citrifolia Linn.* To induce diabetes, an intraperitoneal administration of STZ at a dosage of 50 milligram per kilogram body weight was administered. Plant extract's antidiabetic effects were contrasted with those of the common medication Glibenclamide.

3.5.2 Diabetes Induction In Rats

After a week of acclimatization, the animals were left for fasting overnight. Diabetes was brought on by intraperitoneal administration of STZ that had just been dissolved in citrate buffer (pH 4.5). These rats were given a 5% glucose solution of water to drink overnight in order to combat the drug-induced hypoglycemia brought on by the immense release of insulin. After three days, level of glucose in blood was determined, and rats were found diabetic and added to study if their blood concentration was more than 250 mg/dl. On the fourth day following the streptozotocin injection, the plant extract was administered; this was regarded as the first day of therapy, which lasted for 21 days.

3.6 Statistical Evaluation

Statistical evaluation was accomplished using Duncun's Multiple Range Test, and $p<0.05$ was considered substantial. All of data of outcomes was presented using a one-way ANOVA with Mean ± S.E.M.

4. RESULTS AND DISCUSSION

4.1 Preliminary Phytochemical Study

Table 1: Preliminary Phytochemical Study.

TEST FOR	RESULT
Flavonoids	+ve
Saponins	+ve
Tannins	+ve
Terpenoids	+ve
Glycosides	+ve
Phytosterols	+ve
Protein	+ve
Carbohydrates	+ve
Alkaloids	+ve

4.2 Pharmacological Activity

4.2.1 Influence of Ethanolic Extract Of *Morinda citrifolial (EEMC)* on Body Weight in Streptozotocin Stimulated Diabetic Animals.

Table 2: Effect on Body Weight.

Group	Treatment	Average Body Weight(gm) (in days)			
		1st Day	7th Day	14th Day	21st Day
1.	Normal control	148.9±2.9	150.63±2.3	156.5±2.4	164.85±2.9
2.	Diabetic control STZ (150mg/kg)	150.65±1.0	142.21±2.9	137.05±2.8	134.3±2.0
3.	Glibenclamide (5mg/kg)	154.06±1.23	147.9±2.3	144.18±1.2	139.05±1.07
4.	*EEMC (*200mg/kg)	156.7±1.49	146.5±1.32	142.75±1.9	136.5±3.15
5.	EEMC (400mg/kg)	150.42±2.14	143.95±1.9	140.33±1.8	142.8±0.9

Records were stated as Mean ± SD, N=6 The table displays average body weight for each group over the course of the study. Average body weight at day 21 confirmed a reduction in GP2, GP3, GP2, and GP5 compared to the first day. Body weight of GP2 (diabetic animals) substantially reduced (P<0.05) in comparison within the groups.

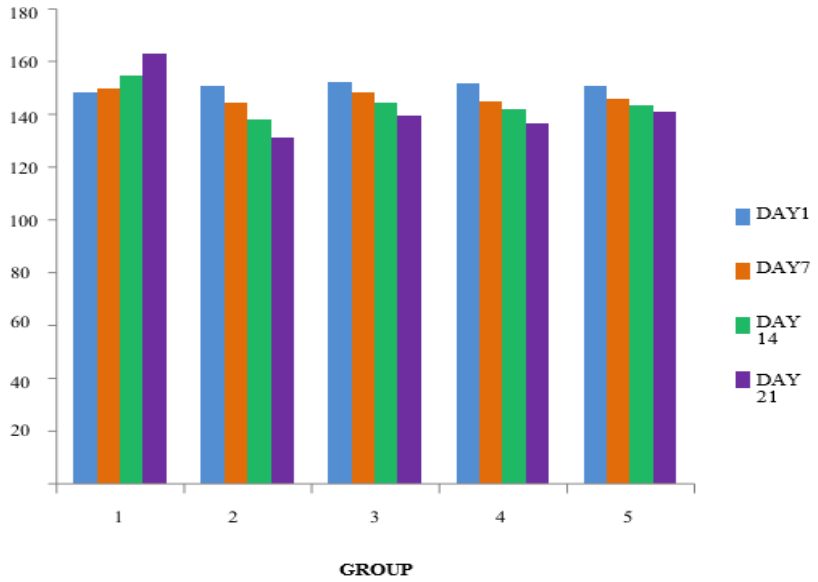

Fig 4: Mean weight of diabetic Wistar rats caused by streptozotocin following three weeks of therapy with an ethanolic preparation of *Morinda citrifolia Linn.*

4.2.2 Effect of Ethanolic Extract Of *Morinda citrifolia Linn* On Whole Blood Glucose (WBG) In Streptozotocin Induced Diabetic Rats

Table 3: Effect On Whole Blood Glucose (WBG).

GROUP	TREATMENT	Whole Blood Glucose (mg/dL)			
		1st Day	7th Day	14th Day	21st Day
1.	Normal control	76.3±3.02	75.07±0.67	83.05±0.80	96.32±0.44
2.	Diabetic control STZ (150mg/kg)	385.5±1.46	420.05±1.52	417.02±1.41	433.3±1.3
3.	benclamide (5mg/kg)	334.62±2.04	265.97±1.42	224.58±0.69	178.1±1.19
4.	*EEMC (*200mg/kg)	354.22±7.53	271.81±1.01	245.48±1.44	187.93±1.06
5.	*EEMC* (400mg/kg)	422.4±4.97	390.72±1.15	240.03±1.52	189.23±9.58

Records were conveyed as Mean±SD, N=6 Average blood glucose displayed a major drop in GP3, GP4, and GP5 when relating the 21st day with the 1st day. On day 21, GP3, GP4, and GP3 had lower mean blood glucose levels than GP2. There was a statistically substantial (p<0.05) difference among GP1, GP2, GP3, GP4, and GP5. When comparing GP2 to GP3, GP4, and GP5, a statistically substantial (p<0.05) variation was observed in both groups.

On day 21, GP3, GP4, and GP3 had lower mean blood glucose levels than GP2. There was a statistically substantial (p<0.05) difference relating GP1 and GP2, GP3, GP4, and GP5. There was a statistically substantial (p<0.05) variation between GP2 and GP3, GP4, and GP5 groups.

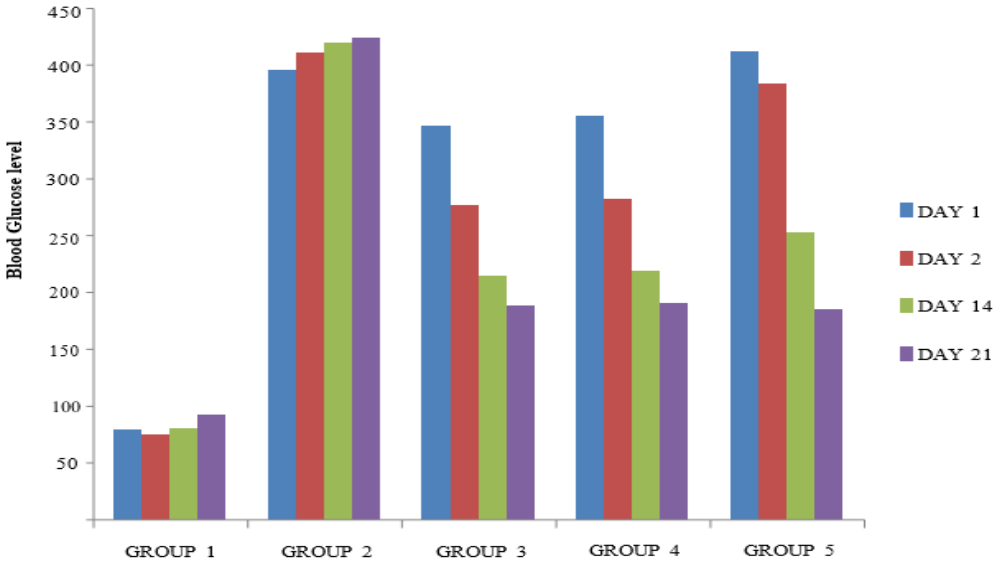

Fig: 5 Graphical Representation Of Mean Blood Glucose Level.

DISCUSSION

Numerous herbs, some of which have been shown to have hypoglycemic properties, have been used traditionally to treat diabetes. According to these studies, the antidiabetic action is caused by substances such polysaccharides, flavonoids, terpenoids, tannins, and steroids. Moreover, phenolic chemicals, steroids, tannins, flavonoids, saponins, and carbohydrates are present in EEMC. The combined action of these chemicals in the extract may have caused the plant's observed hypoglycemic effects.

When STZ was administered to rats, the pancreatic β-cells were rapidly destroyed, resulting in decreased glucose-stimulated insulin release and insulin resistance—two characteristics that are characteristic of type II diabetes. Currently, diabetes mellitus can be treated with insulin and oral hypoglycemic medications. However, because of the negative effects of the current medications, there is an increasing interest in herbal therapies. The current study shows that EEMC has both hypoglycemic and protective effects on the serum lipid profile of rats with STZ diabetes. Comparing EEMC- of treated diabetic rats to diabetic controlled rats, we found a substantial ($P < 0.05$) drop in blood glucose.

The potential mechanism of EEMC's hypoglycemic action could be because of blood glucose transfer to peripheral tissue, augmented secretion of insulin, or other mechanisms like stimulating peripheral tissue's uptake of glucose, inhibiting endogenous glucose production, or activating gluconeogenesis in the liver and muscles.

Hyperlipidemia is linked to diabetes. Triglycerides are hydrolyzed under normal circumstances by the lipoprotein lipase enzyme, which is known to be activated by insulin. When β-cells are destroyed, plasma insulin levels drop, causing hyperlipidemia. The substantial regulation of plasma lipid levels raises the possibility that the EEMC works via enhancing insulin secretion..

5. CONCLUSION

The findings support anti-diabetic properties of an ethanolic extract of the bark of the *Morinda citrifolia* plant. To clarify their method of action, it is also vital to conduct additional research in order to extract and identify the hypoglycemic components in this plant.

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