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Research Article

Study of the Antidiabetic Activity of the Ethanol Extracts of the Leaves and Juice of the Fruits of *Morinda citrifolia*

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Abstract

The present study aims to evaluate the effect on blood glucose of the ethanolic extract of the leaves and juice of *Morinda citrifolia* (rubiaceae) leaves and fruit in a model of type 2 diabetes. After maceration in ethanol (95%), followed by filtration, the resulting extract is concentrated using a rotary evaporator to remove the extraction solvent. The juice extract is obtained by pressing, followed by filtration. The resulting filtrate is subjected to a series of extractions with ethanol and then concentrated using a rotary evaporator. The extracts are tested in normoglycemic rats in a glucose tolerance test, as well as in type 2 diabetic rats. They had virtually no effect on the basal blood glucose levels of normoglycemic rats, with values of 0.85 ± 0.03 vs 0.78 ± 0.035 g/L and 0.87 ± 0.04 vs 0.76 ± 0.015 g/L respectively at T0 and T4h and at oral doses of 50 mg/kg and 100 mg/kg for the ethanol extract of the juice. For the ethanol extract of the leaves, the values were estimated at 0.815 ± 0.04 vs 0.66 ± 0.015 g/L and 0.792 ± 0.025 vs 0.695 ± 0.03 g/L respectively at oral doses of 50 mg/kg and 100 mg/kg. The tested extracts showed antihyperglycemic activity in a glucose tolerance test. Indeed, at oral doses of 50 and 100 mg/kg of ethanolic extracts of the leaves and juice, the hyperglycemic peaks after glucose administration (4 g/kg orally) were reached at 1.80 ± 0.1 and 1.52 ± 0.16 g/L, respectively, at baseline (T0), then at 1.29 ± 0.25 g/L and 1.45 ± 0.41 g/L at 30 minutes (t30min), compared to 2.03 ± 0.28 g/l in the control group. Furthermore, the juice extract exhibited antihyperglycemic effects in a model of alloxan-induced insulin secretion disorder. Indeed, at a dose of 50 mg/kg orally, blood glucose, after eight (08) days of observation, were 1.5 ± 0.51g/L vs 3.96 ± 0.40 in the control group (physiological saline) and 1.9 ± 0.94 in the group treated with glibenclamide. The compounds contained in the leaves and fruits of *Morinda citrifolia* exhibit anti-hyperglycemic properties. These results are explained by the presence in the extract of chemical compounds such as flavonoids, whose role in modulating sensitivity and regulating carbohydrate metabolism has been demonstrated in previous studies.

Keywords

Morinda Citrifolia, Hyperglycemic, Antidiabetic, Normoglycemic

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1. Introduction

Diabetes mellitus is a chronic metabolic disease characterized by persistent hyperglycemia, resulting from a defect in insulin secretion or action, or both. This chronic hyperglycemia is responsible, in the long term, for specific complications affecting the eyes, kidneys, nerves, heart, and blood vessels [1]. According to the World Health Organization (WHO), the global prevalence of diabetes continues to rise, and the diabetic population is expected to exceed 300 million individuals by 2025. [2]. The management of type 1 diabetes relies primarily on insulin therapy, requiring several daily injections of exogenous insulin, which can be burdensome and a source of discomfort for patients [3]. In order to improve the quality of life of people with diabetes, new therapeutic alternatives are being explored, including the use of medicinal plants with antihyperglycemic potential.

Oral antidiabetic drugs, such as sulfonylureas, biguanides, alpha-glucosidase inhibitors, and glinides, are widely used in type 2 diabetes, but their use can be accompanied by sometimes severe side effects, prompting some patients to turn to herbal medicine [4]. The use of plant extracts in diabetes management is a well-established practice in traditional medicine, particularly in Africa, where nearly 80% of the population in developing countries uses them at least once.

Among the plants studied for their antidiabetic properties, *Morinda citrifolia* (commonly known as Noni) is attracting increasing interest. Ethanolic extracts of the fruit and leaves of this plant have demonstrated significant hypoglycemic effects in various animal models and in vitro. Several studies have highlighted the ability of these extracts to reduce blood glucose levels, improve insulin sensitivity, and decrease glycated hemoglobin (HbA1c) [5].

From a phytochemical perspective, *Morinda citrifolia* is rich in bioactive compounds such as flavonoids, anthraquinones, iridoids, polyphenols, saponins, tannins, and vitamin C, which may contribute to its antidiabetic and antioxidant effects [6]. These properties make Morinda citrifolia a promising candidate for the development of new natural therapeutic agents against diabetes.

In this context, this study aims to evaluate the antihyperglycemic activity of the ethanol extract of *Morinda citrifolia* fruit and leaf juice, and to test its efficacy on different experimental models of hyperglycemia.

2. Material and Methods

2.1. Materials

2.1.1. Plant Material

The plant was harvested in December 2023 in the garden of the Faculty of Medicine, Pharmacy, and Dentistry at Cheikh Anta Diop University of Dakar (UCAD). After harvesting, the leaves were washed and then dried in the dark at room temperature in the laboratory of the Research Group on Bioactive Substances (GRSB). They were ground using an electric grinder to obtain a fine powder, which was carefully stored in jars to prevent any contamination.

Figure 1. *Plant matter.*

2.1.2. Animal Material

The animals used in this study were male or female Wistar rats, selected according to specific criteria to ensure the validity of the results:

1) Weight: between 124 and 240 g
2) Prior selection: no rats had been selected for previous studies
3) Health status: no eye lesions were noted
4) Reproductive status: females must not be pregnant
5) Age: the average age is 6 to 8 months

The rats are kept in the animal facility of the Pharmacology and Pharmacodynamics Laboratory at Cheikh Anta Diop University in Dakar, where they are exposed to a regular light cycle, with light during the day and darkness at night. The selected rats are weighed, numbered, and housed in cages lined with wood shavings for their comfort. They receive an appropriate diet consisting of "chicken feed" from the SENTENAC Mills in Dakar, twice a day. They also have free access to water.

Figure 2. *Animal Equipment.*

2.2. Methods

2.2.1. Preparation of the Ethanol Extract of *Morinda citrifolia* Leaves

One hundred (100) grams of this powder are macerated in 600 mL of ethanol for 72 hours. After filtration, the resulting extract is concentrated using a rotary evaporator to remove the extraction solvent.

2.2.2. Preparation of the Ethanol Extract of *Morinda citrifolia* Fruit Juice

The pressing-filtration method is used. The resulting filtrate is transferred to a separatory funnel and subjected to a series of extractions with ethanol. The juice extract is then placed in a rotary evaporator to remove the solvent.

2.2.3. In vivo study of the Effect of Ethanol Extracts

The experiments are carried out within the Pharmacology and Pharmacodynamics Laboratory of the Faculty of Medicine, Pharmacy and Odontology, of Cheikh Anta Diop University of Dakar.

The products are administered by gavage using a feeding tube. The extract is suspended in isotonic saline (IS), and different concentrations were prepared from the raw extract and the solvent used, these are: 5 mg/mL, for the dose 50 mg/Kg per os and 10mg/mL for the dose 100 mk/Kg per os. Animals with normal blood glucose levels are divided into groups, each receiving a single oral dose of the different extracts. A negative control group receives physiological saline, while the positive control group receives glibenclamide solution (the reference product), a hypoglycemic drug. Depending on the method used, blood glucose is measured using an ACCU-CHEK Instant glucometer with test strips on a drop of blood taken from the tip of the animal's nose.

2.2.4. Trials in Normoglycemic Rats

Twenty (20) rats were carefully selected and divided into five groups of four animals each to ensure a rigorous evaluation of the treatment effects. Before the start of the experiment, all rats were fasted for 12 hours, thus ensuring homogeneous experimental conditions. as illustrated in Table 1.

Before administering the treatments, a baseline blood glucose measurement was performed on all rats at T_0, thus determining their fasting blood glucose level.

Immediately after this measurement, the rats received either physiological saline or the product to be tested, depending on their respective group.

Blood glucose levels were measured at regular intervals over a four-hour period, corresponding to times T_1, T_2, T_3, and T_4. These successive blood glucose measurements will allow for the analysis of the changes induced by the administered treatments and the evaluation of the efficacy of the product being tested [7].

Table 1. Treatments for Normoglycemic Rats.

batches	Dose	Treatment with	Voice
batche 1	10 mL/kg	Physiological saline solution	Per os
Batche 2	50 mg/kg	Ethanol extract of Morinda citrifolia leaves	
batche 3	100 mg/kg		
batche 4	50 mg/kg	Ethanol extract of the juice of Morinda citrifolia fruits	
batche 5	100 mg/kg		

2.2.5. Trials in Rats with Temporary Hyperglycemia

In this study, we conducted trials on rats that received a glucose load after twelve (12) hours fast.

An initial blood sample was taken to determine the animals baseline blood glucose levels. Subsequently, the rats were gavaged with a glucose solution at a dose of 4 g/kg body weight to induce a controlled rise in blood glucose.

The rats were carefully selected and randomly divided into five groups of four animals each to evaluate the effect of the treatment on blood glucose (Table 1).

An initial blood sample was taken 90 minutes before administration of the test product to assess the initial impact of the treatment. Subsequently, blood samples were taken just before administration of the glucose solution, and then every 30 minutes for a period of 120 minutes [8].

Table 2. Treatment of Rats with Temporary Hyperglycemia.

batches	Dose	Treatment with	Voice
batche 1	10 mL/kg	Physiological saline solution	Per os
Batche 2	50 mg/kg	Ethanol extract of Morinda citrifolia leaves	
batche 3	100 mg/kg		
batche 4	50 mg/kg	Ethanol extract of the juice of Morinda citrifolia fruits	
batche 5	100 mg/kg		

2.2.6. Type 2 Diabetes

Sustained hyperglycemia was induced by subcutaneous injection of an alloxan monohydrate solution (Sigma A7413-25MG; 98) at a concentration of 100 mg/mL at a dose of 100 mg/kg.

Twenty rats received a subcutaneous injection of alloxan monohydrate at a dose of 100 mg/kg body weight of freshly prepared alloxan solution with 0.9%. Seventy-two (72) hours after alloxan administration, the rats glycosuria was determined using test strips. Animals exhibiting marked glycosuria and with blood glucose levels between 2 and 4 g/L were considered to have type 2 diabetes and were included in the

experiment. They were divided into three groups of three.

- A control group treated with physiological saline at a dose of 10 mL/kg/day orally for 8 to 7 days.
- A group treated with glibenclamide solution at a dose of 0.3 mg/kg/day orally for 8 to 7 days.
- A group treated with the ethanol extract of *Morinda citrifolia* fruit juice at a dose of 50 mg/kg orally for 8 to 7 days. Blood samples were taken every 48 hours and blood glucose levels were measured [8].

3. Analysis

The results are expressed as mean ± standard error of the mean (Mean ± ESM). The homogeneity of the basic parameters was confirmed by analysis of variance (ANOVA). The results were compared using Fisher's exact test. A p-value < 0.05 was considered statistically significant, and (n) represents the number of experiments in each group.

4. Results

4.1. Tests of *Morinda citrifolia* Extracts in Normoglycemic Rats

4.1.1. On the Ethanol Extract of Fruit Juice

The yield values shown in Table 3 demonstrate that the parts of the plant studied are rich in secondary metabolites, including polyphenols, sugars, tannins, flavonoids, etc. These results, considered quite high, are certainly accentuated by the nature of the extraction solvent, ethanol, which is polar.

Table 3. *Extraction Yields in Juices and Leaves.*

Part of the plant	Mass (g)	Volume of solvent (mL)	Mass of the extract (g)	Yield (%)
Fruit juice	200	350	10.50	5.25%
Leaves	100	600	12.04	12.03%

About the normoglycemic test, the Figure 3 shows that administration of the ethanol extract solution at doses of 50 and 100 mg/kg did not result in a significant decrease in blood glucose levels in normoglycemic rats compared to the control group. Indeed, blood glucose values were 0.95 ± 0.065 g/L at T0 and 0.847 ± 0.035 g/L at T4H for the control group, 0.855 ± 0.03 g/L at T0 and 0.785 ± 0.035 g/L for the group treated with the 50 mg/kg dose, and 0.875 ± 0.04 g/L at T0 and 0.767 ± 0.015 g/L for the group receiving the solution of interest at a dose of 100 mg/kg.

These results suggest that the ethanol extract of Morinda citrifolia fruit juice does not cause hypoglycemia in normoglycemic rats.

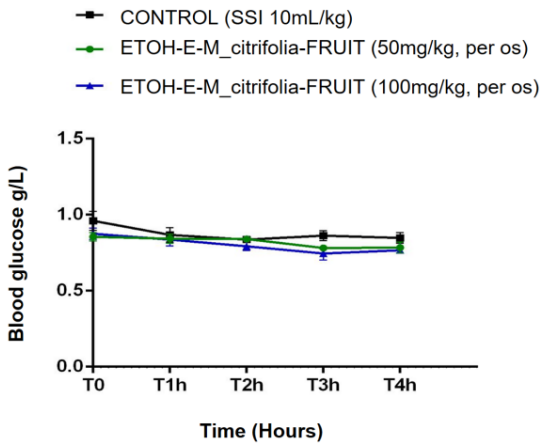

Figure 3. *Mean Blood Glucose Levels of the Ethanol Extract of Morinda Citrifolia Fruit Juice in Normoglycemic Rats.*

4.1.2. On the Ethanol Extract of the Leaves

The ethanol extract of the leaves shows a similar profile. The Figure 3 shows that the administration of the ethanol extract solution at doses of 50 and 100 mg/kg does not lead to a significant decrease in blood glucose in normoglycemic rats, compared to the control group. Indeed, the glycemic values were 0.950 ± 0.065 g/L at T-0H and 0.815 ± 0.040 g/L at T-4H for the control group, 0.855 ± 0.030 g/L at T-0H and 0.785 ± 0.035 g/L at T-4H for the group treated with a dose of 50 mg/kg, and 0.875 ± 0.040 g/L at T-0H and 0.767 ± 0.015 g/L at T-4H for the group receiving the solution of interest at a dose of 100 mg/kg.

These results suggest that the ethanol extract of Morinda citrifolia fruit juice does not induce hypoglycemia in normoglycemic rats.

The data are summarized in Figure 4.

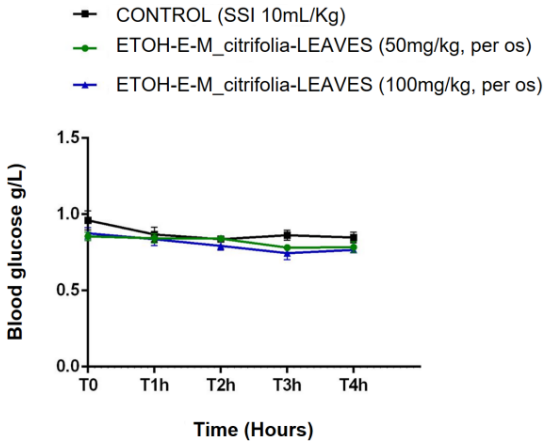

Figure 4. *Mean Blood Glucose Levels of the Ethanol Extract of Morinda Citrifolia Leaves in Normoglycemic Rats.*

4.2. Tests on Rats with Induced Hyperglycemia

Oral administration of glucose at a dose of 4 g/kg to normoglycemic rats previously treated with physiological saline induced significant hyperglycemia, with a peak glucose level observed at 30 minutes (2.13 ± 0.31 g/L versus a baseline glucose level of 0.74 ± 0.04 g/L). This 188% increase reflects the normal physiological response to a large glucose load, characterized by rapid intestinal glucose absorption and a transient rise in blood glucose.

4.2.1. Impact of Pretreatment on Glycemic Response on the Ethanol Extract of *Morinda citrifolia* Fruit Juice

Pretreatment with the ethanol extract of *Morinda citrifolia* fruit at two doses (50 mg/kg and 100 mg/kg) modifies this glycemic response. Indeed, at 30 minutes post-load, the glycemic peaks are markedly attenuated: 1.290 ± 0.250 g/L for 50 mg/kg and 1.450 ± 0.410 g/L for 100 mg/kg, compared to 2.130 ± 0.155 g/L in the control group. This reduction represents a 39.4% and 31.9% attenuation of the hyperglycemic peak, respectively, demonstrating a significant capacity of the extract to modulate the postprandial glycemic response.

The variation in blood glucose, expressed as a percentage, is calculated based on the following formula:

$$\%\ reduction = \frac{control\ value - processed\ value}{control\ value} \times 100$$

The variation in blood glucose (difference between the baseline value at T-0 min and the peak at T-30 min) was reduced in the treated groups: 0.49 ± 0.32 g/L for 50 mg/kg and 0.57 ± 0.46 g/L for 100 mg/kg, compared to 1.39 ± 0.165 g/L in the control group. This reduction in the magnitude of hyperglycemia of 64.7% (50 mg/kg) and 59.0% (100 mg/kg) suggests that *Morinda citrifolia* fruit extract significantly improves glucose tolerance.

At T-120min, the residual blood glucose was 1.15 ± 0.085 g/L for the control group, against 0.85 ± 0.17 g/L (50 mg/kg) and 0.81 ± 0.10 g/L (100 mg/kg), representing respective reductions of 26.1% and 29.6% (Figure 5).

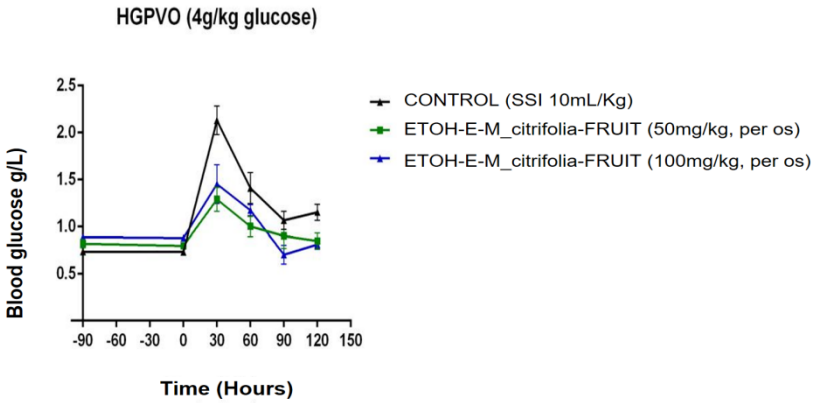

Figure 5. *Anti-Hyperglycemic Effect of the Ethanol Extract of Morinda Citrifolia Fruit Juice (50, 100 mg/kg, orally).*

4.2.2. Impact of Pretreatment on Glycemic Response on the Ethanol Extract of *Morinda citrifolia* Leaves

Pretreatment with the ethanol extract of *Morinda citrifolia* leaves at two doses (50 mg/kg and 100 mg/kg) also significantly modifies this glycemic response. Indeed, 30 minutes post-load, glycemic peaks are markedly attenuated: 1.806 ± 0.1 g/L for 50 mg/kg and 1.525 ± 0.165 g/L for 100 mg/kg, compared to 2.13 ± 0.155 g/L in the control group. This reduction represents a 15.2% and 28.4% attenuation of the hyperglycemic peak, respectively, demonstrating the extracts dose-dependent ability to modulate the postprandial glycemic response.

The variation in blood glucose (difference between the baseline value at T-0 min and the peak at T-30 min) was also significantly reduced in the treated groups: 1.036 ± 0.19 g/L for 50 mg/kg and 0.628 ± 0.245 g/L for 100 mg/kg, compared to 1.39 ± 0.156 g/L in the control group. This reduction in the magnitude of hyperglycemia was 25.5% (50 mg/kg) and 54.8% (100 mg/kg).

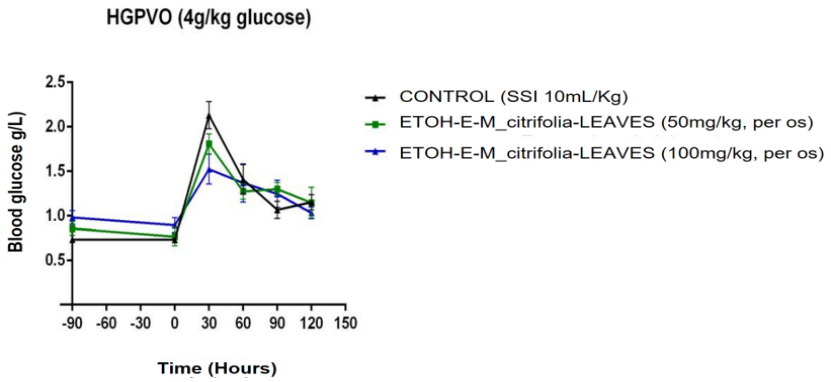

Figure 6. *Antihyperglycemic Effect of the Ethanol Extract of Morinda Citrifolia Leaves.*

4.3. Tests on Diabetic Rats

In the control group, blood glucose levels remained stable, fluctuating between 3.89 ± 0.20 g/L on day 0 and 3.96 ± 0.40 g/L on day 8, indicating persistent hyperglycemia without significant improvement. The glibenclamide group showed a progressive decrease in blood glucose levels, from 3.6 ± 0.56 g/L to 1.9 ± 0.94 g/L over 8 days, representing a reduction of 47.2%. The group treated with the extract of Morinda citrifolia juice also showed a clear decrease in blood glucose, from 2.37 ± 0.38 g/L to 1.5 ± 0.51 g/L, i.e. a reduction of 36.7%, with a biphasic kinetics characterized by stabilization between days 0 and 2, followed by a progressive decrease.

Intergroup comparisons using Fisher's exact test (LSD) revealed statistical significance ($p < 0.05$; n=4) between the extract group and the control group on days 4, 6, and 8, as shown in Figure 7. On day 8, the difference in blood glucose between the control and glibenclamide groups was 2.06 g/L, corresponding to a 52.0% reduction, while the difference between the control and the extract group was 2.46 g/L, a 62.1% reduction. Furthermore, the extract group had a blood glucose level 0.4 g/L lower than the glibenclamide group.

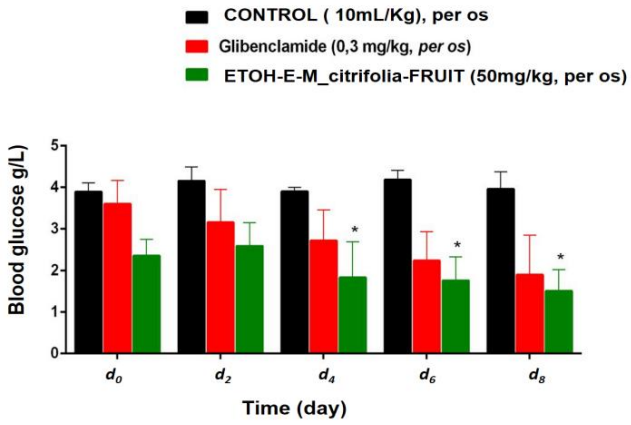

Figure 7. *Evolution of Blood Glucose in Type 2 Diabetic Rats After Daily Administration of the Ethanol Extract of Morinda Citrifolia Fruit Juice at a Dose of 50 mg/kg/day orally.*

5. Discussion

Phytotherapy for diabetes is currently experiencing significant growth due to the increasing discovery of plant extracts effective in treating diabetes [9].

In this study, we evaluated the hypoglycemic, antihyperglycemic, and antidiabetic effects of ethanolic extracts of the leaves and fruits of Morinda citrifolia (Rubiaceae) on blood glucose levels in normoglycemic rats, in a model of hyperglycemia induced by glucose overload (4 g/kg), and in an alloxan-induced type 2 diabetic rat model.

5.1. Effects in Normoglycemic Rats

In healthy rats, oral administration of *Morinda citrifolia* at 50 and 100 mg/kg did not induce severe hypoglycemia, a key element for product safety. Several studies report that noni regulates blood glucose levels without causing alarming hypoglycemic episodes. For example, administering Noni juice to a normoglycemic subject results in only a slight decrease in blood glucose levels, without exceeding physiological thresholds, which attests to a good safety profile [10].

The absence of a major hypoglycemic effect in normoglycemic rats is explained by a "glucoregulatory" effect, increasing insulin sensitivity rather than excessively stimulating pancreatic insulin secretion when it is not needed. Furthermore, Noni modestly inhibits intestinal glucose absorption, a mechanism similar to that of alpha-glucosidase inhibitors but to a lesser extent and without causing a sudden drop in blood glucose [11].

5.2. Effect on Induced Hyperglycemia (Glucose Load Test)

Following an oral glucose load (4 g/kg), rats become transiently hyperglycemic. Administering extracts of *Morinda citrifolia* (50 and 100 mg/kg) a few minutes before or immediately after the load allows us to measure its potential to accelerate the return to normal blood glucose levels. Several studies reveal that Noni fruit extract has a dose-dependent effect on reducing blood glucose levels after a glucose load in

rats. Oral administration of 50 mg/kg and 100 mg/kg of fruit extract shows that:

A dose of 50 mg/kg is more effective than 100 mg/kg in reducing the rise in blood glucose levels after glucose administration. This reduction is observable as early as 30 minutes after the load, with a faster return to normal blood glucose levels compared to untreated controls.

In parallel with certain oral antidiabetic drugs, high-dose Noni fruit extract shows a marked reduction, reflecting a limitation of intestinal glucose reabsorption and/or improved peripheral utilization of blood glucose [10].

Reductions of 28% to 70% in post-load blood glucose have been reported, depending on the dose and protocol used (De Carvalho et al., 2015). These results are comparable to some classic antidiabetic drugs such as metformin, although the mechanism of action of Noni differs [12].

Extracts of *Morinda citrifolia* exert their effect through several complementary mechanisms:

• Inhibition of intestinal absorption: reduction of the rapid entry of glucose into the bloodstream via partial inhibition of alpha-amylase and alpha-glucosidase.

• Stimulation of peripheral glucose uptake: activation of AMP-activated protein kinase, a crucial pathway for glucose uptake in muscles and the liver.

• Effect on insulin sensitivity/production: certain bioactive compounds in noni potentiate the action of insulin or stimulate pancreatic secretion, particularly in the context of insulin resistance, without excessive stimulation under normal physiological conditions.

5.3. Study in Alloxan-induced Type 2 Diabetic Rats (dose 50 mg/kg)

In animal models, the induction of type 2 diabetes by alloxan administration results in stable hyperglycemia, secondary to partial destruction of pancreatic β cells. A dose of 50 mg/kg is often considered optimal for maximizing efficacy while minimizing the risk of side effects, according to most trials.

This study demonstrates a significant reduction in fasting blood glucose (a 47.2% reduction in 8 days) in rats treated with the 50 mg/kg extract, compared to the diabetic control group. These results are consistent with the work of Nayak [13]. It should be noted that this decrease is often accompanied by:

1) an improvement in postprandial blood glucose levels,
2) a decrease in glycated hemoglobin (HbA1c),
3) an increase in liver glycogen and body mass,
4) an improvement in the lipid profile (decrease in triglycerides and LDL, increase in HDL) [3].

The efficacy of Noni is sometimes comparable to, or slightly lower than, that of reference drugs such as metformin or glibenclamide, but with the advantage of reduced oxidative stress and better hepatic tolerance.

However, longer-term dose-response studies and human clinical trials are still needed to validate the full range of benefits and long-term safety, as well as to clarify potential interactions with conventional treatments. Ethanol extracts of *Morinda citrifolia* at 50 and 100 mg/kg exhibit marked antidiabetic activity in rats, demonstrating a regulatory effect on blood glucose in normoglycemic models, effective reduction of acute hyperglycemia, and overall improvement of the metabolic profile in alloxan-induced type 2 diabetic rats. This efficacy relies on multiple mechanisms: slowing of glucose absorption, stimulation of insulin sensitivity, and antioxidant and cytoprotective effects. Noni thus represents a promising natural therapeutic option, justifying increased research on this plant for its rational and safe use in humans.

6. Conclusion

Research on the antidiabetic activity of *Morinda citrifolia* extracts highlights the therapeutic potential of this plant in managing hyperglycemia, using both its fruit and leaves. Ethanol extracts administered at different doses (50 and 100 mg/kg) to rats in induced hyperglycemia models demonstrated a significant reduction in postprandial blood glucose levels, with a dose-dependent effect. The 50 mg/kg dose was the most effective for the fruit extract. While leaf extracts were effective in limiting glycemic spikes, their overall effect was slightly less pronounced than that of the fruit extract. However, a good safety profile was observed, with no hypoglycemia induced in normoglycemic rats.

These results support the potential integration of *Morinda citrifolia* as an adjunct in diabetes management strategies, particularly for controlling postprandial hyperglycemia, reducing oxidative stress, and improving the overall metabolic profile. However, any extrapolation to humans requires further investigation, including clinical trials, to confirm efficacy, safety, optimal dosage, and the assessment of potential drug interactions.

The antidiabetic activity shown in this study may be due to a single bioactive molecule or to the synergy of several molecules present in the sample. Therefore, further studies are needed to isolate and characterize these molecules within the samples.

In short, *Morinda citrifolia* appears to be a promising plant resource, warranting particular attention in the development of new natural solutions for diabetes management.

Abbreviations

HbA1c	glycated hemoglobin
HDL	High-Density Lipoprotein
LDL	Low-Density Lipoprotein
AMP	Adenosine Monophosphate
ESM	standard error of the mean
GRSB	laboratory of the Research Group on Bioactive Substances

Conflicts of Interest

The authors declare no conflicts of interest in the Conflicts of Interest.

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