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RESEARCH ARTICLE

REVISED Hypoglycemic effect of the aqueous extract from *Acalypha argomuelleri* Briq. (Euphorbiaceae) 'Sweet stick' leaves in *Rattus rattus* var. *albinus*

[version 3; peer review: 2 approved, 1 not approved]

Previously titled: Hypoglycemic effect of the aqueous extract from *Acalypha argomuelleri* Briq. 'Sweet stick' leaves in *Rattus rattus* var. *albinus*

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v3 First published: 19 Aug 2025, 14:800
<https://doi.org/10.12688/f1000research.164673.1>
Second version: 15 Sep 2025, 14:800
<https://doi.org/10.12688/f1000research.164673.2>
Latest published: 10 Oct 2025, 14:800
<https://doi.org/10.12688/f1000research.164673.3>

Abstract**Introduction**

Diabetes mellitus (DM) is a chronic metabolic disease representing a global public health concern and is associated with severe complications such as cardiovascular and renal diseases. Although several species of the genus *Acalypha* have demonstrated biological activity, no prior studies have evaluated the hypoglycemic effect of *Acalypha argomuelleri* Briq., making this study relevant.

Method

The hypoglycemic effect of the aqueous leaf extract of *A. argomuelleri* Briq. (AAAE) was evaluated in an experimental model using *Rattus rattus* var. *albinus* (males). A randomized, prospective design was employed, consisting of a control group and three treatment groups

Open Peer Review**Approval Status**   

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version 1 19 Aug 2025	 view	 view	

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receiving doses of 100, 150, and 300 mg/kg of the extract, respectively. Hyperglycemia was induced via oral glucose administration.

Results

The qualitative phytochemical analysis of AAAE revealed the presence of flavonoids, phenols, cardiogenic glycosides, and diterpenes, with no reducing sugars. The 300 mg/kg dose produced a significant and sustained reduction in blood glucose levels, reaching near-normal values at 90 minutes, demonstrating a dose- and time-dependent hypoglycemic effect.

Discussion

The study confirmed that AAAE has a dose-dependent hypoglycemic effect, with optimal efficacy at 300 mg/kg. This dose showed a faster and more sustained reduction in glucose levels compared to 100 and 150 mg/kg, suggesting higher efficacy at elevated concentrations. The identified flavonoids and phenols, associated with glucose metabolism modulation and pancreatic β -cell protection, likely explain the observed effect. The absence of reducing sugars indicates the hypoglycemic effect is linked to secondary metabolites.

Conclusions

The AAAE exhibited a significant dose- and time-dependent hypoglycemic effect, with optimal efficacy at 300 mg/kg after 90 minutes. These findings support the potential of *A. argomuellieri* Briq. as a natural alternative for blood glucose control, though further studies are needed to assess its safety and efficacy in clinical models.

Keywords

Diabetes mellitus, Hypoglycemic effect, aqueous extract, *Acalypha argomuellieri* Briq

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Competing interests: No competing interests were disclosed.

Grant information: This research received institutional funding from the University of San Martín de Porres with project code: E21102023008.

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How to cite this article: Morales Ramos JG, Loja Herrera B, Rodríguez Alayo NM *et al.* **Hypoglycemic effect of the aqueous extract from *Acalypha argomuellieri* Briq. (Euphorbiaceae) 'Sweet stick' leaves in *Rattus rattus* var. *albinus* [version 3; peer review: 2 approved, 1 not approved]** F1000Research 2025, 14:800 <https://doi.org/10.12688/f1000research.164673.3>

First published: 19 Aug 2025, 14:800 <https://doi.org/10.12688/f1000research.164673.1>

REVISED Amendments from Version 2

In this revised version, we incorporated the suggestions made by Reviewer 2 in order to improve clarity, methodological precision, and transparency of the manuscript.

In the Materials and Methods section, we reorganized the structure for greater clarity and added missing details. Specifically, we specified the sex of the study animals, indicating that only male rats were used. In addition, we included references to Cerrate (1969) and Romagosa et al. (2000) for the collection and identification of the botanical material.

For the phytochemical screening, we clarified that the procedure followed García Granados and confirmed that this was a qualitative test. In the revised version, we also indicated that the analysis included a semiquantitative estimation based on the intensity of the color reaction, which avoids the use of notations such as +++ or –.

In the experimental design, we included the missing information regarding the dose of glucose administered (5 ml per rat) and clarified that the animals were fasted prior to the oral glucose tolerance test. We also emphasized that the animals used were males, as suggested by the reviewer.

Regarding the measurement times for blood glucose, we maintained the intervals of 30, 60, and 90 minutes, providing references (Tripathi et al., 2014; Narmadha et al., 2017) to justify that this design is widely used in preclinical studies with plant extracts and is sufficient to capture both the post-load peak and the early return phase of blood glucose. We acknowledged that longer follow-up times (120 and 180 minutes) can provide additional information, and we committed to include them in future studies, especially in diabetic models and chronic evaluations.

These modifications significantly improve the methodological transparency and scientific clarity of the manuscript.

Any further responses from the reviewers can be found at the end of the article

1. Introduction

The World Health Organization (WHO) defines Diabetes mellitus (DM) as a chronic metabolic disease characterized by elevated blood glucose levels. DM causes complications such as vascular diseases, heart conditions, blindness, renal failure, and neurological disorders. Type 1 diabetes (T1D), also known as insulin-dependent diabetes, is a chronic condition where the pancreas produces little or no insulin, which cannot be prevented. In contrast, Type 2 diabetes (T2D) typically occurs in adults, is the most common form, and is frequently associated with obesity. T2D can be prevented by avoiding complications and premature death.¹

In 2022, an estimated 828 million adults worldwide had DM, with prevalence increasing in 155 countries for men and 132 for women. Between 1990 and 2022, age-standardized prevalence rose from 7% to 14%, justifying the need to explore alternative treatments.²

In the Americas, 112 million adults over the age of 18 are living with DM. According to data released in a report by the Pan American Health Organization (PAHO), under the heading ‘country profiles - diabetes disease burden, 2023’, revealed that DM (excluding diabetic kidney disease) increased and that the total number of deaths in 2019 was 141 812 distributed in middle-to-high income groups.³

A projection for 2045 in Latin America and the Caribbean (LAC) estimated that the number of people with DM would reach 49 million, with a prevalence of 11.9%. Globally, it is projected that by 2035, DM2 cases would rise to 643 million, a 50% increase from current figures.⁴ A review study concluded that individuals with T2DM in Latin American developing countries face a higher risk of cardiovascular or all-cause mortality compared to those in developed countries.⁵

Conventional therapies for DM1 include insulin administration, while DM2 relies on oral hypoglycemic agents such as metformin. The American Diabetes Association (ADA) 2024 guidelines recommend GLP-1 analogs and SGLT2 inhibitors as first-line treatments for MN2 patients with cardiovascular disease (CV), heart failure, or chronic kidney disease.⁶

Hypoglycemia has been exposed as one of the most serious adverse side effects of anti-diabetic treatments. Numerous epidemiological studies have highlighted the importance of a diet rich in plant foods including vegetables, fruits, spices and condiments in the prevention and treatment of DM. Various plants are used for their anti-diabetic and hypoglycemic effects, such as *Morus alba* L. (‘mulberry’), *Juglans regia* L. (‘walnut’), which are widely used throughout the world. In Peru, there is a wide diversity of plant species with hypoglycemic effects, some of which belong to traditional medicine and are being studied for their use and toxicity.⁷

Various parts of the plant have been used to obtain extracts and identify their metabolites. Among the widely studied antidiabetic plants, *M. alba* “mulberry” stands out, whose metabolites present in the leaves include flavonoids such as rutin and quercetin-3-triglyceride, which were shown to have hypoglycemic and pharmacological effects on DM2 in animal models and humans, as synthesized in our ongoing phytochemical and pharmacological reviews.^{8–11}

Another plant to consider is *A. wilkesiana* Müll. Arg. whose aqueous extract prepared from its leaves revealed the presence of bioactive principles such as: coumarins, polyphenols, flavins, terpenes, tannins and saponosides, which have a potentiating effect on diabetic nephropathy.¹²

In Iran, the hydrosol of *J. regia* is traditionally used to regulate blood sugar in patients with DM. Various bioactive metabolites have been identified in it, including flavonoids, phenolic compounds, limonene, myrcenes, linalool, beta-pharnesene, borneol monoterpenes, caffeic acid and coumaric acids, sinapic acid, ferulic acid, juglone, 1,4-naphthoquinone, 3-3'-bisjuglone, cyclo-tri-juglone, regiolone, triptenes, betulin and botulinic acid.^{13–16}

In Peru, several medicinal plants, such as *Geranium ayavacense* Linnaeus. and *Geranium ruizii* Hieron ('pasuchaca'), are recognized in traditional medicine for their medicinal properties. These plants have demonstrated hypoglycemic effects in experimental models using hyperglycemic rats (*Rattus rattus* var. *albinus*), with leaves are used in infusions and flowers in hydroethanolic extracts. Other species with similar therapeutic properties include *Psoralea glandulosa* Linnaeus. ('cullen'), *Physalis angulata* Linnaeus ('mullaca'), and *Smallanthus sonchifolius* (Poepp.) H. Rob ('yacón').^{17–20}

Numerous studies on the genus *Acalypha* have demonstrated its pharmacological properties, including antimicrobial effects (*A. integrifolia* and *A. wilkesiana*), anti-inflammatory effects (*A. fruticosa* Forsskal.), and anticancer effects (*A. monostachya*).^{21–24}

Acalypha argomuelleri Briq., commonly known as 'Sweet stick', is a species distributed from Ecuador to Peru. It is a shrub that primarily grows in tropical rainforest, found in the Andean region between 2,000 and 2,800 m.s.n.m. Taxonomically, it belongs to the class Equisetopsida, subclass Magnoliidae, order Malpighiales, family Euphorbiaceae, and the genus *Acalypha*. Euphorbiaceae is one of the largest plant families, comprising numerous genera and approximately 6,300 species; *Acalypha* is the third largest genus within this family, including around 500 species.^{25,26}

This study aimed to assess the hypoglycemic effect of the aqueous extract of *Acalypha argomuelleri* Briq. (EAAA) using an experimental model, as no scientific evidence is currently available regarding its medicinal properties. Despite its traditional use in folk medicine, the therapeutic potential of this species remains unexplored in the scientific literature. Therefore, this research seeks not only to address this gap but also to investigate the potential of *Acalypha argomuelleri* as a natural alternative for glycemic control—an approach that could prove beneficial for communities that rely heavily on traditional medicine.

2. Methods

The study was carried out between January and December 2024. During this period, the following stages were completed: collection and botanical identification of the plant material, conditioning and acclimatisation of the experimental animals, as well as the preparation and administration of the alcoholic extract, followed by that of the aqueous extract of *Acalypha argomuelleri* Briq. The experimental phase was then carried out in the experimental physiology laboratory of the Universidad Nacional Pedro Ruiz Gallo between June and December. Blood glucose measurements were taken at specific times according to the experimental design, and the data obtained were statistically analysed to evaluate the hypoglycaemic effect of the extract. Although extended measurements (120 y 180 minutes) may provide additional information, our study focused on the early hypoglycaemic response, adequately captured within 90 minutes. Future studies will consider longer follow-up times, especially in diabetic and chronic models.

The research followed a quantitative, true experimental approach, appropriate for the study as it allows the establishment of causal relationships between the administration of the extract and changes in glucose levels. The study was prospective with a longitudinal design. A completely randomized design with control and treatment groups was used to evaluate the hypoglycemic effect of the aqueous extract of *A. argomuelleri* (AEAA) in hyperglycemic *Rattus rattus* var. *albinus*.

- a. The male rats were housed in metal cages containing sterile wood shavings. The temperature was controlled at 20–24 °C, the humidity at 50–60%, and the lighting was on a 12-hour cycle. They were fed a standard diet and had access to water at all times. No environmental enrichment was applied.

- a. The protocol avoided painful procedures. Nontoxic doses were used, and animals were monitored regularly.
- b. There were no adverse events.
- c. Humane endpoints were not established for the study as no serious harm was expected. Animals were monitored twice daily.

The corresponding permits were obtained from the National Forest and Wildlife Service (SERFOR) (Resolutions No. D000120-2023-MIDAGRI-SERFOR-ATFFS-CAJAMARCA and No. D000167-2024) for the collection of *Acalypha argomuelleri* Briq., as well as authorization from the Research Department of the Lambayeque Regional Hospital (HRL), including approval from the Institutional Research Ethics Committee for the use of animals (No. 026-2025).

The collection of *A. argomuelleri* Briq. leaves at the flowering stage were carried out in the district of Querocoto, Chota province, Peru. The leaves of the plant were used, taking into account the traditional medicinal use by the population. The coordinates of the collection area were 6°24'53"S 79°04'03"W. In situ plant samples were taken and transported to the Universidad Nacional de Trujillo, where they were deposited in the Herbarium Truxillensis (HUT) (Trujillo–La Libertad) for proper identification and registration under number 65645 on 20/09/2024.

No previous protocol was registered in a public database. The experimental design was reviewed and approved by the Hospital ethics Committee.

Preparation of the aqueous extract from *Acalypha argomuelleri* Briq. leaves

For the preparation of the aqueous extract of *A. argomuelleri* (AEAA), the method described by García-Granados²⁷ was used, which involved the following steps:

1. Drying: The leaves were cleaned and dried at room temperature until a constant weight was achieved.
2. Grinding: The dried leaves were ground until they reached an approximate size of 2 mm.
3. Extraction: 200 g of plant material were placed in 300 mL of water at 100°C for 45 minutes. Subsequently, the mixture was filtered, pressed, and reduced to a final volume of 162 mL.
4. Concentration: The liquid was dried in an oven at 42°C for 48 hours, followed by cooling in a desiccator. By weight difference, a dry residue of 16.5 g was obtained.
5. Preparation of Solutions: Based on the dry extract, 25 mL solutions were prepared at concentrations of 100, 150, and 300 mg/mL, respectively.

Phytochemical analysis

The phytochemical analysis of AEAA was performed using a spot test and classified as qualitative with semi-quantitative estimation, evaluating the intensity of the colorimetric reaction (abundant, moderate, or scarce) according to the degree of colour developed, following the method described by Dueñas-Deyá.²⁸ The presence of metabolites was determined based on specific colorimetric reactions for each group of compounds. The intensity of the color reaction indicated the presence or absence of bioactive components using the following scale:

- Absent (–)
- Present (+)

To indicate the presence of sugars, the Benedict's test was used following the methodology described by García-Granados.²⁷

Experimental design

The study was conducted with 33 adult males rats (*Rattus rattus* var. *albinus*), aged between 4 and 6 months, weighing between 190 and 230 gr., and divided into four experimental groups. The control group initially consisted of 9 rats, while each of the three treatment groups included 8 rats. To ensure sample size homogeneity and to meet the assumptions of

Analysis of Variance (ANOVA), the statistical analysis was performed considering 8 rats per group over a period of six months.

A hyperglycemic state was induced in the rats through oral administration of glucose (5 mL). Subsequently, the aqueous extract of *Acalypha argomuelleri* Briq. was administered orally in three different doses (100 mg/kg, 150 mg/kg, and 300 mg/kg). Blood glucose levels were recorded under preprandial conditions, first determining the basal level and then the hyperglycemic level, with measurements taken at 30, 60, and 90 minutes after extract administration. These intervals are widely used in glucose tolerance tests in preclinical models with plant extracts, as they allow both the post-load peak and the initial phase of blood glucose return to be captured. Blood glucose was measured using an ACCU-CHEK glucometer and test strips, selected for their accuracy and reliability, as supported by previous studies. These intervals are widely used in preclinical glucose tolerance tests with plant extracts.^{29,30}

No additional environmental enrichment was applied, which is a recognized but common limitation in preclinical pharmacological studies.

Statistical analysis

Data analysis was performed using SPSS software version 22.0, applying single and double-entry statistical tests. To compare the groups, an Analysis of Variance (ANOVA) based on the “F” distribution was used for multiple comparisons, followed by Duncan’s post hoc test. Results with a p-value < 0.05 were considered statistically significant.

There was no blinding at any stage of the experiment.

3. Results

3.1 Phytochemical profile of the aqueous extract of *Acalypha argomuelleri* Briq.

The qualitative phytochemical analysis revealed the presence of several bioactive compounds. The results are summarized in the following table:

Constituent	Test performed	Presence in the leaf
Diterpenes	Cooper acetate test	+
Cardiotonic glycosides	Keller-Kilani test	+
Phenols	Ferric chloride test (12.5%)	+
Flavonoids	Shinoda test	+

The qualitative phytochemical analysis revealed an abundant presence of phenols, a moderate amount of flavonoids and diterpenes, and a small quantity of cardiotonic glycosides. Reducing sugars were not detected. These findings suggest that the flavonoids and phenols present in the extract may be linked to the observed hypoglycemic effect, given their potential to modulate enzymatic activity and protect pancreatic β -cells.

3.2 Blood glucose in the control group

The blood glucose data from the control group rats (0 mL/kg), which did not receive treatment with AEAA, served as the reference baseline to compare the effects observed in the treated experimental groups. Basal glucose levels and the progressive reduction in blood glucose levels over time (30, 60, and 90 minutes) were monitored. These measurements showed variation among individuals, reflecting natural fluctuations in glucose levels.

The data observed in [Table 2](#) showed the glucose response in rats treated with AEAA at a dose of 100 mg/kg. Basal glucose measurements ranged from 99 mg/dL to 124 mg/dL, with an average of 111 mg/dL, which were found to be within the normal range. The highest recorded hyperglycemia peak was 342 mg/dL. At 30 minutes, most rats exhibited a significant increase in blood glucose levels. By 60 minutes, a variable decrease was observed, with some rats maintaining elevated levels, and at 90 minutes, a progressive reduction occurred, though some rats retained high levels.

At this dose, AEAA appears to induce a significant hyperglycemia peak at 30 minutes in some rats, suggesting a variable response. However, glucose levels did not decrease uniformly among all rats, as some maintained elevated levels up to 90 minutes. Although the response to the 100 mg/kg dose was not entirely uniform it appears to indicate that AEAA may have a glucose-regulating effect, which acted following an initial hyperglycemic peak, with some rats showing a gradual reduction in their glucose levels over time.

Table 1. Glucose response in rats treated with AEAA (Control).

Rat	Weight (g)	Extract dose (mL/kg)	Basal glucose (mg/dL)	Glucose 30 min (mg/dL)	Glucose 60 min (mg/dL)	Glucose 90 min (mg/dL)
1	200	0	132	200	194	186
2	216	0	104	196	141	229
3	200	0	101	200	213	198
5	172	0	96	186	185	63
6	215	0	89	181	190	105
7	200	0	112	183	213	198
8	220	0	140	200	170	181
9	170	0	100	211	197	190

Table 2. Glucose response in rats treated with AEAA (100 mg/kg).

<i>Acalypha argomuelleri</i> (100 mg/kg)							
Rat	Weight (g)	Extract dose (mL/kg)	Basal glucose (mg/dL)	Hyperglycemia	Glucose 30 min (mg/dL)	Glucose 60 min (mg/dL)	Glucose 90 min (mg/dL)
1	329	0.140	121	342	156	179	180
2	268	0.110	116	155	286	256	219
3	295	0.120	124	289	131	129	130
4	286	0.120	99	256	300	152	127
5	298	0.130	115	279	201	121	99
6	266	0.110	115	160	281	250	160
7	326	0.140	120	332	178	166	120
8	286	0.120	101	256	300	152	110

The results shown correspond to rats treated with AEAA at a dose of 150 mg/kg. The average basal glucose was found to be 101 mg/dL, and the hyperglycemia peak reached a maximum of 220 mg/dL. Regarding glucose progression, a less pronounced increase was observed at 30 minutes compared to the 100 mg/kg dose. By 60 minutes, a more uniform decrease was seen in most rats, and at 90 minutes, greater stability in values with a tendency toward normalization was noted. This suggests that, given the more consistent glucose reduction at 60 and 90 minutes and fewer individual fluctuations, the extract at this dose may better regulate glucose absorption, potentially making it more effective at stabilizing glucose levels (Table 3).

In summary, the data from the third treatment with AEAA at a dose of 300 mg/kg indicated an average basal glucose of 78 mg/dL, while hyperglycemia peak reached a maximum of 391 mg/dL. Regarding glucose progression, extreme variability was observed at 30 minutes, with some rats showing high values. By 60 minutes, a more controlled decrease was observed. At 90 minutes, glucose levels were lower compared to the other doses. The interpretation, given the lower glucose levels observed, suggested that 300 mg/kg of AEAA might be the most effective dose for sustained glucose reduction and could have a long-term regulatory effect (Table 4).

Table 5, analyzed the results using the arithmetic mean ($\bar{x}$), standard deviation (σ), and coefficient of variation (CV), with the following interpretations:

Low CV (<10%): Homogeneous data, stable response.

Moderate CV (10%–30%): Acceptable variability.

High CV (>30%): High dispersion, unstable response.

Table 3. Glucose response in rats treated with AEAA (150 mg/kg).

<i>Acalypha argomuellerei</i> (150 mg/kg)							
Rat	Weight (g)	Extract dose (mL/kg)	Basal glucose (mg/dL)	Hyperglycemia	Glucose 30 min (mg/dL)	Glucose 60 min (mg/dL)	Glucose 90 min (mg/dL)
1	385	0.288	95	206	188	165	166
2	306	0.229	102	184	158	142	148
3	287	0.215	108	162	145	134	126
4	328	0.246	96	220	158	140	118
5	288	0.216	110	188	166	145	136
6	384	0.288	106	192	169	145	133
7	285	0.215	105	194	168	133	112
8	304	0.220	100	180	147	130	105

Table 4. Glucose response in rats treated with AEAA (300 mg/kg).

<i>Acalypha argomuellerei</i> (300 mg/kg)							
Rat	Weight (g)	Extract dose (mL/kg)	Basal glucose (mg/dL)	Hyperglycemia	Glucose 30 min (mg/dL)	Glucose 60 min (mg/dL)	Glucose 90 min (mg/dL)
1	200	0.240	70	143	93	93	94
2	180	0.216	82	391	170	158	151
3	190	0.228	72	146	149	146	138
4	200	0.240	86	148	133	139	114
5	180	0.216	80	284	363	123	97
6	210	0.252	55	135	140	101	92
7	170	0.204	92	161	117	110	113
8	187	0.224	76	163	151	155	123

Table 5. General Interpretation of the Mean ($\bar{x}$), Standard Deviation (σ), and Coefficient of Variation (CV%) in glucose response in rats treated with AEAA.

Etapas	Weight (gr)	Basal (mg/dL)	Hyperglycemia (mg/dL) 2.5 ml glucose	30 min	60 min	90 min	N
Control (Without Extract)	$\bar{x}$ =196.09 σ =20.07 CV=10.24	$\bar{x}$ =104.89 σ =21.23 CV=20.24	$\bar{x}$ =196.78 σ =13.97 CV=7.10	$\bar{x}$ =214.33 σ =77.70 CV=36.25	$\bar{x}$ =186.89 σ =73.56 CV=39.36	$\bar{x}$ =156.56 σ =43.66 CV=27.89	9
Treatment 1 AEAA 100 mg/kg	$\bar{x}$ =294.25 σ =23.46 CV=7.97	$\bar{x}$ =113.88 σ =9.14 CV=8.03	$\bar{x}$ =258.63 σ =69.85 CV=27.01	$\bar{x}$ =229.13 σ =70.05 CV=30.57	$\bar{x}$ =175.63 σ =51.23 CV=29.17	$\bar{x}$ =143.13 σ =40.38 CV=28.91	8
Treatment 2 AEAA 150 mg/kg	$\bar{x}$ =320.88 σ =41.69 CV=12.99	$\bar{x}$ =102.75 σ =5.47 CV=5.32	$\bar{x}$ =190.75 σ =17.30 CV=9.07	$\bar{x}$ =162.38 σ =13.74 CV=8.46	$\bar{x}$ =141.75 σ =10.95 CV=7.73	$\bar{x}$ =130.50 σ =19.90 CV=15.25	8
Treatment 3 AEAA 300 mg/kg	$\bar{x}$ =189.63 σ =13.14 CV=6.93	$\bar{x}$ =76.63 σ =11.33 CV=14.78	$\bar{x}$ =196.38 σ =92.13 CV=46.92	$\bar{x}$ =164.50 σ =83.51 CV=50.77	$\bar{x}$ =128.13 σ =25.01 CV=19.52	$\bar{x}$ =115.25 σ =21.34 CV=18.52	8

For glucose variation without AEAA application (Day 0), a normal response curve was observed following glucose administration, showing an initial high peak (214.33 mg/dL) and a progressive reduction as metabolism progressed. The high CV in subsequent minutes suggested individual differences in glucose metabolism.

Regarding the glucose variation across the three treatments, the results are presented as follows:

Treatment 1 with 100 mg/kg

The variability analysis revealed a high CV in the glucose response, indicating that the 100 mg/kg dose of the extract did not regulate glucose homogeneously, as hyperglycemia remained elevated and variable.

Treatment 2 with 150 mg/kg

EAAA at 150 mg/kg stabilized glucose more effectively compared to the 100 mg/kg dose, reducing hyperglycemia in a more homogeneous and controlled manner. This was attributed to a more consistent decrease in glucose levels, with low variability observed in post-administration values.

Treatment 3 with 300 mg/kg

At this dose, basal glucose levels were the lowest, suggesting that the extract may have a long-term hypoglycemic effect. An extremely high CV% was observed in the first 30 minutes, indicating inconsistent initial effects of the 300 mg/kg dose across individuals. However, glucose levels progressively decreased by 90 minutes, leveling off and showing a sustained reduction. These values were the lowest among all groups, suggesting that this dose was the most effective for long-term glucose regulation.

Regarding the statistical tests to assess the presence of significant differences in glucose levels at 30, 60, and 90 minutes among the experimental groups (Control, 100 mg/kg, 150 mg/kg, and 300 mg/kg of AEAA), an analysis of variance (ANOVA) and the Waller-Duncan multiple range test were performed. The ANOVA in [Table 6](#) showed significant differences among the treatments ($p = 0.000$), indicating that at least one group exhibited a distinct response in glucose reduction.

The Duncan test ($\alpha = 0.05$) ([Table 7](#)) was used to identify differences between groups. The results revealed that the 300 mg/kg dose showed a significant difference compared to the control group, indicating that this treatment at 90 minutes produced a significant reduction in blood glucose levels compared to untreated rats. At 60 minutes, the same treatment exhibited an intermediate effect but remained significantly different from the 30 minutes time point, which the least effective.

In contrast, the 100 mg/kg and 150 mg/kg doses showed no significant differences compared to the control group, suggesting they may not be sufficiently effective to impact blood glucose reduction. A practical interpretation of AEAA's efficacy highlights the importance of higher doses (e.g., 300 mg/kg), which may be necessary to achieve a more consistent and effective effect.

A realistic interpretation of EAAA's efficacy would suggest the importance of higher concentrations, which may be necessary to achieve a more consistent and effective therapeutic effect.

Table 6. ANOVA of glucose response in rats treated with AEAA.

	Source of variation	Sum of squares	df	Mean square	F	Sig. (p-value)
Mg/dL	Entre grupos	37823.083	2	18911.542	8.524	0.000
	Dentro de grupos	206326.156	93	2218.561		
		244149.240	95			

Table 7. Results of the duncan test for blood glucose levels at 30, 60 and 90 minutes.

Waller-Duncan			
Glucose	Sample size (N)	Subset for $\alpha = 0.05$	
		1	2
90 min	32	139.41	
60 min	32	158.34	158.34
30 min	32		187.66

4. Discussion

Phytochemical analysis of *A. argomuellieri* leaves revealed the presence of flavonoids in moderate proportions, high levels of phenolic compounds, and the absence of sugars. These bioactive compounds, commonly found in other *Acalypha* species, may have been responsible for the observed effects on glucose regulation due to their highly significant hypoglycemic medicinal properties. Previous studies have documented that the hypoglycemic effects of plants associated with the presence of flavonoids and phenols, for example *M. alba* y *A. wilkesiana*, are often attributed to their ability to enhance the function of pancreatic tissue, specifically the β -cells. This effect may be achieved either by stimulating insulin secretion or by reducing intestinal glucose absorption.^{12,31}

These results (Table 1) suggest that, in the absence of AEAA, the glycemic homeostasis of the rats remained relatively stable over time, although individual fluctuations were observed. Such variations could be influenced by physiological factors such as basal metabolism, prior diet, or compensatory responses to fasting before treatment administration.³²

The results obtained with AEAA at a dose of 100 mg/kg showed a variable response in blood glucose levels in rats, indicating a partially regulatory effect with individual differences in response and, consequently, a lack of uniformity in outcomes. This variability could be related to the action of the extract's bioactive compounds—mainly flavonoids and phenols—which are known to modulate glucose metabolism. Additionally, these variations might be attributed to genetic factors, differences in extract absorption, or the complexity of interactions involving flavonoids and phenols.³³

At a dose of 150 mg/kg, a progressive decrease in blood glucose levels was observed in most rats, reaching near-normal values at 60 and 90 minutes. The lower individual variability and greater stability in glucose levels at 90 minutes suggest that this dose of AEAA may be more effectively modulating glucose absorption and metabolism than the 100 mg/kg dose. This effect could be attributed to the action of bioactive compounds, primarily flavonoids and phenols, which according to various studies, can influence glycemic homeostasis through mechanisms such as the inhibition of digestive enzymes (α -glucosidase y la α -amylase) and stimulation of insulin secretion.³⁴ Furthermore, the observed response in this treatment indicates that, although the effect is significant, individual differences persist, which may be linked to genetic factors or variations in the absorption and bioavailability of the extract.³⁵

In contrast, the results obtained with AEAA at a dose of 300 mg/kg showed a faster, sustained, and more uniform reduction in blood glucose levels. The average basal glucose recorded before hyperglycemia induction was 78 mg/dL reaching a peak of 391 mg/dL, which is characteristic of the experimental model. However, by 90 minutes glucose values were significantly lower compared to other treatments, suggesting that this dose has a more pronounced and long-lasting hypoglycemic effect.

This more consistent response could be linked to a higher concentration of bioactive compounds that optimize glucose utilization in peripheral tissues, promoting more effective regulation of glycemic homeostasis.³⁶ Additionally, it has been proposed that flavonoids and phenols present in *Acalypha* species not only stimulate insulin secretion but also protect pancreatic β -cells by reducing oxidative stress and modulating the expression of pro- and anti-apoptotic genes.^{37,38}

The 300 mg/kg dose demonstrated the highest hypoglycemic efficacy, with a sustained reduction in blood glucose levels to near-normoglycemia values at 90 minutes. This finding combined with the absence of reducing sugars in the extract, suggests that the optimal concentration of flavonoids and phenols may act effectively through a multifactorial mechanism targeting multiple metabolic pathways: (1) inhibition of α -glucosidase, (2) modulation of intestinal glucose absorption, and (3) protection of pancreatic β -cells against oxidative stress — key mechanisms associated with antidiabetic effects in plants such as *M. alba* and other *Acalypha* species.⁸

However, the variability observed (CV > 50% at 30 minutes) highlights the influence of individual factors such as basal metabolism, bioavailability of active compounds, and hormonal fluctuations,³⁹ which could affect treatment response and therapeutic efficacy. Future studies—including a comprehensive phytochemical analysis and chronic diabetes models—will clarify whether *A. argomuellieri* Briq. Possesses additional antidiabetic effects (e.g., improvement insulin resistance or reduction of systemic oxidative stress). Current evidence indicates that the hypoglycemic effect of AEAA is dose-dependent, suggesting that the highest dose is the most effective long-term. This finding aligns with other studies in experimental models, where doses ranging from 200 to 500 mg/kg showed significant glucose reduction by 120 minutes.^{40–42}

Eight rats per group were used, which is an adequate and commonly accepted number in preclinical pharmacological evaluation studies. This sample size allowed statistically significant differences to be observed between groups, although it is recognized that further studies with larger samples could strengthen the evidence and facilitate the exploration of additional mechanisms.

While the results obtained provide evidence of the hypoglycemic effect of *A. argomuelleri* Briq., it is important to note that this study was conducted in an experimental model using healthy albino rats. Future studies could evaluate the extract's impact on induced diabetes models to determine its effectiveness under pathological conditions. Additionally, more detailed phytochemical analyses would be relevant to identify the compounds responsible for the hypoglycemic effect and elucidate their mechanism of action.

Taken together, these findings suggest that AEAA could represent a natural alternative in complementary medicine for blood glucose control, with potential therapeutic applications in the management of type 2 diabetes mellitus (T2DM). Even though EAAA showed a significant hypoglycaemic effect in the animal model, it is not possible to assign a percentage of efficacy in humans without conducting controlled clinical studies. It would be prudent, and by analogy with other phytochemicals used as adjuvants, to consider that it would have a modest effect as a complementary therapy, provided that standardised extracts are available. The next phase of this study will involve evaluating the antidiabetic effect in a specific animal model for DM2 and, in addition, characterising the specific bioactive metabolites by conducting toxicological studies to ensure their safety and identify the compounds responsible for the observed activity. Likewise, in order to move towards a marketable pharmaceutical product, sequential steps are required, including standardisation under GMP (Good Manufacturing Practices) standards, pharmacokinetics and clinical trials in all phases.

It is suggested that the findings could be a basis for studies in other animal models or in humans, although a direct clinical application is not yet proposed.

5. Conclusions

This study represents a pioneering contribution to the evaluation of the hypoglycemic effect of the aqueous extract of *Acalypha argomuelleri* Briq. (AEAA) in albino rats, as no prior documented research exists on the species in relation to blood glucose regulation. The key findings are as follows:

- The aqueous extract of *Acalypha argomuelleri* Briq. At a dose of 300 mg/kg, significantly reduced blood glucose levels in *Rattus rattus* var. *albinus* compared to the control group, demonstrating a dose-dependent hypoglycemic effect.
- The efficacy of the aqueous extract of *Acalypha argomuelleri* Briq. Increased with treatment duration, showing a progressive reduction in glucose levels due to its cumulative and sustained effect.
- The 90 minute treatment exhibited the greatest reduction in glucose levels, representing the optimal timepoint to maximize the hypoglycemic effect without inducing adverse effects.

Ethical considerations

The corresponding permits were obtained from the National Forest and Wildlife Service (SERFOR) (Resolutions No. D000120-2023-MIDAGRI-SERFOR-ATFFS-CAJAMARCA and No. D000167-2024) for the collection of *Acalypha argomuelleri* Briq., as well as authorization from the Research Department of the Lambayeque Regional Hospital (HRL), including approval from the Institutional Research Ethics Committee for the use of animals (No. 026-2025).

Data availability statement

Underlying data

Zenodo. Hypoglycemic effect of the aqueous extract from *Acalypha argomuelleri* Briq. 'Sweet stick' leaves in *Rattus rattus* var. *albinus*, <https://doi.org/10.5281/zenodo.16732470>.⁴³

This project contains the following underlying data:

- TOLERANCE TEST DATABASE (Excel file).xlsx (Individual blood glucose data in rats by experimental group and day of evaluation).
- ANOVA DATA SPSS.spv - (Results of the ANOVA analysis applying SPSS to the experimental data).
- Duncan_Acalypha_test (1).txt - (Results of the Duncan/Tukey post hoc test with detailed statistical significance by pairs).

- [BASE DOF DATES TEST OF TOLERANCE.xlsx](#)
- [MEDIA, DS Y CV ACALYPHA.docx](#)
- [RESAULTS JANUARY 31.pdf](#)

The data is available under the terms of the [Creative Commons Attribution 4.0 International licence](#) (CC BY 4.0).

Reporting guidelines

Zenodo. Hypoglycemic effect of the aqueous extract from *Acalypha argomuelleri* Briq. 'Sweet stick' leaves in *Rattus rattus* var. *albinus*, <https://doi.org/10.5281/zenodo.16732470>.⁴³

This project contains the following underlying data:

[Author Checklist - Full 19_07_25.pdf](#)

The data is available under the terms of the [Creative Commons Attribution 4.0 International licence](#) (CC BY 4.0).

References

- Organización Mundial de la Salud (OMS): *Diabetes: Datos y cifras*. OMS; Accessed: Mar. 23, 2025.
[Reference Source](#)
- Zhou B, et al.: **Worldwide trends in diabetes prevalence and treatment from 1990 to 2022: a pooled analysis of 1108 population-representative studies with 141 million participants**. *Lancet*. Nov. 2024; **404**(10467): 2077–2093.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Organización Panamericana de la Salud (OPS): *Diabetes - OPS/OMS | Organización Panamericana de la Salud*. OPS/OMS; Accessed: Mar. 23, 2025.
[Reference Source](#)
- Magliano DJ, Boyko EJInternational Diabetes Federation: **IDF Diabetes Atlas 2021, 10th Edition Committee**. *Online version of IDF Diabetes Atlas*. Accessed: Mar. 23, 2025.
[Reference Source](#)
- Carrillo-Larco RM, Barengo NC, Albitres-Flores L, et al.: *The risk of mortality among people with type 2 diabetes in Latin America: A systematic review and meta-analysis of population-based cohort studies*. John Wiley and Sons Ltd.; Mar. 04, 2019.
[Publisher Full Text](#)
- Flores L, Vidal J: **Has the first treatment of type 2 diabetes mellitus changed?** *Medicina Clínica (English Edition)*. Nov. 2024; **163**(10): 509–511.
[Publisher Full Text](#)
- Ansari P, et al.: **Plant-Based Diets and Phytochemicals in the Management of Diabetes Mellitus and Prevention of Its Complications: A Review**. *Nutrients*. Oct. 2024; **16**(21): 3709.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Morales Ramos JG, Esteves Pairazamán AT, Mocarro Willis MES, et al.: **Medicinal properties of 'Morus alba' for the control of type 2 diabetes mellitus: a systematic review**. *F1000Res*. Oct. 2021; **10**: 1022.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Ge Q, et al.: **Analysis of mulberry leaf components in the treatment of diabetes using network pharmacology**. *Eur. J. Pharmacol.* Aug. 2018; **833**: 50–62.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Chan EWC, Lye PY, Wong SK: **Phytochemistry, pharmacology, and clinical trials of Morus alba**. *Chin. J. Nat. Med.* Jan. 2016; **14**(1): 17–30.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Swathi P, Gana Manjusha K, Vivekanand M, et al.: **Effect of Morus alba against Hyperglycemic and Hyperlipidemic Activities in Streptozotocin Induced Diabetic Nephropathy**. *Biosci. Biotechnol. Res. Asia*. Dec. 2017; **14**(4): 1441–1447.
[Publisher Full Text](#)
- Mendame WLM, Mintsba BAE, Nguerna A-MN, et al.: **Phytochemical screening and effects of aqueous extract of Acalypha wilkesiana Müll. Arg on isolated toad heart**. *J. Phytopharmacol.* Jun. 2022; **11**(3): 159–163.
[Publisher Full Text](#)
- Moravej H, et al.: **Chemical Composition and the Effect of Walnut Hydrosol on Glycemic Control of Patients With Type 1 Diabetes**. *Int. J. Endocrinol. Metab.* Jan. 2016; **14**(1): e34726.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Rabiei K, Ebrahimzadeh MA, Saeedi M, et al.: **Effects of a hydroalcoholic extract of Juglans regia (walnut) leaves on blood glucose and major cardiovascular risk factors in type 2 diabetic patients: a double-blind, placebo-controlled clinical trial**. *BMC Complement. Altern. Med.* Jul. 2018; **18**(1): 206.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- María PAX, Alexander AA, Teresa MCM, et al.: **Actividad antibacterial de extractos de Nogal Juglans regia**. *Revista de Investigación en Ciencias de la Salud*. Vol. 18, Jul. 2023; : pp. 8–13. México. Accessed: Mar. 24, 2025.
[Reference Source](#)
- Perales-Flores JD, et al.: **Actividad antioxidante, tóxica y antimicrobiana de Rosmarinus officinalis, Ruta graveolens y Juglans regia contra Helicobacter pylori**. *Biotechnia*. Nov. 2023; **25**(1): 88–93.
[Publisher Full Text](#)
- Gonzales Lliontop LF, Chotón Calvo M d R, Ruiz JRC: **Efecto hipoglucemiante de las hojas y flores de Geranium ayavacense L. 'pasuchaca' sobre la glicemia en Rattus rattus var. Albinus**. *Revista Científica Dékamu Agropec*. Sep. 2021; **2**(1): 15–24.
[Publisher Full Text](#)
- Díaz Ortega JL, Benites Castillo S, Romero CV, et al.: **Efecto del extracto hidroetanólico de geranium ruizii hieron sobre la hiperglicemia inducida en rattus rattus variedad albinus**. *Interciencia: Revista de ciencia y tecnología de América*. Jan. 2023; **48**(1): 40–45. Accessed: Mar. 24, 2025. 0378-1844.
[Reference Source](#)
- Ramírez Verástegui J: **Efecto hipoglucemiante del infuso de planta total de Psoralea glandulosa 'cullen' En rattus Var albinus normoglicémicas**. *Revista Peruana de Medicina Integrativa*. Aug. 2016; **1**(2): 12–16.
[Publisher Full Text](#)
- Minchola-Castañeda K, Luzuriaga-Tirado E, Montalvo-Rodríguez A, et al.: **Propiedades beneficiosas del yacón (smallanthus sonchifolius) en la salud**. *Más Vida*. Sep. 2022; **4**(3): 87–98.
[Publisher Full Text](#)
- Seebaluck-Sandoram R, Lall N, Fibrich B, et al.: **Antibiotic-potentiating activity, phytochemical profile, and cytotoxicity of Acalypha integrifolia Willd. (Euphorbiaceae)**. *J. Herb. Med.* Mar. 2018; **11**: 53–59.
[Publisher Full Text](#)
- Sherifat KO, Itohan AM, Adeola SO, et al.: **ANTI-FUNGAL ACTIVITY OF ACALYPHA WILKESIANA: A PRELIMINARY STUDY OF FUNGAL ISOLATES OF CLINICAL SIGNIFICANCE**. *Afr. J. Infect. Dis.* Dec. 2023;

- 17(1): 74–74.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
23. Fawzy GA, Al-Taweel AM, Perveen S, *et al.*: **Bioactivity and chemical characterization of *Acalypha fruticosa* Forssk. growing in Saudi Arabia.** *Saudi Pharm. J.* Jan. 2017; **25**(1): 104–109.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 24. Guillén-Meléndez GA, *et al.*: **Cytotoxic Effect in vitro of *Acalypha monostachya* Extracts over Human Tumor Cell Lines.** *Plants.* Oct. 2021; **10**(11): 2326.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 25. Gómez Reyes A, Murillo-A J, García H: *Los géneros de euphorbiaceae, peraceae, phyllanthaceae y picrodendraceae del departamento de Santander, Colombia.* Vol. 1. Bogotá: Universidad Nacional de Colombia. Facultad de Ciencias. Instituto de Ciencias Naturales; Primera edición 2021. Accessed: Mar. 26, 2025.
[Reference Source](#)
 26. Levin GA, Cardinal-McTeague WM, Steinmann VW, *et al.*: **Phylogeny, Classification, and Character Evolution of *Acalypha* (*Euphorbiaceae*: *Acalyphoideae*).** *Syst. Bot.* Jun. 2022; **47**(2): 477–497.
[Publisher Full Text](#)
 27. García-Granados RU, Cruz-Sosa F, Alarcón-Aguilar FJ, *et al.*: **Análisis fitoquímico cualitativo de los extractos acuosos de *Thalassia testudinum* Banks ex König et Sims de la localidad de Champotón, Campeche, México, durante el ciclo anual 2016–2017.** *Polibotanica.* Jul. 2019; 151–168.
[Publisher Full Text](#)
 28. Dueñas-Deyá A, Castañeda-Bautista R, Martín-Cruz L, *et al.*: **Estudio fitoquímico de la especie endémica cubana *Zanthoxylum pseudodumosum*, una planta con potencial actividad antifúngica.** *Revista Cubana de Química.* Dec. 2020; **32**(3): 406–419. Accessed: Mar. 26, 2025.
[Reference Source](#)
 29. Tripathi AK, Kohli S: **Pharmacognostical standardization and antidiabetic activity of *Syzygium cumini* (Linn.) barks (*Myrtaceae*) on streptozotocin-induced diabetic rats.** *J. Complement. Integr. Med.* 2014 Jun; **11**(2): 71–81.
[PubMed Abstract](#) | [Publisher Full Text](#)
 30. Narmadha R, Devaki K: **Toxicological evaluation and oral glucose tolerance test of ethanolic leaf extract of *Barleria cristata* L. in wistar albino rats.** *Int. J. Basic Clin. Pharmacol [Internet].* 2017 Feb. 2 [cited 2025 Sep. 12]; **2**(6): 742–746.
[Reference Source](#)
 31. González-Blas MV, García-Armas JM, Herrera-Gutiérrez LA: **Flavonoides y Fenoles totales con actividad hipoglucemiante en semillas de *Syzygium jambos*.** *Revista Salud Amazónica y Bienestar.* Jan. 2022; **1**(1): e272.
[Publisher Full Text](#)
 32. Figueroa-García M d C, Rivera-Valencia M, Sosa-Durán EE, *et al.*: **Perfil glicémico durante el ayuno en ratas macho-Wistar con diabetes tipo 2.** *Revista del Hospital Juárez de México.* Nov. 2016; **83**(1–2): 23–30. Accessed: Mar. 26, 2025.
[Reference Source](#)
 33. Díaz-Núñez D, Rivera-Torres B: **Revisión exploratoria sobre la evidencia de cultivos andinos con efecto hipoglucemiante y de sus componentes bioactivos.** *Rev. Peru Med. Exp. Salud Publica.* Dec. 2023; **40**(4): 474–484.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 34. Prajna PP, Rajan R, Shana KM, *et al.*: **Traditional uses, phytochemistry and pharmacology of *Acalypha hispida* burm: A systematic review.** *World J. Biol. Pharm. Health Sci.* Nov. 2022; **12**(2): 087–093.
[Publisher Full Text](#)
 35. Rahman MM, *et al.*: **Exploring the plant-derived bioactive substances as antidiabetic agent: An extensive review.** *Biomed. Pharmacother.* Aug. 2022; **152**: 113217.
[PubMed Abstract](#) | [Publisher Full Text](#)
 36. Tran N, Pham B, Le L: **Bioactive Compounds in Anti-Diabetic Plants: From Herbal Medicine to Modern Drug Discovery.** *Biology (Basel).* Aug. 2020; **9**(9): 252.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 37. Alam S, *et al.*: **Antidiabetic Phytochemicals From Medicinal Plants: Prospective Candidates for New Drug Discovery and Development.** *Front. Endocrinol (Lausanne).* Feb. 2022; **13**: 1–35.
[Publisher Full Text](#)
 38. Al-Ishaq RK, Abotaleb M, Kubatka P, *et al.*: **Flavonoids and Their Anti-Diabetic Effects: Cellular Mechanisms and Effects to Improve Blood Sugar Levels.** *Biomolecules.* Sep. 2019; **9**(9): 430.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 39. Dueñas Martín M, Iriondo-Dehond A, Dolores M, *et al.*: **Efecto de los compuestos fenólicos en el metabolismo de los carbohidratos.** *Revista Española de Nutrición Comunitaria = Spanish Journal of Community Nutrition.* 2018; **24**(1): 25–32.
[Publisher Full Text](#)
 40. Núñez-Tuesta L, Aranda-Ventura J, Villacrés-Vallejo J, *et al.*: **Efecto reductor del extracto acuoso de hojas de *Justicia spicigera* contra la hiperglicemia en ratones BALB/C.** *Revista Peruana de Medicina Integrativa.* Dec. 2022; **7**(4).
[Publisher Full Text](#)
 41. Acevedo Correa D, Mantilla Escalante DC, Duran Lengua M, *et al.*: **Regulación de los niveles de glucosa mediante la inducción de extracto acuoso de *Pseudoelephantopus spicatus*.** *Biotechnología en el Sector Agropecuario y Agroindustrial: BSAA.* 2024; **22**(1): 40–52. ISSN-e 1909-9959, ISSN 1692-3561.
[Publisher Full Text](#)
 42. Siraj MA, *et al.*: **Anti-Inflammatory and Antioxidant Activity of *Acalypha hispida* Leaf and Analysis of its Major Bioactive Polyphenols by HPLC.** *Adv. Pharm. Bull.* Jun. 2016; **6**(2): 275–283.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 43. Morales Ramos JG, Herrera BL, Rodríguez Alayo NM, *et al.*: **Hypoglycemic effect of the aqueous extract from *Acalypha argomuellieri* Briq. 'Sweet stick' leaves in *Rattus rattus* var. *albinus*.** [Data set]. *Zenodo.* 2025.
[Publisher Full Text](#)

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Current Peer Review Status:   

Version 3

Reviewer Report 14 October 2025

<https://doi.org/10.5256/f1000research.188409.r422492>

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Antonio Galán de Mera 

Universidad San Pablo-CEU, Madrid, Spain

As I indicated last time, my decision is ACCEPTED.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Plant systematics, Biogeography, Pharmacognosy.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 2

Reviewer Report 24 September 2025

<https://doi.org/10.5256/f1000research.187885.r410404>

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MARIO ANTONIO BOLARTE ARTEAGA

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Bolarte Arteaga Mario Antonio

Universidad Continental - Los Olivos Lima, Lima Region, Lima District, Peru

1. INTRODUCTION

The introduction to the manuscript presents a clear and well-structured overview of the scientific

and ethnobotanical context of *Acalypha argomuelleri* as a species of medicinal interest, citing other native Peruvian and foreign species. The authors successfully articulate the importance of preclinical studies in animal models with the need to scientifically validate the traditional uses reported in local communities. Likewise, an adequate literature review is included that places the work within the framework of current research on hypoglycaemic plants, allowing the reader to understand both the relevance from a biological point of view and the value from another point of view, which is the cultural value of the natural resource studied. The writing is fluid, coherent, and sufficient to justify the objective of the study, so I believe that this section does not require additional modifications. The manuscript addresses a relevant topic in the field of pharmacognosy and complementary medicine, evaluating the hypoglycaemic effect of *Acalypha argomuelleri*, a little-studied species with potential therapeutic application.

1. METHODOLOGY

The methodology presented in the manuscript is clear and consistent with the objectives set out. The glucose tolerance test procedure, the administration of the extract in different doses, and the recording of the glycaemic response are described accurately, ensuring reproducibility in future studies. Likewise, the use of statistical analysis using ANOVA followed by Duncan's test is relevant and correctly applied, lending strength to the results. I believe that the methodology section does not require further modification, as it meets the standards of rigour and transparency expected in this type of research.

1. RESULTS

The results section is organised in a clear and coherent manner, adequately presenting both the experimental data and its statistical analysis. The tables accurately indicate the variations in glucose levels following the administration of the extract in different doses, which facilitates understanding of the findings. In addition, Duncan's test is correctly described, allowing significant differences between groups to be identified. The writing is objective and avoids premature interpretations, limiting itself to presenting the findings as they were obtained. I consider the results to be sufficient, well presented, and requiring no further modification.

1. DISCUSSION

The discussion is solid and adequately fulfils the purpose of interpreting the results in light of existing scientific evidence. The authors make relevant comparisons with other plants known for their hypoglycaemic activity, which places their findings in a broader context and gives the study international relevance. Furthermore, there is a balance between the interpretation of the data and the recognition of limitations, as well as the mention of future lines of research, demonstrating a forward-looking and responsible approach. The writing is clear, coherent and well structured, allowing the reader to understand both the scope and potential of the extract of the plant studied. I consider that this section does not require any modifications.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Pharmacogenomics, Medicina plants and Pharmacology

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 25 Sep 2025

Jorge Guillermo Morales Ramos

We thank the reviewer for approving the article without comments.

Competing Interests: No competing interests were disclosed.

Reviewer Report 16 September 2025

<https://doi.org/10.5256/f1000research.187885.r414413>

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Antonio Galán de Mera 

Universidad San Pablo-CEU, Madrid, Spain

I agree with this new amended version and recommend acceptance

Thank you very much.

Kind regards

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Plant systematics, Biogeography, Pharmacognosy.

I confirm that I have read this submission and believe that I have an appropriate level of

expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 08 September 2025

<https://doi.org/10.5256/f1000research.181218.r407373>

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Aku Enam Motto

University of Lomé, Lomé, Togo

RESEARCH ARTICLE

Hypoglycemic effect of the aqueous extract from *Acalypha argomuelleri* Briq. 'Sweet stick' leaves in *Rattus rattus* var. *albinus*

Abstract

Introduction

Reformulate it

Material and methods

The authors should follow the structure for more clarification and understanding

Animals

Plant collection and identification

Preparation of the aqueous extract

Phytochemical screening

This is a qualitative test, so there is no need to write +++ or ---

Absence - and Presence +

Experimental design

The authors should mention the dose of glucose administered to the rats

The authors did not mention whether the manipulation occurred in fasted rats or not

Precision of the sex of the animals is also needed.

The measurement of the glycemia must be extended in 2 hours (30 min, 60 min, 60 min; 120 and 180 min)

For this kind of evaluation of the hypoglycemic activity, there are a lot of adequate protocols nowadays

(refer to 1&2)

For a better understanding, the authors must complete the test.

Statistical analysis

References

1. Agalatossi H, Motto A, Lawson-Evi P, Eklug-Gadegbeku K: Antihyperglycemic and Antioxidant Properties of *Sida linifolia* Juss. ex Cav. (Malvaceae) Hydroalcoholic Extract in ICR Mice. *Asian Science Bulletin*. 2025; **3** (1): 8-19 [Publisher Full Text](#)

2. Dackey Y, Hanvi D, Motto A, Atchou K, et al.: Potential Anti-hyperglycemic Activity of the Polyherbal Combination of *Carica papaya* L., *Persea americana* Mill., and *Theobroma cacao* L. Leaves Extract: In vitro, Ex vivo, In vivo Studies. *Journal of Advances in Medical and Pharmaceutical Sciences*. 2025; **27** (2): 54-66 [Publisher Full Text](#)

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

No

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

No source data required

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Physiology, Pharmacology, toxicology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response 21 Sep 2025

Jorge Guillermo Morales Ramos

Abstract

The sex of the rats was added to the summary.

Introduction

Reformulate

It has been reformulated by adding Peruvian plants with hypoglycaemic effects (page 3, paragraph 10), article v2.

Materials and methods

Authors should follow the structure for greater clarity and understanding.

Animals

The reviewer's suggestion was accepted, incorporating the sex of the study animals and indicating that they were male.

Plant collection and identification

The methods of Cerrate and Romagosa et al. were used for the collection of botanical material.

Cerrate E. Manera de preparar plantas para un herbario. Lima: Editorial UNMSM; 1969.

Romagosa J, Rosales S, Rupérez RF, Crespo R. Enciclopedia de medicina naturalista y alternativa; 2000.

Preparation of the aqueous extract

Phytochemical screening

The methodology mentioned the method followed by García Granados (paragraph 7, p.3, ref. 27), which describes the stages of the process.

This is a qualitative test, so it is not necessary to write +++ or ---.

Absence - and Presence +

Version 2 of the article states that the test was qualitative with semi-quantitative estimation (p. 3, paragraph 1, Phytochemical analysis, ref. 28).

Experimental design

The authors should mention the dose of glucose administered to the rats.

Paragraph 2 of the experimental design section indicates that the dose of glucose administered was 5 ml.

The authors did not mention whether the manipulation was performed on fasted rats or not.

The experimental design section mentions the conditions referred to by the reviewer (p. 7, paragraph 2).

It is also necessary to specify the sex of the animals.

We appreciate the reviewer's suggestion to include the sex of the rats, which were males paragraph 2(a).

Blood glucose measurement should be extended to 2 hours (30 min, 60 min, 60 min; 120 and 180 min).

We appreciate the reviewer's suggestion regarding the inclusion of additional times (120 and 180 minutes). In our study, 30, 60, and 90 minutes were selected because these intervals are widely used in glucose tolerance tests in preclinical models with plant extracts, as they allow both the post-load peak and the early phase of blood glucose return to be captured (Tripathi et al., 2014; Narmadha, et al., 2017). With this design, it was possible to identify the maximum hypoglycaemic effect of the extract in the critical window where changes are most evident. While we recognise that extended measurements up to 120 or 180 minutes may provide additional information, the main objective of this exploratory study was to evaluate the early hypoglycaemic response, which is adequately reflected in the 90 minutes. Undoubtedly, future studies —especially in diabetic models and chronic evaluations— will include longer times.

Tripathi AK, Kohli S. Pharmacognostical standardization and antidiabetic activity of *Syzygium cumini* (Linn.) barks (Myrtaceae) on streptozotocin-induced diabetic rats. J Complement Integr Med. 2014 Jun;11(2):71-81. doi: 10.1515/jcim-2014-0011. PMID: 24760764.

Narmadha R, Devaki K. Toxicological evaluation and oral glucose tolerance test of ethanolic leaf extract of *Barleria cristata* L. in wistar albino rats. Int J Basic Clin Pharmacol [Internet]. 2017 Feb. 2 [cited 2025 Sep. 12];2(6):742-6. Available from:

<https://www.ijbcp.com/index.php/ijbcp/article/view/1359>

Competing Interests: None

Reviewer Report 03 September 2025

<https://doi.org/10.5256/f1000research.181218.r410405>

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Antonio Galán de Mera 

Universidad San Pablo-CEU, Madrid, Spain

I think this is a very interesting type of manuscript that scientifically demonstrates the traditional use of certain plants in Peru that could be adopted by occidental medicine. Perhaps it would be useful to indicate whether the extracts could have secondary effects (although this is not the aim of this work) and what the subsequent steps would be in order to develop a pharmaceutical preparation.

Although it is a pharmacological manuscript, the botanical aspects of the plant should be dealt with in more detail. For example, the way in which its ecology is dealt with is very superficial, when it is precisely a natural resource that could lead to the establishment of a nature reserve.

Other points:

In the title, add the family after *Acalypha argomuelleri* Briq. (**Euphorbiaceae**).

The caption for **Table 6** should be in English.

In paragraph 6 of the introduction, I believe that if the new plant that causes hypoglycaemia is Peruvian, more plants from Peru that cause this effect should be added, and not just *Geranium ayavacense*. Furthermore, three paragraphs below, a very similar paragraph is repeated, and what is detailed in it should be included here. Join two paragraphs.

In paragraph 7, line 4: THESE ARE NOT SYSTEMATIC REVIEWS OF PLANTS (BOTANICAL EXPRESSION), THEY ARE PHYTOCHEMICAL AND PHARMACOLOGICAL REVIEWS: It should be stated: as synthesised in our ongoing phytochemical and pharmacological reviews.

Paragraph 12 and 13 of the introduction:

'the humid tropical biome': This is taken from IPNI, but IPNI is not accurate for ecological data. What is its distribution in Peru? Add some bibliographical references about its distribution. There is no humid tropical biome. It should be indicated whether it is a humid tropical forest, humid tropical shrubs, a savannah-type forest, etc., and also the bibliographical reference from which this information is taken. IF WE ARE DISCUSSING ABOUT A NATURAL RESOURCE, IT IS VERY IMPORTANT TO CORRECTLY INDICATE THE ECOLOGICAL CONDITIONS OF THE LOCATION. A PHARMACOLOGICAL STUDY CAN LEAD TO A WHOLE CONSERVATION STRATEGY.

'traditional use in folk medicine': What is it used for in traditional medicine? Please specify it, and add a bibliographical reference.

Methods, paragraph 5: WHY HAVE ONLY THE LEAVES BEEN USED? AND WHY HAVE THEY BEEN COLLECTED WHEN THE PLANT IS IN BLOOM? PERHAPS BECAUSE THAT IS HOW IT IS DONE IN

TRADITIONAL MEDICINE? THE REASON SHOULD BE STATED.

In that paragraph, after Peru: Cajamarca Department, Peru. Also add coordinates and date of collection. National University of Trujillo: Is the registered name IN ENGLISH? OR IS IT UNIVERSIDAD NACIONAL DE TRUJILLO?

After registration, the voucher number must be added to the HUT herbarium, which is the acronym for the herbarium.

Discussion: Phytochemical analysis: The intensity of the color reaction qualitatively indicated...but also quantitative? I believe you are showing colour intensity according to quantity, so wouldn't that also be quantitative analysis? Furthermore, in paragraph 2 of the **results**, the authors wrote the sentence 'Qualitative phytochemical analysis revealed an abundant presence of phenols, a moderate amount of flavonoids and diterpenes, and a small **quantity** of cardiogenic glycosides'.

Discussion, paragraph 1: The authors wrote: 'Previous studies have documented that the hypoglycemic effects of plants associated' **Which plants?**

Paragraph 10 of the discussion states: '*Taken together, these findings suggest that AEAA could represent a natural alternative in complementary medicine for blood glucose control, with potential therapeutic applications in the management of type 2 diabetes mellitus (T2DM).*

However further studies are required to validate its efficacy in humans.' What success rate could extracts from this plant have in humans, considering that it is used in traditional medicine? Could a medicine be manufactured that could be dispensed in pharmacies? These would be interesting points to add to the discussion.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Plant systematics, Biogeography, Pharmacognosy.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 08 Sep 2025

Jorge Guillermo Morales Ramos

1. In the title, add the family after *Acalypha argomuelleri* Briq. (**Euphorbiaceae**).

Answer: The addition suggested by the reviewer was made.

2. The caption for **Table 6** should be in English.

Answer: The legend for Table 6 was translated.

3. In paragraph 6 of the introduction, I believe that if the new plant that causes hypoglycaemia is Peruvian, more plants from Peru that cause this effect should be added, and not just *Geranium ayavacense*. Furthermore, three paragraphs below, a very similar paragraph is repeated, and what is detailed in it should be included here. Join two paragraphs.

Answer: The suggested paragraphs were merged, mentioning some plants of Peruvian origin that were already mentioned in the article.

4. In paragraph 7, line 4: THESE ARE NOT SYSTEMATIC REVIEWS OF PLANTS (BOTANICAL EXPRESSION), THEY ARE PHYTOCHEMICAL AND PHARMACOLOGICAL REVIEWS: It should be stated: as synthesised in our ongoing phytochemical and pharmacological reviews.

Answer: The reviewer's suggestion has been added to the text.

5. Paragraph 12 and 13 of the introduction:

'the humid tropical biome': This is taken from IPNI, but IPNI is not accurate for ecological data. What is its distribution in Peru? Add some bibliographical references about its distribution. There is no humid tropical biome. It should be indicated whether it is a humid tropical forest, humid tropical shrubs, a savannah-type forest, etc., and also the bibliographical reference from which this information is taken. IF WE ARE DISCUSSING ABOUT A NATURAL RESOURCE, IT IS VERY IMPORTANT TO CORRECTLY INDICATE THE ECOLOGICAL CONDITIONS OF THE LOCATION. A PHARMACOLOGICAL STUDY CAN LEAD TO A WHOLE CONSERVATION STRATEGY.

Answer: The additions suggested by the reviewer were made, indicating the ecology of the plant, its use and traditional preparation.

6. 'traditional use in folk medicine': What is it used for in traditional medicine? Please specify it, and add a bibliographical reference.

Answer: The reviewer's suggestion was accepted and the reference was added.

7. Methods, paragraph 5: WHY HAVE ONLY THE LEAVES BEEN USED? AND WHY HAVE THEY BEEN COLLECTED WHEN THE PLANT IS IN BLOOM? PERHAPS BECAUSE THAT IS HOW IT IS DONE IN TRADITIONAL MEDICINE? THE REASON SHOULD BE STATED.

In that paragraph, after Peru: Cajamarca Department, Peru. Also add coordinates and date of collection. National University of Trujillo: Is the registered name IN ENGLISH? OR IS IT UNIVERSIDAD NACIONAL DE TRUJILLO?

After registration, the voucher number must be added to the HUT herbarium, which is the acronym for the herbarium.

Answer: The relevant corrections were made, adding the use and preparation of the plant, as well as an explanation of how the leaves were used in the experiment. Coordinates and

the date of collection were also added, according to the herbarium voucher.

Discussion:

8. Phytochemical analysis: The intensity of the color reaction qualitatively indicated...but also quantitative? I believe you are showing colour intensity according to quantity, so wouldn't that also be quantitative analysis? Furthermore, in paragraph 2 of the **results**, the authors wrote the sentence 'Qualitative phytochemical analysis revealed an abundant presence of phenols, a moderate amount of flavonoids and diterpenes, and a small **quantity** of cardiogenic glycosides'.

Answer: The suggestion to replace qualitative phytochemical analysis with semi-quantitative phytochemical analysis is accepted.

Discussion, paragraph 1: The authors wrote: 'Previous studies have documented that the hypoglycemic effects of plants associated' **Which plants?**

Paragraph 10 of the discussion states: '*Taken together, these findings suggest that AEAA could represent a natural alternative in complementary medicine for blood glucose control, with potential therapeutic applications in the management of type 2 diabetes mellitus (T2DM).*

However further studies are required to validate its efficacy in humans.' What success rate could extracts from this plant have in humans, considering that it is used in traditional medicine? Could a medicine be manufactured that could be dispensed in pharmacies? These would be interesting points to add to the discussion.

Answer: We thank the reviewer for the clarification and suggestion regarding the structure of the paragraph, and the relevant changes have been made in the paragraphs 1 y 10.

Competing Interests: None

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