

Hypoglycemic effect of aqueous leaf extracts of *Vernonia amygdalina* and *Ficus exasperata* following separate and concurrent administrations

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ABSTRACT

Background: Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia due to either insufficient insulin production or insulin resistance. The increasing global prevalence of diabetes necessitates the need to explore alternative treatment options. *Vernonia amygdalina* and *Ficus exasperata* are widely used traditional herbal remedies with potential antidiabetic properties. This study aimed to assess the effects of these plants, both individually and in combination, on blood glucose levels in normoglycemic individuals following glucose-induced hyperglycemia.

Objectives: This study evaluated the glucose-lowering effects of aqueous extracts of *Vernonia amygdalina* and *Ficus exasperata*, both separately and in combination, in normoglycemic individuals, comparing their efficacy to that of the standard drug, Glimepiride.

Methods: Participants were randomly assigned to four groups. Group A (n=5) served as the standard and received 2 mg of Glimepiride. Groups B (n=10), C (n=10), and D (n=10) were administered varying dosages of *Vernonia amygdalina*, *Ficus exasperata*, or a combination of both, respectively. Specifically, within each group Subgroup B1 (n=5) received 200 mg/kg of *V. amygdalina*, and Subgroup B2 (n=5) received 400 mg/kg. Subgroup C1 (n=5) received 200 mg/kg of *F. exasperata*, while Subgroup C2 (n=5) received 400 mg/kg. Subgroups D1 and D2 were given a combination of both extracts at 200 mg/kg and 400 mg/kg, respectively. Blood glucose levels were measured at baseline, 30 minutes post-glucose ingestion (0.5 hour), and 1, 2, and 4 hours post-treatment. Data were analyzed using repeated one-way ANOVA followed by Bonferroni post-hoc comparisons to assess the statistical significance of the glucose-lowering effects.

Results: *Vernonia amygdalina* at 200 mg/kg significantly ($p < 0.05$) reduced blood glucose levels at 2 hours and 4 hours post-treatment. The 400 mg/kg dose exhibited a more potent and sustained effect, with significant reductions at all time points. *Ficus exasperata* at both 200 mg/kg and 400 mg/kg also showed significant hypoglycemic effects, with the 400 mg/kg concentration being more effective. The combination of both extracts produced moderate to strong hypoglycemic effects, particularly at the 400 mg/kg dose, with significant ($p < 0.05$) reductions observed at all time points. Glimepiride consistently resulted in significant ($p < 0.05$) glucose reductions at all intervals, outperforming the herbal extracts.

Conclusion: Both *Vernonia amygdalina* and *Ficus exasperata*, individually and in combination, exhibit potent glucose-lowering effects. Their efficacy, especially at higher doses, is comparable to Glimepiride, suggesting their potential as alternative or complementary treatments for managing blood glucose levels in diabetes.

Keywords: Antihyperglycemic effect, Diabetes mellitus, Glimepiride, *Ficus exasperata*, Herbal medicine, *Vernonia amygdalina*

Effet hypoglycémique des extraits aqueux de feuilles de *Vernonia amygdalina* et de *Ficus exasperata* après administrations séparées et concomitantes

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RÉSUMÉ

Contexte: Le diabète sucré est un trouble métabolique chronique caractérisé par une hyperglycémie due soit à une production insuffisante d'insuline, soit à une résistance à l'insuline. La prévalence mondiale croissante du diabète nécessite d'explorer d'autres options thérapeutiques. *Vernonia amygdalina* et *Ficus exasperata* sont des remèdes traditionnels à base de plantes médicinales largement utilisés, dotés de propriétés antidiabétiques potentielles. Cette étude a cherché à évaluer les effets de ces plantes, à la fois individuellement et en combinaison, sur les niveaux de glucose sanguin chez des individus normoglycémiques suite à une hyperglycémie induite par le glucose. Objectifs: Cette étude a évalué les effets hypoglycémiques des extraits aqueux de *Vernonia amygdalina* et de *Ficus exasperata*, à la fois séparément et en combinaison, chez des individus normoglycémiques, en comparant leur efficacité à celle du médicament standard, le Glimépiride.

Méthodes: Les participants ont été répartis aléatoirement en quatre groupes. Le groupe A (n=5) a servi de groupe témoin et a reçu 2 mg de Glimépiride. Les groupes B (n=10), C (n=10) et D (n=10) ont reçu des doses variables de *Vernonia amygdalina*, de *Ficus exasperata* ou d'une combinaison des deux, respectivement. Plus précisément, dans chaque groupe, le sous-groupe B1 (n=5) a reçu 200 mg/kg de *V. amygdalina* et le sous-groupe B2 (n=5) a reçu 400 mg/kg. Le sous-groupe C1 (n=5) a reçu 200 mg/kg de *F. exasperata*, tandis que le sous-groupe C2 (n=5) a reçu 400 mg/kg. Les sous-groupes D1 et D2 ont reçu une combinaison des deux extraits à raison de 200 mg/kg et 400 mg/kg, respectivement. La glycémie a été mesurée au départ, 30 minutes après l'ingestion de glucose (0,5 heure) et 1, 2 et 4 heures après le traitement. Les données ont été analysées à l'aide d'une ANOVA unidirectionnelle répétée suivie de comparaisons post-hoc de Bonferroni pour évaluer la signification statistique des effets hypoglycémiques.

Résultats: La dose de 200 mg/kg *Vernonia amygdalina* a réduit de manière significative ($p < 0,05$) la glycémie 2 heures et 4 heures après le traitement. La dose de 400 mg/kg a eu un effet plus puissant et plus durable, avec des réductions significatives à tous les moments. *Ficus exasperata* à la fois à la dose de 200 mg/kg et à 400 mg/kg a également montré des effets hypoglycémiques significatifs, la concentration de 400 mg/kg étant plus efficace. La combinaison des deux extraits a produit des effets hypoglycémiques modérés à forts, en particulier à la dose de 400 mg/kg, avec des réductions significatives ($p < 0,05$) observées à tous les moments. Le glimépiride a systématiquement entraîné des réductions significatives ($p < 0,05$) de la glycémie à tous les intervalles, surpassant les extraits végétaux.

Conclusion: *Vernonia amygdalina* et *Ficus exasperata*, individuellement ou en combinaison, présentent tous deux de puissants effets hypoglycémiques. Leur efficacité, notamment à des doses plus élevées, est comparable à celle du glimépiride, ce qui suggère leur potentiel en tant que traitements alternatifs ou complémentaires pour la gestion de la glycémie chez les diabétiques.

Mots clés: Effet antihyperglycémique, Diabète sucré, Glimépiride, *Ficus exasperata*, Phytothérapie, *Vernonia amygdalina*

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood sugar levels (hyperglycemia) resulting from either the body's insufficient production of insulin or its inability to effectively use the insulin it produces. This condition has become a significant global health concern, with its prevalence rising at an alarming rate worldwide.¹ Diabetes ranks among the leading causes of mortality globally, contributing to millions of fatalities yearly, either directly or through complications related to the disease.²

Over recent decades, the global prevalence of diabetes has increased dramatically. In 2019, approximately 463 million adults were diagnosed with diabetes, accounting for 9.3 % of the world's adult population. Projections indicate that this figure could rise to 578 million by 2030 and 700 million by 2045, highlighting the escalating nature of this disease.³ The increase in diabetes cases is closely linked to lifestyle factors, including a rise in sedentary behavior, poor dietary habits, and the growing prevalence of obesity, particularly in urban areas.⁴ In low- and middle-income countries, where healthcare systems are often inadequate, the impact of diabetes is particularly severe, exacerbating existing health inequalities and contributing to higher rates of morbidity and mortality.⁵

Type 2 diabetes, which constitutes the majority of diabetes cases, is characterized by insulin resistance and a relative deficiency in insulin production.⁶ Its pathophysiology is complex, involving genetic, environmental, and behavioral factors. Key risk factors include obesity, sedentary lifestyles, unhealthy dietary habits, and advancing age.³ The metabolic disturbances in Type 2 diabetes stem primarily from the impaired action of insulin in skeletal muscles, adipose tissue, and the liver. This leads to hyperglycemia, which, if not controlled, can result in complications like cardiovascular disease, neuropathy, nephropathy, and retinopathy.⁷

Given the limitations of conventional diabetes treatments, including side effects and high costs, there has been an increased interest in alternative therapies like herbal medicine. Herbal medicine, which involves the use of plant-derived substances for therapeutic purposes, has been practiced for thousands of years and remains an integral part of healthcare in many cultures. The renewed interest in the therapeutic potential of medicinal plants, driven by the need for more accessible and cost-effective treatment options.⁸ Among the plants

gaining attention for their antidiabetic potential are *Vernonia amygdalina* and *Ficus exasperata*, both of which have shown promising results in studies evaluating their glucose-lowering effects.

Vernonia amygdalina, commonly known as "Bitter Leaf," is a perennial shrub widely used and recognized in traditional African medicine for treating various ailments, including diabetes.⁹ Its therapeutic potential, has garnered increasing interest, especially in managing chronic diseases like diabetes mellitus. The leaves of *Vernonia amygdalina* are dark green and elliptical, growing up to 15 cm in length.¹⁰ The plant typically reaches a height of about 2-5 meters and is usually propagated through stem cuttings.¹⁰ The leaves' bitter taste is due to various phytochemicals believed to contribute to its medicinal properties.¹¹

Similarly, *Ficus exasperata*, known as the "Sandpaper Tree," is another medicinal plant traditionally used in various parts of Africa for managing diabetes and inflammatory conditions.¹² Belonging to the Moraceae family, it thrives in tropical habitats such as forest edges, riverbanks, and savannas. The tree features broad, ovate leaves with a rough texture, which can grow up to 20 cm in length.¹²

Vernonia amygdalina and *Ficus exasperata* are two plants that have been traditionally utilized in various African communities to manage diabetes and related metabolic disorders. These plants have been integral to the traditional healthcare systems in Africa, where they are commonly used to prepare decoctions and infusions aimed to help lower blood glucose levels.⁸

The antidiabetic effects of *Vernonia amygdalina* and *Ficus exasperata* are primarily attributed to their rich phytochemical profiles, which include flavonoids, alkaloids, tannins, saponins, and terpenoids.¹³ These bioactive compounds demonstrate various pharmacological effects, such as enhancing insulin sensitivity, inhibition of carbohydrate-hydrolyzing enzymes, and protection against oxidative stress.¹⁰ In particular, flavonoids such as quercetin and luteolin, found in both *Vernonia amygdalina* and *Ficus exasperata*, are known for their potent antioxidant properties, which play a critical role in mitigating the oxidative stress linked to diabetes. Since oxidative stress is a significant factor in the pathogenesis of diabetes and its complications, these compounds are especially valuable in managing the disease.¹⁴

METHODS

Experimental design

This study assessed the effects of *Vernonia amygdalina* and *Ficus exasperata* on blood glucose levels, both individually and in combination. A total of 35 healthy volunteers, weighing between 46 and 96 kg, participated in the experiment. The study design involved administering aqueous extracts of both plants to the participants. Initially, participants' weights and fasting blood sugar levels were measured. This was followed by an Oral Glucose Tolerance Test (OGTT), in which they consumed 75 g of glucose dissolved in 250 ml of water to induce hyperglycemia. After confirming elevated blood sugar levels, the plant extracts were administered and blood glucose levels were monitored at 1, 2, and 4 hours post-administration to evaluate the effects of the extracts on hyperglycemia.

Volunteers grouping

Participants were selected after giving written informed consent, and were randomly divided into four groups. Group A (n=5) served as the control and received 2 mg of Glimperide. Groups B (n=10), C (n=10), and D (n=10) were administered varying dosages of *Vernonia amygdalina*, *Ficus exasperata*, or a combination of both, respectively. Each group was further split into two subgroups of 5 volunteers. Subgroup B1 received 200 mg/kg of *V. amygdalina*, and Subgroup B2 received 400 mg/kg. Subgroup C1 received 200 mg/kg of *F. exasperata*, while Subgroup C2 received 400 mg/kg. Subgroups D1 and D2 were given a combination of both extracts at 200 mg/kg and 400 mg/kg, respectively.

Induction of hyperglycaemia and estimation of blood glucose

Volunteers fasted for 9-10 hours prior to glucose administration. After the fasting period, hyperglycemia was induced by orally administering 75 g of glucose dissolved in 250 ml of water. Blood glucose levels were measured at 0.5, 1, 2, and 4 hours post-glucose ingestion using a glucometer with ACCU-CHEK Active test strips. This approach allowed a thorough assessment of the glucose-lowering effects of the plant extracts administered.

Collection of plant materials

The leaves of *Vernonia amygdalina* and *Ficus exasperata* were obtained from the medicinal garden of the Faculty of Pharmacy at Obafemi Awolowo University (OAU), Ile-Ife, Nigeria. The species were authenticated and recorded at the Faculty's Herbarium, where herbarium numbers were assigned. To minimize exposure to sunlight, the leaves were carefully harvested from middle-aged trees in the late afternoon. After collection, the leaves were spread on newspapers to protect them from light before extraction was carried out the next day.

Preparation of plant materials: Extraction

To replicate traditional medicinal practices, the selected plants were processed to produce aqueous extracts. The leaves were first thoroughly rinsed under running water to remove any impurities. For each study group, 400 g of leaves were weighed and then boiled in 2 L of water for 30 minutes, mimicking traditional decoction preparation,⁸ with 1 g of leaves corresponding to 5 ml of water. After boiling, the mixture was allowed to sit for 10 minutes before administration, ensuring the preservation of the active components.

Research ethical approval

Ethical clearance for this study was obtained from the Health Research Ethics Committee (HREC) of Institute of Public Health, Obafemi Awolowo University, Ile-Ife, Osun State, Nigeria.

Statistical analysis

Data were expressed as mean \pm standard error of the mean (SEM) in bar charts. Analysis was conducted using Graph Pad Prism 5 software (Graph Pad Software Inc., USA). Differences across time intervals were analysed using One-way Analysis of Variance (ANOVA), followed by Bonferroni post-hoc comparisons. Statistical significance was defined as $p < 0.05$.

RESULTS

Vernonia amygdalina (200 mg/kg)

Figure 1 shows a significant increase in blood glucose levels post-induction ($p = 0.0250$) compared to baseline levels. Following treatment with *Vernonia amygdalina*, a reduction in blood glucose levels was observed at 1 hour ($p = 0.2214$), 2 hours ($p = 0.0482$), and 4 hours ($p = 0.0180$), demonstrating a sustained hypoglycemic effect over time.

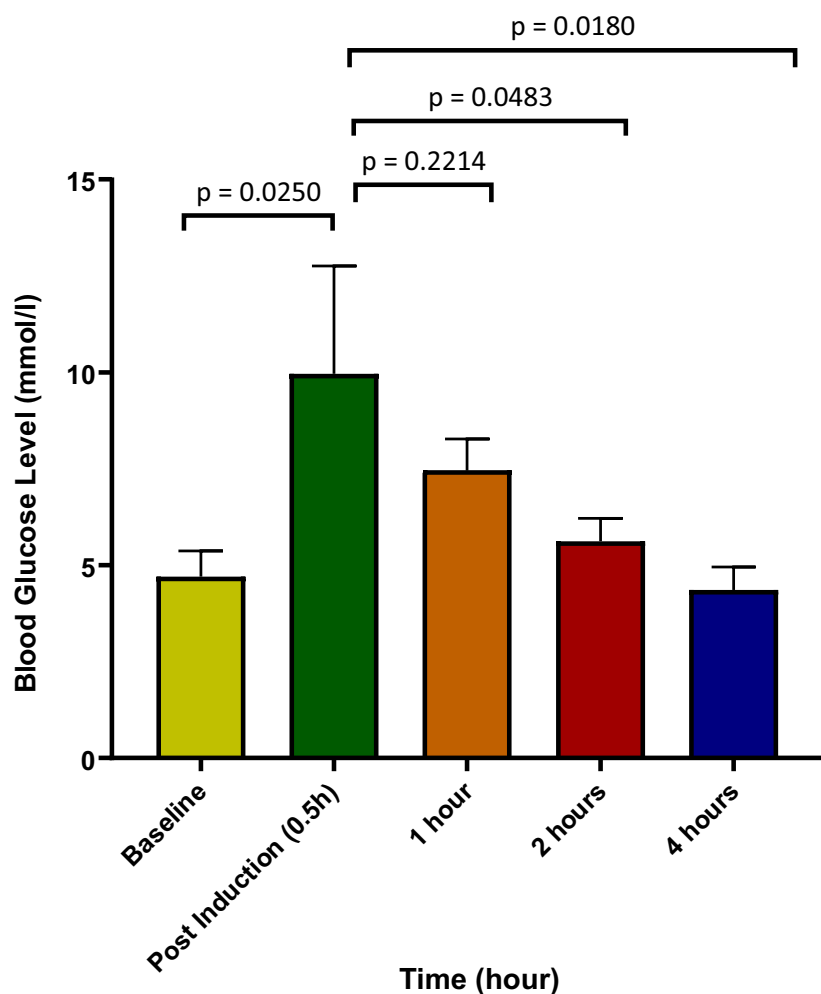


Figure 1: Effect of aqueous extract of *Vernonia amygdalina* (200 mg/kg) on blood sugar level (mmol/L) of normoglycemic individuals before and after induction of hyperglycemia, and after consumption of the extract.

***Vernonia amygdalina* (400 mg/kg)**

Figure 2 presents the results of the administration of *Vernonia amygdalina* at a higher dose of 400 mg/kg. Following the induction of hyperglycemia, a significant increase in blood glucose levels was observed ($p = 0.0058$). Subsequent administration of the extract led to significant reductions in blood glucose levels at 1 hour ($p = 0.0174$), 2 hours ($p = 0.0109$), and 4 hours ($p = 0.0059$), indicating a potent and sustained hypoglycemic effect.

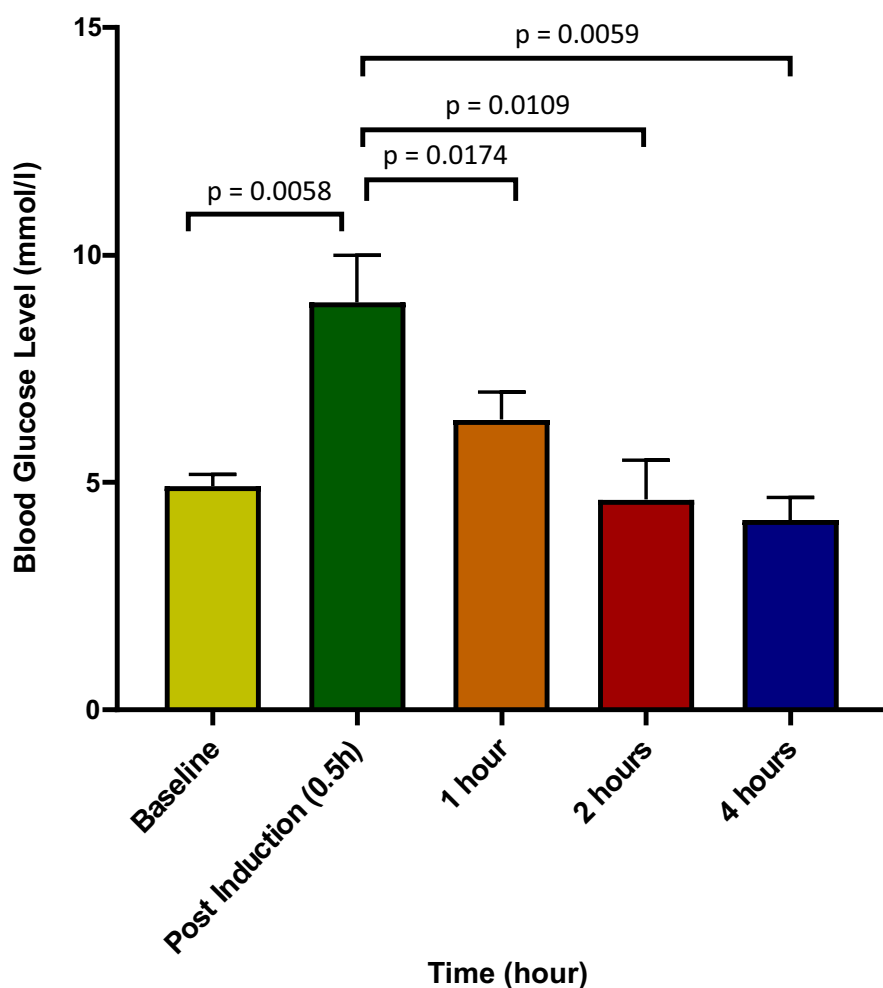


Figure 2: Effect of aqueous extract of *Vernonia amygdalina* (400 mg/kg) on blood sugar level (mmol/L) of normoglycemic individuals before and after induction of hyperglycemia, and after consumption of the extract.

***Ficus exasperata* (200 mg/kg)**

Figure 3 illustrates the effect of *Ficus exasperata* at a dose of 200 mg/kg on blood glucose levels. Following the induction of hyperglycemia, a significant increase in blood glucose levels was observed ($p = 0.0344$). However, treatment with this extract resulted in significant reductions in blood glucose levels at 1 hour ($p = 0.0409$), 2 hours ($p = 0.0247$), and 4 hours ($p = 0.0343$), indicating a consistent hypoglycemic effect.

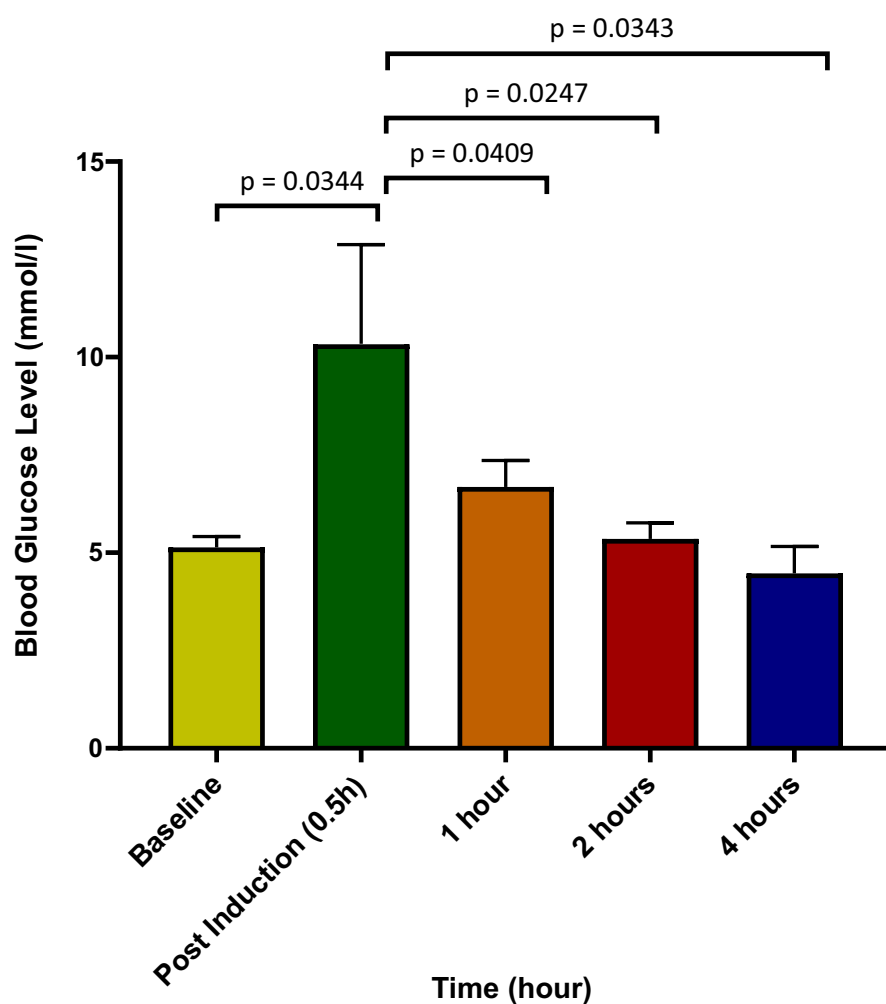


Figure 3: Effect of aqueous extract of *Ficus exasperata* (200 mg/kg) on blood sugar level (mmol/L) of normoglycemic individuals before and after induction of hyperglycemia, and after consumption of the extract.

***Ficus exasperata* (400 mg/kg)**

Figure 4 presents the effect of *Ficus exasperata* (400 mg/kg) on blood glucose levels. Following the induction of hyperglycemia, a significant increase in blood glucose levels was observed ($p = 0.0085$). Treatment with the extract resulted in further significant reductions in glucose levels at 1 hour ($p = 0.0372$), 2 hours ($p = 0.0047$), and 4 hours ($p = 0.0015$), demonstrating the extract's potent hypoglycemic properties.

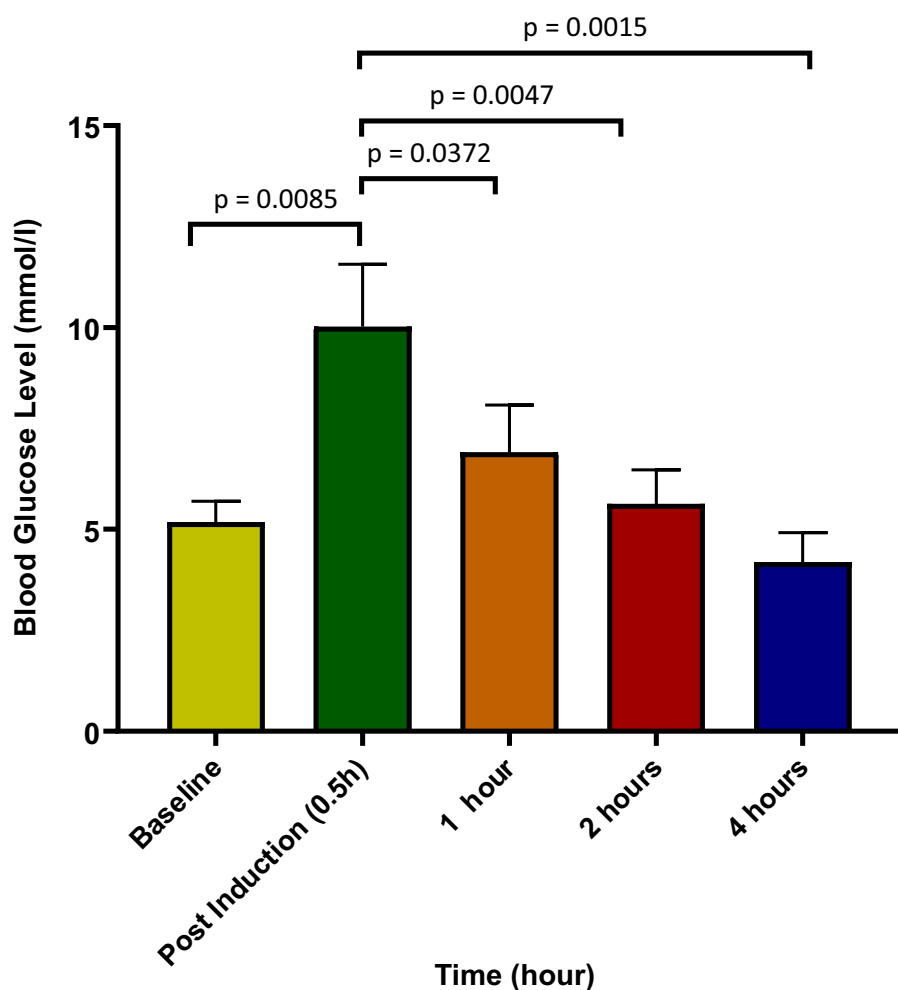


Figure 4: Effect of aqueous extract of *Ficus exasperata* (200 mg/kg) on blood sugar level (mmol/L) of normoglycemic individuals before and after induction of hyperglycemia, and after consumption of the extract.

Combination of *Vernonia amygdalina* and *Ficus exasperata* (200 mg/kg)

Figure 5 depicts the combined effect of *Vernonia amygdalina* and *Ficus exasperata* at a dose of 200 mg/kg on blood glucose levels. After inducing hyperglycemia, a significant increase in blood glucose levels was recorded ($p = 0.0364$). The combination treatment resulted to significant reductions in blood glucose levels at 1 hour ($p = 0.0729$), 2 hours ($p = 0.0352$), and 4 hours ($p = 0.0282$), indicating a moderate hypoglycemic effect.

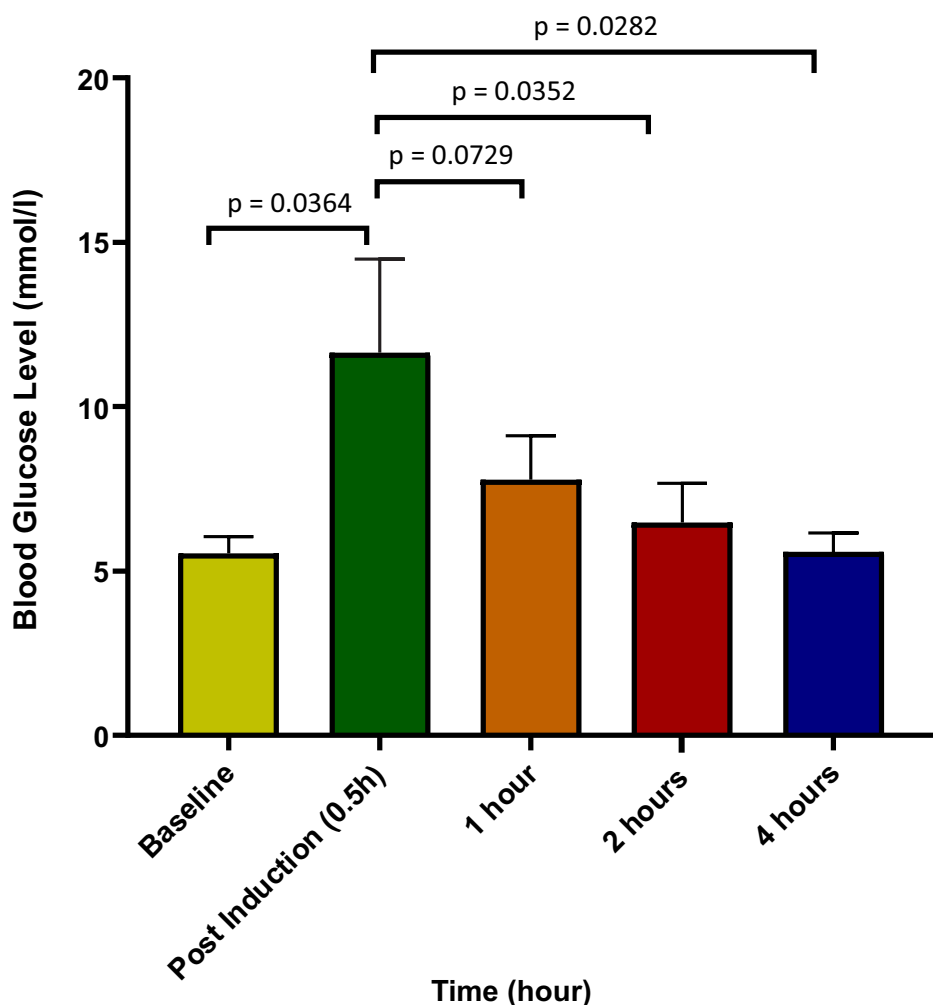


Figure 5: Effect of the combination of the aqueous extract of *Vernonia amygdalina* and *Ficus exasperata* (200 mg/kg) on blood glucose level of normoglycemic individuals before and after induction of hyperglycemia, and after consumption of the extract.

Combination of *Vernonia amygdalina* and *Ficus exasperata* (400 mg/kg)

Figure 6 illustrates the effect of the combination of *Vernonia amygdalina* and *Ficus exasperata* at a dose of 400 mg/kg. Following the induction of hyperglycemia, a significant increase in blood glucose levels ($p = 0.0161$) was noted. This increase was followed by significant reductions at 1 hour ($p = 0.0117$), 2 hours ($p = 0.0459$), and 4 hours ($p = 0.0136$), indicating a strong and sustained hypoglycemic effect.

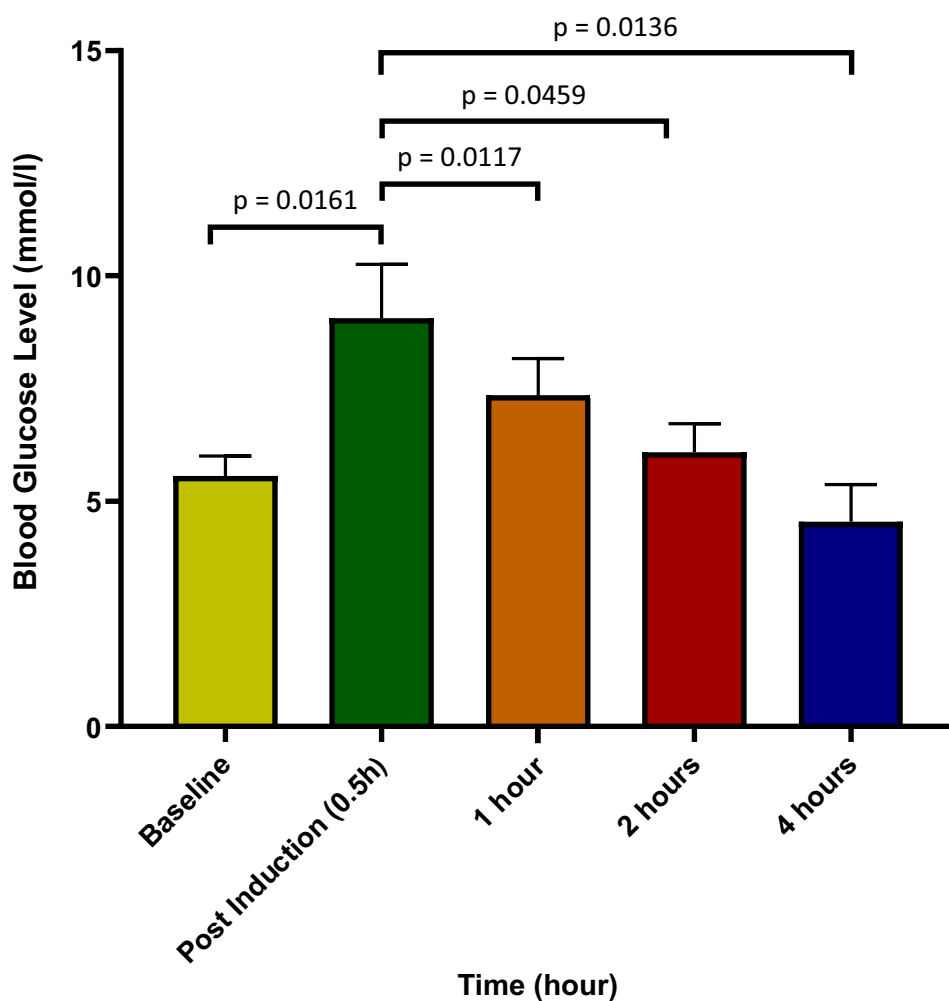


Figure 6: Effect of the combination of the aqueous extract of *Vernonia amygdalina* and *Ficus exasperata* (400 mg/kg) on blood glucose level of normoglycemic individuals before and after induction of hyperglycemia, and after consumption of the extract.

Glimepiride (2 mg, Standard)

Figure 7 shows the effect of 2 mg of Glimepiride, which served as the standard treatment in this study. The administration of Glimepiride after the induction of hyperglycemia resulted in a significant increase in blood glucose levels ($p = 0.0024$). However, subsequent treatment showed significant reductions in blood glucose levels at 1 hour ($p = 0.0181$), 2 hours ($p = 0.0092$), and 4 hours ($p = 0.0028$), confirming the standard's potent hypoglycemic efficacy.

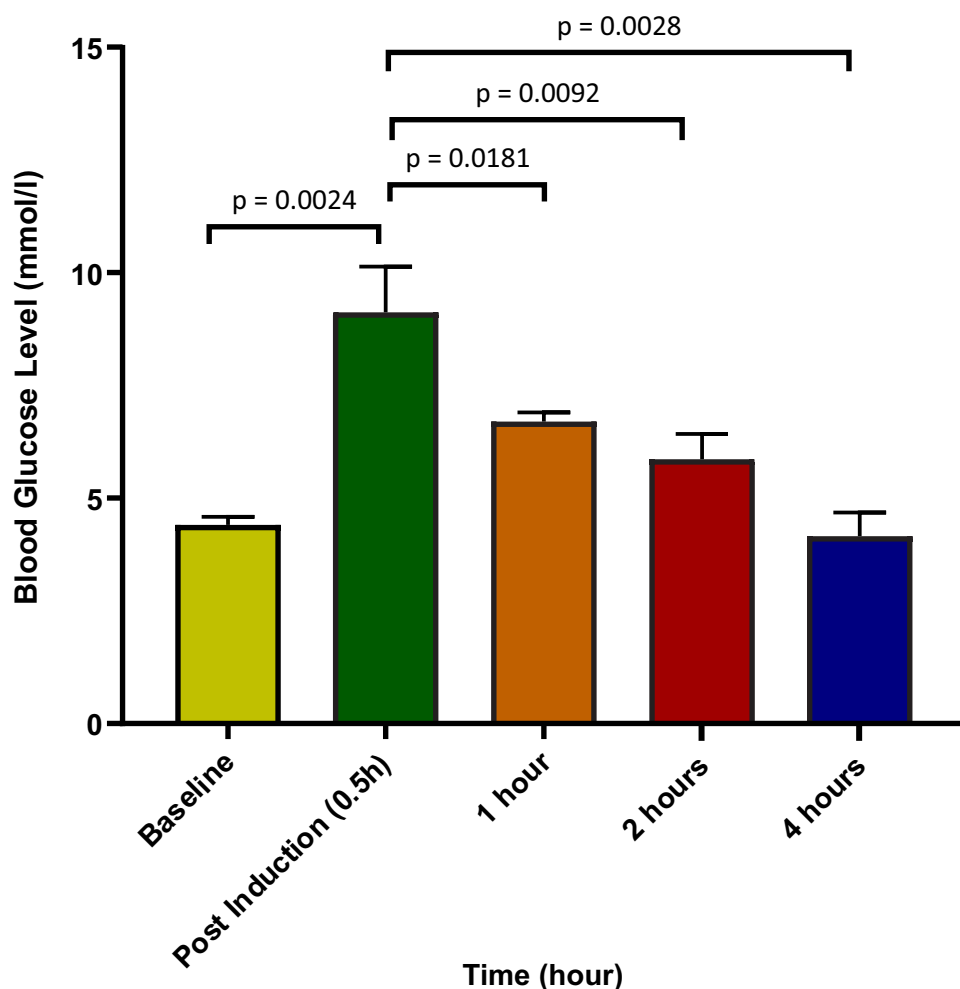


Figure7: Effect Glimepiride (2mg) on blood glucose level of normoglycemic individuals before and after induction of hyperglycemia, and after consumption of the extract.

DISCUSSION

The current study investigated the hypoglycemic effects of *Vernonia amygdalina* and *Ficus exasperata*, both individually and in combination, on blood glucose levels in normoglycemic individuals. The results indicated that both plants exhibited significant glucose-lowering effects comparable to the standard antidiabetic drug, Glimepiride, particularly at higher doses. These findings support the potential use of these herbal extracts in managing blood glucose levels, aligning with previous research¹⁰ that has highlighted the antidiabetic properties of these plants.

Vernonia amygdalina, also known as bitter leaf, has been widely recognized in traditional medicine for its antidiabetic properties.² In this study, *Vernonia amygdalina* at a dose of 200 mg/kg showed significant ($p < 0.05$) glucose-lowering effects at 2 hours and 4 hours post-administration. The delayed yet sustained hypoglycemic effect observed at this dose suggests that

the bioactive compounds in *Vernonia amygdalina* may exert a prolonged effect on glucose metabolism, possibly through enhanced insulin sensitivity or inhibition of gluconeogenesis.¹⁰

The 400 mg/kg dose demonstrated a more pronounced antihyperglycemic effect, with significant reductions ($p < 0.05$) in blood glucose levels observed as early as 1 hour and sustained up to 4 hours. This dose-dependent response suggests that higher concentrations of *Vernonia amygdalina* may offer both immediate and lasting effect on blood glucose levels. The effectiveness of *Vernonia amygdalina* at 400 mg/kg is comparable to that of Glimepiride, a well-established antidiabetic drug, indicating that this plant extract could be a viable alternative for managing diabetes, especially within traditional medicine practices.

The efficacy of *Vernonia amygdalina* can be attributed to

its rich phytochemical content, including saponins, flavonoids, alkaloids, steroids and terpenes which have been reported to have good antidiabetic, hypolipidemic and antihyperglycemic activities.¹⁵ These compounds are known to enhance glucose uptake in peripheral tissues, reduce hepatic glucose production, and improve insulin sensitivity, also, are believed to play a crucial role in enhancing insulin sensitivity and modulating glucose metabolism. Moreover, the antioxidant properties of these phytochemicals may play a role in mitigating oxidative stress, which is a known contributor to insulin resistance and β -cell dysfunction in diabetes.¹⁰

Ficus exasperata, also known as sandpaper tree, has a rich history in traditional medicine for its reported antidiabetic properties.¹² In this study, doses of 200 mg/kg and 400 mg/kg of *Ficus exasperata* produced significant reductions in blood glucose levels ($p < 0.05$) at all measured time points - 1 hour, 2 hours, and 4 hours post-treatment. The hypoglycemic effect was notably stronger at the higher dose, supporting previous findings that suggest a dose-dependent relationship between *Ficus exasperata* and its antidiabetic effect. The consistent glucose-lowering effect across multiple time points suggests that *Ficus exasperata* may act by enhancing insulin secretion or increasing glucose uptake in peripheral tissues.¹⁶ These effects are likely due to the plant's diverse phytochemical constituents, including flavonoids, saponins, and alkaloids, which are known to influence glucose metabolism. These compounds may enhance tissue glucose uptake and inhibit carbohydrate absorption in the intestines, leading to reduced blood glucose levels while showing insulin-mimetic properties.¹⁷ Furthermore, *Ficus exasperata*'s anti-inflammatory and antioxidant actions may protect pancreatic β -cells from oxidative damage, and improving insulin secretion, thus contributing to its overall antidiabetic effect.¹⁴

The combination of *Vernonia amygdalina* and *Ficus exasperata* at a dose of 200 mg/kg produced moderate hypoglycemic effects, with significant reductions in blood glucose levels ($p < 0.05$) observed at 2 hours and 4 hours post-treatment. At the higher dose of 400 mg/kg, the combination treatment led to significant reductions ($p < 0.05$) at all measured time points post-treatment. The effectiveness of this higher-dose combination was comparable to Glimpiride, particularly at the later time points, suggesting that the combined extracts provide a strong and sustained hypoglycemic effect.

The synergistic effect observed with the combination of *Vernonia amygdalina* and *Ficus exasperata* at 400 mg/kg could be attributed to the complementary mechanisms of action of their respective phytochemicals. For instance, while *Vernonia amygdalina* may primarily enhance insulin sensitivity and reduce hepatic glucose output,¹⁸ *Ficus exasperata* may inhibit intestinal glucose absorption and stimulate insulin secretion.¹⁶ Together, these actions could provide a more comprehensive approach to managing blood glucose levels, potentially offering a more effective treatment option for diabetes management.

Glimpiride, a well-known sulfonylurea, consistently lowered blood glucose levels at all time points, demonstrating highly significant reductions with p -values < 0.05 . The rapid and sustained antidiabetic effect of Glimpiride is well-documented, as it acts primarily by stimulating insulin release from pancreatic β -cells,⁸ which is indicative of its potent insulin-releasing effects, making it a reliable standard for comparison. The herbal extracts, especially at higher concentrations, closely matched the efficacy of Glimpiride. The slight delay in onset of action observed with the herbal extracts compared to Glimpiride may be due to differences in their mechanisms of action, with the herbs likely involving multiple pathways, such as improving insulin sensitivity, enhancing glucose uptake, and inhibiting carbohydrate absorption.

The comparable efficacy of these extracts to a standard pharmaceutical agent like Glimpiride highlights the need for further research into their safety profiles, and potential for integration into conventional diabetes management protocols.

The demonstrated efficacy of *Vernonia amygdalina* and *Ficus exasperata* both individually and in combination, especially at higher doses, suggests that these plants could be valuable components of an integrative approach to diabetes care. This also underscores the importance of exploring herbal combinations in the development of novel antidiabetic therapies.

CONCLUSION

This study has provided substantial evidence that *Vernonia amygdalina* and *Ficus exasperata* possess significant antihyperglycemic effects, both individually and in combination. The results suggest that these plant extracts, particularly at higher doses, can effectively reduce blood glucose levels, with efficacy approaching

that of the standard antidiabetic drug, Glimepiride. These findings support the traditional use of these plants in the management of diabetes and highlight their potentials as complementary or alternative therapies.

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