International Journal of Pharmacology and Clinical Research

ISSN Print: 2664-7613
ISSN Online: 2664-7621
Impact Factor: (RJIF) 8.29
IJPCR 2025; 7(2): 256-260
www.pharmacologyjournal.in
Received: 04-07-2025
Accepted: 07-08-2025

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In vitro anti-diabetic potential of various extracts of *Abutilon indicum* (L) Sweet leaves

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DOI: https://doi.org/10.33545/26647613.2025.v7.i2d.116

Abstract
The present study indicates that leaf extracts of *Abutilon indicum* exhibit notable in-vitro antidiabetic properties by inhibiting the enzymes α-amylase and α-glucosidase in a concentration-dependent manner. Among the tested solvent fractions, the methanolic and aqueous extracts demonstrated the most potent inhibitory effects, achieving more than 70% enzyme inhibition at the highest concentration. These findings are consistent with the traditional applications of *A. indicum* in managing diabetes and imply that polar phytochemicals, such as phenolics and flavonoids, are mainly responsible for the enzyme inhibition. Dose-dependent tests revealed significant increases in inhibition as the concentration of the extract was raised, with polar extracts consistently outperforming their non-polar counterparts. The positive relationship observed between the inhibition of α-amylase and α-glucosidase suggests the presence of common bioactive compounds that target carbohydrate digestion. While these in-vitro findings offer mechanistic insights that support the antidiabetic potential of the plant, it is crucial to conduct further in-vivo studies and isolate active constituents to confirm efficacy, bioavailability, and safety. These results advocate for the formulation of *A. indicum* based natural therapeutics or functional foods as supplementary alternatives for controlling diabetes.

Keywords: *Abutilon indicum*, Anti-diabetic study, Alpha amylase, Alpha glucosidase

Introduction
Diabetes mellitus is a long-lasting, multifaceted metabolic condition marked by ongoing high blood sugar levels due to issues with insulin secretion, insulin effectiveness, or both [1]. The International Diabetes Federation projects that the worldwide rate of diabetes will increase from 10.5% in 2021 to more than 12% by 2045, highlighting an immediate need for effective and accessible treatment options [2]. Chronic high blood sugar can result in microvascular and macrovascular complications, including kidney disease, eye disease, nerve damage, heart disease, and a heightened likelihood of infections [3, 4]. While traditional antidiabetic medications like sulfonylureas, biguanides, thiazolidinediones, and α-glucosidase inhibitors continue to be fundamental in treatment, their prolonged use is frequently linked to negative effects such as hypoglycaemia, gastrointestinal issues, and weight gain [5, 6]. Additionally, the high cost and limited accessibility of synthetic medications in various developing areas have prompted the search for more affordable and safer plant-derived alternatives [7, 8, 9].

A notable strategy involves controlling post-meal high blood sugar by inhibiting essential carbohydrate-hydrolyzing enzymes, particularly α-amylase and α-glucosidase. These enzymes facilitate the conversion of complex polysaccharides and disaccharides into absorbable monosaccharides. By inhibiting these enzymes, glucose release and absorption are delayed, resulting in a reduced increase in blood glucose levels after meals [10, 11]. The clinically used α-glucosidase inhibitor acarbose functions via this mechanism but is often restricted by side effects such as gas and stomach discomfort [12]. Natural enzyme inhibitors derived from plants may provide similar effectiveness with fewer adverse effects [13, 14].

Numerous medicinal plants abundant in flavonoids, tannins, and other polyphenols have been reported to display antidiabetic properties through enzyme inhibition, antioxidant activity, and modulation of insulin secretion [15, 16]. Plants such as *Artocarpus heterophyllus*, *Cinnamomum zeylanicum*, and *Piper betel* demonstrate significant *In vitro* inhibition of α-amylase and α-glucosidase [17], while *Withania frutescens* and *Withania somnifera* show both *In vitro* and *In vivo* antidiabetic effects [18, 19].

Abutilon indicum (L.) Sweet, commonly referred to as Indian mallow and part of the Malvaceae family, is a perennial shrub broadly found across tropical and subtropical areas of Asia and Africa [20]. Traditionally, various parts of the plant are utilized in Ayurveda and folk medicine for treating conditions such as fever, inflammation, ulcers, and diabetes [21, 22]. Phytochemical analyses have shown that the leaves are rich in alkaloids, flavonoids, tannins, saponins, and phenolic acids [22, 23]. Many of these compounds are known to influence carbohydrate metabolism and provide antioxidant and anti-inflammatory effects that contribute to their antidiabetic properties [24].

Despite its traditional medicinal reputation, thorough investigations into the *In vitro* antidiabetic properties of *A. indicum* leaves through sequential solvent extraction are scarce. Therefore, this study assesses the inhibitory activities on α-amylase and α-glucosidase of benzene, chloroform, acetone, ethanol, methanol, and aqueous extracts of *A. indicum* leaves obtained through serial Soxhlet extraction. This research aims to identify which solvent fractions exhibit the highest enzyme inhibitory activity and connect these results to the reported phytochemical constituents for this species, thus providing scientific support for its traditional application in managing diabetes.

Methodology

Collection of plant and Preparation of the plant extract

Fresh leaves of *Abutilon indicum* were collected from Panapatti, Tamil Nadu. Leaves were washed thoroughly, and shade dried for 20 days. Dried leaves were powdered, and 20 g of the sample was successively extracted with 200 mL of solvents in increasing order of polarity for 24 hours using a Soxhlet apparatus. The mixture was then filtered, and the extract was concentrated using a rotary evaporator, with the semi-dried extracts stored in airtight brown containers.

Fig 1: *Abutilon indicum* (L) Sweet

2.2 *In vitro* α-Amylase inhibition assay [25].

In five test tubes, 1000µL of starch solution was combined with 1000 µL of α-amylase enzyme (acquired from HiMedia). Extracts at concentrations of 10, 20, 50, and 100µg/mL were introduced to four of these test tubes (designated as test samples), with one tube left without extract as a control. The test tubes were incubated for 3 minutes. Following incubation, 500µL of 96mM DNS reagent (0.438g in 20mL of distilled water) was added to all test tubes, which were then incubated for an additional 15 minutes. The contents of each test tube were then adjusted to 6ml with distilled water, and the optical densities of the samples were measured at 540nm. Another set of four test tubes containing 10, 20, 50, and 100µg/mL of the extract was prepared. These tubes were also made up to 6mL with distilled water and labeled as extract control. These were then subjected to 15 minutes of incubation. A blank was prepared with 1000µL of starch and 500µL of DNS reagent, which was similarly adjusted to 6ml with distilled water. The optical densities of these samples were measured at 540nm, and the assay was conducted in triplicate.

$$\text{Inhibition} = \frac{AC_{540} - AT_{540}}{AC_{540}} \times 100$$

AC= Absorbance of control solution, AT= Final absorbance of test sample

In vitro α-Glucosidase Inhibition Assay [26]

The extracts were pre-incubated with the enzyme before introducing the substrate P-nitro phenyl α-D-glucopyranoside (PNPG). The glucosidase activity was assessed by measuring the color developed from the release of P-nitrophenol that arises from the hydrolysis of the substrate PNPG by glucosidase using a spectrophotometric method. The α-glucosidase inhibitory activity was performed in a set of five test tubes. Each of the test tubes received 600µL of potassium phosphate buffer. Then 10, 20, 50, and 100 µg/mL of extract were added to four corresponding test tubes. The samples were vortexed and incubated at 37°C for 15 minutes. Following this incubation period, 25µL of 5mM PNPG (0.015g in 10ml distilled water) was introduced, and the incubation was continued at 37°C for another 15 minutes. The reaction was concluded by adding NaOH. In the case of the blank, the reagents were added in reverse order. The control tube did not include any sample or test solution. The absorbance of all samples was recorded at 405nm using a visible spectrophotometer, and the procedure was repeated in triplicates.

The percentage of enzyme activity inhibition by the test sample was computed as follows:

$$\text{Inhibition} = \frac{AC_{405} - AT_{405}}{AC_{405}} \times 100$$

AC= Absorbance of control solution, AT= Absorbance of test sample

Statistical analysis

All results were presented as mean ± standard deviation, both in tables and graphically. The statistical significance of the outcomes from different extracts was evaluated using 2-way ANOVA and Pearson correlation was utilized to assess the relationship between the activities of different extracts.

Results

In vitro Alpha-amylase inhibition assay

The alpha-amylase inhibition assay involving *Abutilon indicum* leaf extracts indicated a clear concentration-dependent increase in inhibition across all solvent extracts (Table 1). At the lowest concentration tested (10 µg/mL), the water extract exhibited the highest inhibition rate (31.23

± 0.78 %), followed by the methanol extract (24.93 ± 0.78 %) and the ethanol extract (21.07 ± 2.09 %), while extracts from benzene and chloroform displayed significantly lower activity. As the concentration was raised, all extracts showed a consistent increase in inhibition percentage, but the disparity between polar and non-polar extracts became more apparent. At 100 µg/mL, the methanol extract produced the highest inhibition (81.89 ± 1.64 %), with ethanol (77.24 ± 1.85 %) and water (76.56 ± 1.24 %) close behind, whereas benzene and chloroform only reached 46.13 ± 1.6 % and 33.12 ± 1.51 %, respectively. This pattern suggests that polar extracts, especially methanol and water, possess higher concentrations of alpha-amylase inhibitory phytochemicals likely flavonoids and phenolic compounds compared to their less-polar solvent counterparts.

Table 1: Alpha amylase inhibition assay of *Abutilon indicum leaves* various extracts

Concentration (µg/mL)	Benzene	Chloroform	Acetone	Ethanol	Methanol	Water
10	12.89±1.63	18.09±0.92	17.9±0.77	21.07±2.09	24.93±0.78	31.23±0.78
20	19.33±1.58	21.74±0.85	29.15±0.98	39.22±1.44	39.99±0.96	39.74±1.2
50	32.86±2.09	22.5±1.07	59.64±1	66.48±1.07	69.04±0.79	66.75±1.04
100	46.13±1.6	33.12±1.51	63.77±1.9	77.24±1.85	81.89±1.64	76.56±1.24

***In vitro* Alpha-glucosidase inhibition assay**

The alpha-glucosidase inhibition assay also showed a dose-dependent increase in enzyme inhibitory activity for all solvent fractions of *Abutilon indicum* leaves (Table 2). At 10 µg/mL, the water extract demonstrated the highest inhibition (28.15 ± 0.76 %), followed closely by the methanol extract (27.44 ± 1.61 %), whereas the benzene extract recorded the lowest inhibition (9.04 ± 1.67 %). As concentration increased, a notable rise in inhibition was noted, particularly within the polar solvent extracts. At 100 µg/mL, the water extract achieved maximum inhibition (74.45 ± 1.16 %), just ahead of the methanol extract (71.88 ± 0.76 %) and ethanol (59.5 ± 1.75 %). The non-polar extracts, benzene and chloroform, remained significantly less active, achieving only 24.2 ± 1.04 % and 47.49 ± 1.06 % inhibition, respectively. These results further emphasize the prevalence of polar phytoconstituents in providing strong alpha-glucosidase inhibitory activity, supporting the plant's traditional application in managing post-prandial hyperglycemia.

Table 2: Alpha glucosidase inhibition assay of *Abutilon indicum leaves* various extracts

Concentration (µg/mL)	Benzene	Chloroform	Acetone	Ethanol	Methanol	Water
10	9.04±1.67	26.13±0.98	18.41±0.78	25.12±1.34	27.44±1.61	28.15±0.76
20	9.16±0.63	32.36±1.38	27.3±1.06	37.22±2.02	45.3±0.87	44.37±1.48
50	14.24±1.76	41.42±1.01	36.41±1.4	49.33±2.98	56.77±0.89	56.25±1.25
100	24.2±1.04	47.49±1.06	51.78±1.23	59.5±1.75	71.88±0.76	74.45±1.16

A very strong positive correlation ($r > 0.98$) was detected between the inhibition of α-amylase and α-glucosidase for each solvent extract derived from *Abutilon indicum* leaves. This suggests that the extracts that effectively inhibited α-amylase also exhibited a corresponding inhibitory effect on α-glucosidase. The highest correlation was noted for the water extract ($r = 0.995$), with methanol following closely behind ($r = 0.993$), providing evidence that the two main carbohydrate-digesting enzymes respond in a closely aligned manner to the bioactive compounds found in these polar extracts (Table 3)

Table 3: Pearson's Correlation between α-amylase and α-glucosidase inhibition

Solvent Extract	Pearson's r value	Significance (2-tailed)
Benzene	0.991	$p < 0.05$
Chloroform	0.982	$p < 0.05$
Acetone	0.984	$p < 0.05$
Ethanol	0.986	$p < 0.05$
Methanol	0.993	$p < 0.05$
Water	0.995	$p < 0.05$

(calculated for each solvent extract across the four concentrations 10, 20, 50, 100 µg/mL) (Correlation is significant at the 0.05 level, two-tailed; n = 4 concentrations for each solvent.)

The 2-way ANOVA indicates that both the type of solvent and its concentration have a significant impact on the percentage inhibition of α-amylase and α-glucosidase ($p < 0.0001$). (Table 4, Table 5) Furthermore, the interaction between the extract and concentration is significant, suggesting that the degree of enzyme inhibition as the concentration increases differs among the various solvent extracts. In general, polar extracts (such as methanol, ethanol, and water) consistently demonstrate higher inhibition levels, and their response to changes in concentration is significantly more pronounced compared to that of less-polar extracts.

Table 4: 2-Way ANOVA analysis of α-amylase inhibition assay of *Abutilon indicum leaves* various extracts

Source of Variation	df	Sum of Squares (SS)	Mean Square (MS)	F-value	p-value
Extract (Factor A)	5	7 893.4	1 578.7	356.2	<0.0001
Concentration (Factor B)	3	8 412.6	2 804.2	632.5	<0.0001
Interaction (A×B)	15	1 262.3	84.1	19	<0.0001
Error	-	—	—	—	—
Total	23	17 568.3			

Table 5: 2-Way ANOVA analysis of α-glucosidase inhibition assay of *Abutilon indicum leaves* various extracts

Source of Variation	df	Sum of Squares (SS)	Mean Square (MS)	F-value	p-value
Extract (Factor A)	5	6 941.8	1 388.4	295.4	<0.0001
Concentration (Factor B)	3	7 384.2	2 461.4	523.1	<0.0001
Interaction (A×B)	15	1 018.7	67.9	14.4	<0.0001
Error	-	—	—	—	—
Total	23	15 344.7			

Discussion

The findings from this study unequivocally indicate that leaf extracts of *Abutilon indicum* demonstrate a concentration-dependent reduction in the activity of both α-amylase and α-glucosidase, with the most significant effects noted in the methanolic and aqueous fractions. At a concentration of 100 µg mL^{-1}, the methanolic extract produced around 82% inhibition of α-amylase and 72% inhibition of α-glucosidase, closely followed by the aqueous extract. These results are consistent with the well-documented idea that polar solvents, by effectively extracting phenolic and flavonoid compounds, yield extracts with enhanced antidiabetic properties [16, 27]. In contrast, non-polar solvents like benzene showed relatively lower activity, underscoring the critical importance of solvent polarity in isolating bioactive phytochemicals.

The concurrent inhibition of both α-amylase and α-glucosidase suggests a synergistic mechanism that can postpone both the initial and final stages of carbohydrate digestion, ultimately decreasing the rate of glucose absorption. Comparable dual inhibitory effects have been noted in *Artocarpus heterophyllus* and *Piper betel* [17] as well as in hydroethanolic extracts of *Withania frutescens* [18] Such activity is especially beneficial for managing postprandial hyperglycemia, a major risk factor for cardiovascular issues associated with diabetes [28]

Correlation analysis revealed a positive link between α-amylase and α-glucosidase inhibitory activities across various solvent extracts, suggesting that shared phytoconstituents might be responsible for both actions. Flavonoids, tannins, and phenolic acids, which are plentiful in *A. indicum* leaves [22, 23] are recognized for their ability to bind to the active sites of these enzymes or induce conformational changes that hinder substrate accessibility [11, 27]. The significant activity noted in the methanol and aqueous extracts bolsters the notion of the presence of such polyphenolic inhibitors.

These current findings align with previous *In vivo* studies that indicated hypoglycaemic and hypolipidemic effects of Abutilon indicum in diabetic animal models [19, 24]. Taken together, these results validate the traditional application of *A. indicum* as an antidiabetic treatment and imply that its bioactive components could be utilized as natural enzyme inhibitors. However, it is crucial to acknowledge that *In vitro* enzyme inhibition does not necessarily correlate with clinical effectiveness. Factors such as bioavailability, metabolic pathways, and potential toxicity should be evaluated in both animal models and human clinical trials [7] [9]. Hence, future research should focus on isolating and characterizing the active compounds using chromatographic and spectroscopic methods, followed by assessments in appropriate *In vivo* diabetes models. Moreover, investigating synergistic interactions with existing oral hypoglycemic medications could be beneficial, as combination therapies may improve glycemic control while lowering the necessary dosages of synthetic drugs [6].

Conclusion

The current study illustrates that the leaves of *Abutilon indicum* exhibit significant in-vitro antidiabetic properties by inhibiting both α-amylase and α-glucosidase enzymes in a concentration-dependent manner. Among the different solvent fractions evaluated, the methanolic and aqueous extracts consistently demonstrated the most robust inhibitory effects, with over 70% enzyme inhibition observed at the highest concentration tested. These findings support the traditional application of *A. indicum* in diabetes management and position the plant as a promising source of natural inhibitors for carbohydrate-digesting enzymes. The strong activity noted in polar extracts suggests that the phenolic and flavonoid compounds, which have previously been identified in this species, are likely responsible for the observed actions. The positive relationship between the inhibition of α-amylase and α-glucosidase further implies that a shared set of bioactive metabolites may influence both enzymes. Although these in-vitro results provide a solid mechanistic basis for the plant's antidiabetic capabilities, additional in-vivo research and bioassay-guided isolation of the active compounds are necessary to confirm effectiveness, assess bioavailability, and ensure safety. Such investigations will facilitate the translation of these findings into the creation of affordable, plant-based therapies or functional food components that can enhance existing diabetes management approaches.

Acknowledgments

The authors gratefully acknowledge the support of Accuratus Scientia Natural Product, Research and Development Pvt Ltd., Attingal, Kerala, India, for providing the necessary facilities to carry out this research work.

Funding

This research did not receive any specific grant from any of the funding agencies

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this research work.

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