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Antioxidant and In Vitro Antidiabetic Properties of *Lansium domesticum* Leaves Extracted with Solvents of Varying Polarity

ABSTRACT

Lansium domesticum, a tropical plant traditionally utilized in Southeast Asia, remains underexplored for its pharmacological potential, particularly the bioactivity of its leaves. This study aimed to investigate the influence of solvent polarity on the phytochemical content, antioxidant activity, and enzyme inhibitory potential of *L. domesticum* leaf extracts. Extraction was conducted using methanol, ethanol, and acetone at varying concentrations (50%, 75%, 100%), as well as distilled water. Total phenolic content (TPC) and total flavonoid content (TFC) were quantified, and antioxidant activities were assessed via total antioxidant activity (TAA), DPPH, and FRAP assays. Antidiabetic activity was evaluated in vitro through α-glucosidase and α-amylase inhibition assays. Results indicated that 100% ethanol and acetone extracts exhibited the highest TPC and TFC, correlating strongly with superior antioxidant and enzyme inhibitory activities. The 100% ethanol extract demonstrated the most potent α-glucosidase and α-amylase inhibition, with IC_{50} values of 70.64 µg/mL and 105.13 µg/mL, respectively. Pearson correlation analysis revealed strong negative correlations between phytochemical contents and IC_{50} values, indicating higher bioactivity with increased phenolic and flavonoid concentrations. These findings suggest that pure organic solvents, particularly ethanol, are optimal for extracting bioactive compounds from *L. domesticum* leaves, highlighting their potential for development as natural antioxidants and antidiabetic agents.

Keywords: *Lansium domesticum*, antioxidant, antidiabetic, solvent polarity

INTRODUCTION

Diabetes mellitus is recognized as a prolonged metabolic disorder marked by a persistent increase in blood sugar as a consequence of defective insulin secretion, insulin function, or a combination of the two [1]. Diabetes incidence is rising rapidly across the globe, highlighting the pressing need for improved therapeutic strategies that are effective yet safer than current drugs, many of which cause considerable side effects. Within this framework, medicinal plants and their natural products are considered valuable candidates, offering bioactive compounds with notable antidiabetic and antioxidant potential [2].

An imbalance due to the excessive production of reactive oxygen species (ROS) triggers oxidative stress, which is closely associated with the progression and complications of diabetes [3]. Hence, exploring plant-based antioxidants with the ability to eliminate free radicals and simultaneously inhibit key enzymes involved in carbohydrate digestion, including α-glucosidase and α-amylase, presents a dual therapeutic potential [4,5]. Among the vast array of medicinal

plants, *Lansium domesticum* (commonly known as duku) has long been employed in Southeast Asian traditional medicine for various ailments [6]. However, its pharmacological potential, especially the bioactivity of its leaves, remains underexplored.

Plant extracts exert their therapeutic potential mainly through their phytochemical makeup, with total phenolic (TPC) and flavonoid (TFC) contents being key contributors. Both phenolics and flavonoids possess remarkable antioxidant activities, functioning through free radical neutralization and metal ion chelation involved in oxidative reactions [7]. These molecules also function by blocking carbohydrate-degrading enzymes, resulting in reduced glucose absorption and improved management of postprandial glycemia [8,9]. Thus, evaluating how TPC and TFC relate to various biological activities is fundamental for assessing the functional properties of extracts derived from plants.

Extraction efficiency and the yield of bioactive phytochemicals largely depend on the choice of solvent. Solvent polarity influences the solubility of phenolics, flavonoids, and other secondary metabolites, which in turn determines he bioefficacy of the extracts obtained [10]. For instance, Venkatachalam et al. (2020), the methanol extract of Hopea parviflora recorded the highest levels of antioxidant activity in DPPH, FRAP, and superoxide evaluations [11]. This result indicated that the methanolic extract exhibited stronger antidiabetic potential through inhibition of α-amylase and α-glucosidase compared to the ethanol and ethyl acetate extracts [11]. Similarly, Atanu et al. (2022), that the phytochemical content of ethanol extract from Irvingia gabonensis leaves is significantly higher than n-hexane and chloroform. Following this result, ethanol extracts also possessed the most potent inhibition of the DPPH and hydroxyl radicals among the other two extracts [12]. To date, only scarce comparative data are available concerning the effect of different solvents on the antioxidant and antidiabetic properties of *L. domesticum* leaf extract.

The present work focuses on optimizing the extraction of *L. domesticum* leaves by employing solvents of different polarities, methanol, ethanol, acetone (at concentrations of 100%, 75%, and 50%), and water. Antioxidant capacity was determined through DPPH radical scavenging and FRAP assays. For in vitro antidiabetic evaluation, the degree of inhibition of α-glucosidase and α-amylase enzymes was measured. The findings are expected to identify the most effective solvent system for maximizing the therapeutic potential of *L. domesticum* leaf, thereby supporting its future use in functional food and phytopharmaceutical development.

EXPERIMENTAL SECTION

Chemicals and reagents

Extraction solvents included methanol (≥99.8%), ethanol (≥99.5%), acetone (≥99.5%), and distilled water. Analytical-grade reagents such as DPPH, ferric chloride ($FeCl_3$), potassium ferricyanide [$K_3Fe(CN)_6$], trichloroacetic acid (TCA), sodium carbonate (Na_2CO_3), Folin–Ciocalteu's phenol reagent, sodium nitrite ($NaNO_2$), aluminum chloride ($AlCl_3$), and sodium

hydroxide (NaOH) were obtained from Merck (Darmstadt, Germany). For the phosphomolybdenum assay, ammonium molybdate [$(NH_4)_6Mo_7O_{24}\cdot 4H_2O$], sodium phosphate ($Na_3PO_4$), and sulfuric acid ($H_2SO_4$) were also sourced from Merck. Gallic acid and quercetin (for TPC and TFC determination), together with ascorbic acid (for TAA reference), were purchased from Sigma-Aldrich (St. Louis, MO, USA). Kits for α-glucosidase and α-amylase inhibition were provided by Elabscience (Houston, TX, USA).

Procedure

Plant sample collection and preparation

Fresh leaves of *L. domesticum* were collected from a cultivated area in Deli Serdang, North Sumatera, Indonesia in July 2024. Taxonomic verification and authentication of the plant material were performed by a botanist affiliated with the Herbarium of Universitas Sumatera Utara, and a voucher specimen (No. 3005/MEDA/2024) was deposited for future reference. Freshly collected leaves were rinsed carefully under running tap water and subsequently with distilled water to eliminate any adhering dust or impurities. The cleaned samples were shade-dried at ambient temperature for 7–10 days until a stable weight was obtained. After drying, the leaves were pulverized with a mechanical grinder and sieved through a 60-mesh screen. The resulting powder was preserved in airtight containers at room temperature, shielded from moisture and light, until used for extraction.

Extraction procedure

The extraction of bioactive constituents from *L. domesticum* leaf powder was carried out by maceration. Fifty grams of dried powder were immersed in 500 mL of different solvents, which are methanol, ethanol, acetone (100%, 75%, and 50% v/v, respectively), and distilled water, placed separately in Erlenmeyer flasks. The mixtures were maintained at ambient temperature (25 ± 2°C) with occasional agitation for 72 hours. Following maceration, the solutions were filtered through Whatman No. 1 paper, and the filtrates were concentrated under reduced pressure using a rotary evaporator (EYELA N-1001, Tokyo, Japan) at 40°C. Residual solvent was eliminated by drying the extracts in a silica gel desiccator until constant weight. The dried extracts were stored at 4°C in amber vials for subsequent analysis [13].

Determination of total phenolic content

The Folin–Ciocalteu colorimetric method, with slight modification from Singleton et al. (1999), was employed to determine the total phenolic content of the extracts. A volume of 200 µL of extract (1 mg/mL) was mixed with 1 mL of 10% Folin–Ciocalteu reagent, followed by a 5-minute incubation. Then, 800 µL of 7.5% Na_2CO_3 was added, and the mixture was kept in the dark at room temperature for 30 min. The absorbance was read at 765 nm using a Shimadzu UV-1800 spectrophotometer (Kyoto, Japan). Results were calculated against a gallic acid calibration curve and expressed as mg GAE per g extract [14,15].

Determination of total flavonoid content

The aluminum chloride assay was employed to quantify TFC following Zhishen et al. (1999) with slight adjustments. In this method, 500 µL of extract (1 mg/mL) was mixed with 300 µL of 5% $NaNO_2$. After 5 minutes, 300 µL of 10% $AlCl_3$ was added, and after an additional 6 minutes, 2 mL of 1 M NaOH was introduced. The solution volume was brought to 5 mL with distilled water, vortexed thoroughly, and its absorbance was determined at 510 nm. TFC was expressed as mg QE per g extract using quercetin as the calibration standard [16].

Determination of total antioxidant activity

The phosphomolybdenum method, with modifications based on Govindarajan et al. and Subhasree et al., was employed to measure TAA. A 0.2 mL aliquot of extract solution (25–400 µg/mL in water) was combined with 1.8 mL of reagent containing 0.6 M sulfuric acid, 28 mM sodium phosphate, and 4 mM ammonium molybdate. The reaction mixtures were incubated at 90°C in capped tubes for 90 min and then cooled to room temperature. Absorbance was recorded at 695 nm (Shimadzu UV-1800). Ascorbic acid (5–60 µg/mL) was used to construct the calibration curve, and results were expressed as mg AAE per g of extract [17].

DPPH radical scavenging assay

Free radical quenching ability of the extracts was measured using the DPPH method described by Lubis et al. (2022), with slight adjustments. Briefly, 1 mL of extract solutions (25–400 µg/mL) were mixed with 1 mL of 0.1 mM DPPH in methanol. The mixtures were incubated at ambient temperature in the dark for 30 min. Absorbance was determined at 517 nm with a Shimadzu UV-1800 spectrophotometer. A methanol solution was used as the blank, while DPPH without extract served as the control. Radical scavenging activity was expressed as percentage inhibition calculated using Eq.1 [18]:

$$Inhibition\ (\%) = \frac{A_0 - A_1}{A_0}\ x\ 100 \quad (1)$$

Ferring reducing antioxidant power assay

The reducing capacity of the extracts was assessed using the FRAP assay according to Gonzales-Palma et al. (2016). Briefly, 200 µL of extract was mixed with 500 µL phosphate buffer (0.2 M, pH 6.6) and 500 µL potassium ferricyanide solution (1%). The mixture was incubated at 50°C for 20 min, followed by addition of 500 µL trichloroacetic acid (10%). After centrifugation at 3000 rpm for 10 min, 500 µL of the supernatant was combined with 500 µL distilled water and 100 µL of 0.1% $FeCl_3$. The absorbance was then read at 700 nm. Higher absorbance indicated stronger reducing activity [19].

In vitro antidiabetic activity

α-Glucosidase and α-amylase inhibitory activities were determined using reagent kits from Elabscience (Houston, TX, USA) following the manufacturer's guidelines with minor adjustments. Extracts dissolved in water were prepared at concentrations of 25–500 µg/mL. For α-glucosidase inhibition, 50 µL of extract was combined with the enzyme solution and incubated at 37°C. The

substrate (p-nitrophenyl-α-D-glucopyranoside) was then added, and after incubation, the stop solution supplied by the kit was used to terminate the reaction. Absorbance was read at 405 nm using a BioTek microplate reader. Acarbose was used as the standard. For α-amylase inhibition, 50 µL of extract was incubated with the enzyme solution at 37°C, followed by the addition of soluble starch as substrate. After incubation, the kit color reagent was introduced, and absorbance was recorded at 540 nm. Acarbose acted as a positive control. The inhibition percentage was calculated using Eq. 2 [20,21]:

$$Inhibition\ (\%) = \frac{A_{control} - A_{sample}}{A_{control}}\ x\ 100 \quad (2)$$

In this equation, Acontrol represents the absorbance of the control solution lacking extract, and Asample indicates the absorbance obtained with the extract. IC_{50} values were determined from the inhibition curves plotted using different extract concentrations.

Statistical analysis

All experimental procedures were conducted in triplicate, and data were expressed as mean ± SD. IC_{50} values for antioxidant (DPPH) and enzyme inhibition (α-glucosidase, α-amylase) assays were estimated by nonlinear regression analysis in GraphPad Prism (v9.0). Group differences were analyzed using one-way ANOVA with Tukey's post hoc test, considering $p < 0.05$ as statistically significant. Pearson correlation was also applied to examine the relationship between TPC, TFC, and observed antioxidant/antidiabetic effects. Correlation coefficients and statistical significance were obtained using SPSS Statistics version 26 (IBM Corp., Armonk, NY, USA).

RESULTS AND DISCUSSION

Effect of different solvents on yield and phytochemical content

The isolation of phytochemicals from plant materials typically involves several preparatory steps, such as milling, grinding, and homogenization, with extraction being the most critical for recovering bioactive compounds [22]. The efficiency of extraction is governed by multiple parameters, including the chemical nature of the phytochemicals, the particle size of the sample, the extraction method, solvent polarity, pH, temperature, extraction time, and the composition of the plant matrix [23]. Among these, under consistent time and temperature, the type of solvent and sample composition are considered the most influential factors. In the present study, *L. domesticum* leaf extracts were obtained using water and various concentrations (50%, 75%, and 100%) of aqueous methanol, ethanol, and acetone. Extraction yields ranged from 13.57 ± 1.35% with pure acetone to a maximum of 33.46 ± 2.05% with 50% aqueous ethanol (Table 1). This result suggests that solvent mixtures with intermediate polarity, such as 50% aqueous ethanol, are more effective at extracting a broader range of phytochemicals compared to either pure solvents or water alone. Comparable yields were observed with 50% aqueous acetone (32.56 ± 1.75%) and 75%

aqueous methanol (31.56 ± 1.03%), further supporting the advantage of aqueous-organic combinations. On the other hand, water as a single solvent achieved a moderate yield (21.50 ± 1.50%), while the lowest yield was obtained with 100% acetone, highlighting the limitations of pure organic solvents in extracting diverse phytochemical constituents. The high extraction yields of aqueous solvent mixtures may not only be attributed to the presence of phenolic compounds but also to the co-extraction of other soluble compounds such as proteins and carbohydrates, which tend to have higher solubility in water and ethanol compared to methanol and acetone. The synergistic use of water and organic solvents enhances the solubilization of both polar and semi-polar constituents, leading to improved extraction efficiency. These findings are consistent with previous studies on medicinal plants, which also reported higher yields when using aqueous organic solvent systems [24–26].

The total phenolic content (TPC) of *L. domesticum* leaf extracts was found to vary considerably across different solvent systems (Table 1). The highest TPC value was observed in the extract obtained with 100% ethanol (32.46 ± 2.67 mg GAE/g extract), followed closely by 100% acetone (32.67 ± 2.78 mg GAE/g) and 75% acetone (30.35 ± 1.64 mg GAE/g). These results suggest that pure or highly concentrated organic solvents, particularly ethanol and acetone, are more effective in extracting phenolic compounds, possibly due to their ability to disrupt cell membranes and enhance the solubility of medium to low polarity phenolics [27]. Interestingly, while 50% aqueous ethanol showed the highest extraction yield, its TPC (21.46 ± 1.45 mg GAE/g) was significantly lower than that of the pure ethanol extract. This indicates that a higher extraction yield does not always correspond to higher phenolic content, as co-extraction of non-phenolic components (e.g., carbohydrates, proteins) in aqueous mixtures may dilute the relative concentration of phenolics in the final extract [28]. A similar trend was observed for aqueous methanol and acetone extracts, where increased water content improved yield but not necessarily phenolic purity. The TPC results also reflect the influence of solvent polarity. While water is highly polar, it yielded the lowest TPC (5.35 ± 0.36 mg GAE/g), underscoring its limited efficiency in extracting phenolics, many of which are only moderately polar. In contrast, the presence of organic solvents with intermediate polarity enhances the solubility and mass transfer of phenolics from the plant matrix into the solvent. These findings align with prior reports stating that the polarity of the solvent must match the polarity of the target phenolics to optimize their extraction [29–31].

Table 1. Extraction yield, total phenolic content (TPC), and total flavonoid content (TFC) of *Lansium domesticum* leaf extracts obtained using solvents of varying polarity

Samples	Parameters		
	Extraction yield (%)	**TPC (mg GAE/g)**	**TFC (mg QE/g)**
Water	21.50 ± 1.50	5.35 ± 0.36	4.67 ± 0.12
Methanol			
100% methanol	28.56 ± 1.60	21.64 ± 2.56	10.34 ± 0.67
75% aqueous methanol	31.56 ± 1.03	25.12 ± 1.78	20.46 ± 1.35

50% aqueous methanol	29.46 ± 1.27	10.45 ± 1.21	6.35 ± 0.57
Ethanol			
100% ethanol	18.46 ± 1.67	32.46 ± 2.67	21.35 ± 1.86
75% aqueous ethanol	27.45 ± 1.46	22.34 ± 1.67	12.57 ± 1.07
50% aqueous ethanol	33.46 ± 2.05	21.46 ± 1.45	11.05 ± 1.02
Acetone			
100% acetone	13.57 ± 1.35	32.67 ± 2.78	26.44 ± 2.46
75% acetone	26.68 ± 1.12	30.35 ± 1.64	24.67 ± 1.50
50% acetone	32.56 ± 1.75	27.89 ± 2.12	20.85 ± 1.47

All data are given as mean ± standard deviation (n = 3). Total phenolic content (TPC) was quantified as mg GAE/g extract, whereas total flavonoid content (TFC) was determined as mg QE/g extract.

Subsequently, the total flavonoid content (TFC) exhibited considerable variation depending on the solvent system used for extraction (Table 1). The highest TFC was observed in the extract prepared with 100% acetone (26.44 ± 2.46 mg QE/g extract), followed by 75% acetone (24.67 ± 1.50 mg QE/g) and 100% ethanol (21.35 ± 1.86 mg QE/g). These findings suggest that flavonoids, particularly those with lower polarity, such as aglycones, are more effectively extracted using pure or highly concentrated organic solvents [32]. The high affinity of acetone for non-polar to moderately polar compounds may explain its superior performance in extracting flavonoid constituents. In contrast, aqueous solvent mixtures such as 50% ethanol and 50% methanol yielded moderate TFC values (11.05 ± 1.02 and 6.35 ± 0.57 mg QE/g, respectively), despite producing the highest overall extraction yields. This indicates that maximum extraction yield does not necessarily correlate with high flavonoid content, as aqueous mixtures may co-extract other polar compounds that do not contribute to TFC, thereby lowering the relative concentration of flavonoids in the extract [33]. Water as a sole solvent resulted in the lowest TFC (4.67 ± 0.12 mg QE/g), highlighting its inefficiency in dissolving flavonoid compounds, which often require organic solvents for effective extraction. These results are consistent with the behavior of flavonoids in other plant species, where their solubility and extraction efficiency are strongly dependent on the solvent's polarity, hydrogen-bonding capacity, and ability to penetrate the cell wall [34,35]. Overall, the findings demonstrate that while aqueous-organic solvents enhance total extraction yield, pure organic solvents such as acetone and ethanol are more selective and efficient for isolating flavonoids. This reinforces the importance of solvent optimization based on the specific class of phytochemicals targeted.

Solvents effect on antioxidant activity

The antioxidant capacity of *L. domesticum* leaf extracts was comprehensively evaluated using three complementary assays: Total Antioxidant Activity (TAA), DPPH radical scavenging, and Ferric Reducing Antioxidant Power (FRAP). Across all assays, both extract concentration and solvent type had a pronounced effect on the antioxidant performance of the extracts. TAA results revealed a clear concentration-dependent increase in antioxidant activity for all solvent systems

tested (25–400 µg/mL) (Figure 1). Notably, at 400 µg/mL, extracts obtained using 100% ethanol (98.21 ± 0.47 µg AAE/mL), 100% acetone (93.12 ± 0.47 µg AAE/mL), and 100% methanol (90.82 ± 0.45 µg AAE/mL) exhibited the highest antioxidant performance. These findings highlight the superior ability of pure organic solvents to extract redox-active compounds from plant matrices. The enhanced TAA values in these extracts likely reflect the efficient solubilization of phenolics and flavonoids, known to contribute through both hydrogen atom transfer (HAT) and single electron transfer (SET) mechanisms [36]. In contrast, water demonstrated the lowest antioxidant activity, with a TAA of only 28.56 ± 1.00 µg AAE/mL, indicating its limited ability to extract less polar antioxidant constituents. Although water is widely regarded as a green solvent, its polarity and poor membrane-disrupting capacity may hinder the release of active compounds [37]. Statistical analysis using Tukey's HSD test confirmed significant differences ($p < 0.05$) in TAA among solvent systems. Extracts obtained with 100% ethanol, 100% acetone, and 100% methanol showed significantly higher activity than those extracted with water, 50% methanol, and 50% ethanol, underscoring the influence of solvent polarity, dielectric constant, and hydrogen-bonding capability on extraction efficiency. The TAA trends were strongly aligned with both TPC and TFC data, although some discrepancies, such as the slightly lower TAA in 100% methanol despite its high TPC, suggest that antioxidant activity also depends on compound structure, reactivity, and synergism rather than concentration alone [38].

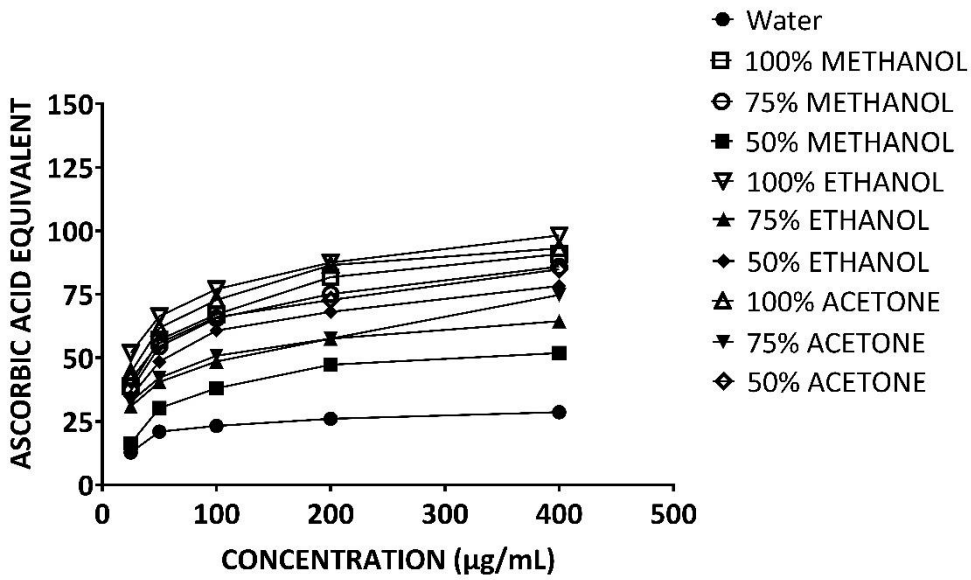

Fig. 1. Total antioxidant activity of *Lansium domesticum* leaf extracts using solvents of varying polarity, expressed as µg AAE/mL across different concentrations (25–400 µg/mL)

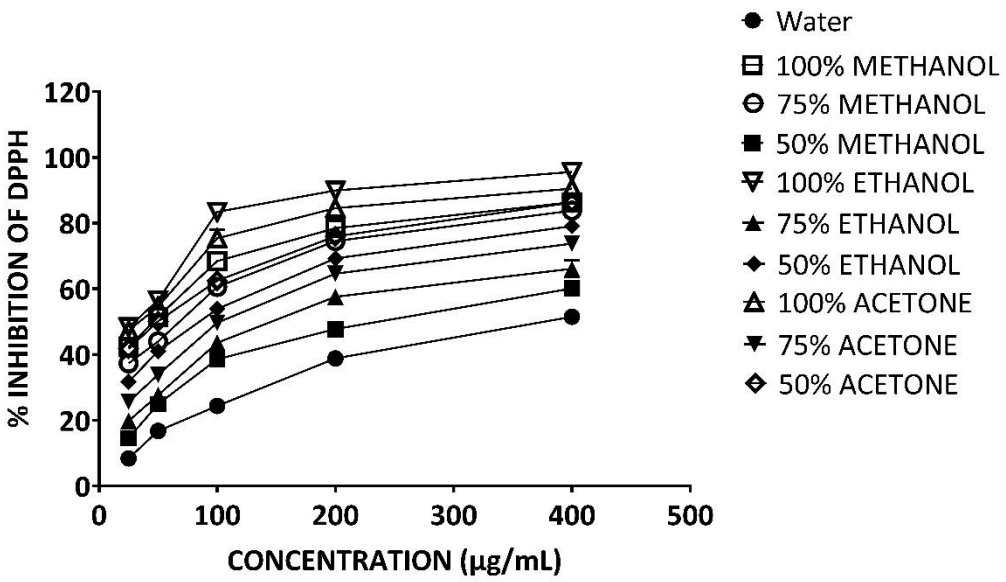

Fig. 2. DPPH radical scavenging activity of Lansium domesticum leaf extracts at various concentrations (25–400 µg/mL)

The DPPH assay supported the TAA findings, showing a similar solvent- and concentration-dependent response (Figure 2). At 400 µg/mL, the highest radical scavenging was recorded in 100% ethanol (95.56 ± 0.99%), followed by 100% acetone (90.46 ± 1.00%), 50% acetone (86.22 ± 1.45%), and 100% methanol (86.34 ± 1.18%). These results confirm the effectiveness of pure or high-content organic solvents in solubilizing compounds capable of neutralizing free radicals via HAT mechanisms [39]. Conversely, water (51.50 ± 1.06%) and 50% methanol (60.09 ± 0.55%) extracts exhibited the weakest activity. The low performance of water may be attributed to its limited capacity to dissolve less polar antioxidant molecules, such as flavonoid aglycones and certain phenolic acids [40]. Although one-way ANOVA could not be applied due to low intra-group variance, Tukey's HSD analysis revealed that 100% ethanol and 100% acetone extracts were significantly more active ($p < 0.05$) than water and most aqueous solvents. These statistical outcomes strengthen the conclusion that solvent polarity is critical in optimizing free radical scavenging capacity. To complement the dose-dependent antioxidant observed in DPPH, IC_{50} values were calculated to quantify the potency of each solvent extract (Table 2). The IC_{50} (half maximal inhibitory concentration) represents the concentration of extract required to achieve 50% inhibition in a given assay. Lower IC_{50} values indicate higher biological activity [41]. Among the tested extracts, 100% methanol showed the strongest DPPH radical scavenging activity, with an IC_{50} of 66.3 µg/mL, followed by 75% aqueous methanol (108.2 µg/mL) and 50% aqueous methanol (95.6 µg/mL). Water extract, on the other hand, exhibited the weakest scavenging activity, with an IC_{50} of 220.0 µg/mL, suggesting limited ability to neutralize free radicals. These results are

consistent with the % DPPH inhibition data, reinforcing that organic solvents are more effective in extracting radical-scavenging compounds.

Table 2. IC_{50} values (µg/mL) of *Lansium domesticum* leaf extracts for antioxidant (DPPH) and in vitro antidiabetic (α-glucosidase and α-amylase inhibition) activities

Extracts	IC_{50} (µg/mL)		
	DPPH Radical Scavenging	**α-glucosidase inhibition**	**α-amylase inhibition**
Water	220.00	706.37	720.45
Methanol			
100% methanol	66.30	70.64	105.13
75% aqueous methanol	108.20	118.19	180.55
50% aqueous methanol	95.60	695.32	680.32
Ethanol			
100% ethanol	42.30	53.32	55.06
75% aqueous ethanol	97.41	604.68	610.34
50% aqueous ethanol	115.40	123.45	254.75
Acetone			
100% acetone	58.33	64.23	65.67
75% acetone	103.40	494.56	480.54
50% acetone	122.90	220.67	273.83

Lower IC_{50} values indicate stronger biological activity. Extracts were prepared using various solvents (water, methanol, ethanol, and acetone) at 50%, 75%, and 100% concentrations. Each value represents the mean of three replicates.

In the FRAP assay, antioxidant potential was reflected in absorbance increases at 593 nm, indicative of ferric-to-ferrous ion reduction (Figure 3). Extracts from 100% ethanol (0.9667 ± 0.01), 100% acetone (0.7667 ± 0.01), and 100% methanol (0.7300 ± 0.01) showed the highest absorbance, consistent with their performance in TAA and DPPH. These solvents are evidently more effective in extracting electron-donating compounds responsible for reducing power via SET mechanisms [42]. In contrast, water (0.1967 ± 0.00) and 50% methanol (0.4033 ± 0.40) showed the lowest absorbance, reflecting limited extraction of redox-active metabolites. Although ANOVA was again inapplicable due to homogeneous values within groups, Tukey HSD analysis confirmed that 100% ethanol and 100% acetone differed significantly ($p < 0.05$) from water and aqueous solvents. The absence of significant differences between 100% ethanol, methanol, and acetone suggests comparable efficiency among these solvents in extracting antioxidant constituents. Overall, FRAP results further support the solvent trends seen in TAA and DPPH, reinforcing that solvent polarity modulates not only extract yield but also antioxidant efficacy. Although no

conversion to μmol Fe^{2+} was performed, absorbance values alone provide a reliable comparative index of reducing capacity.

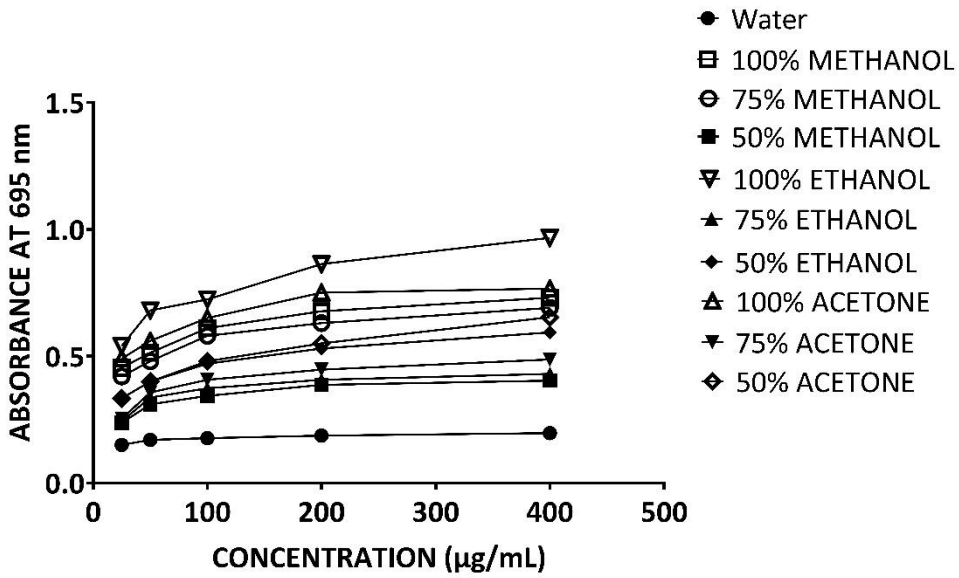

Fig. 3. Ferric reducing antioxidant power (FRAP) of *Lansium domesticum* leaf extracts at various concentrations (25–400 μg/mL)

Solvents' effect on antidiabetic enzyme inhibitor activity

The antidiabetic potential of *L. domesticum* leaf extracts was evaluated through their inhibitory activity against two key carbohydrate-hydrolyzing enzymes, including α-glucosidase and α-amylase. The results demonstrated a clear concentration-dependent inhibition pattern across all solvent systems, with significant differences in efficacy based on solvent polarity and can shown in Figures 4 and 5.

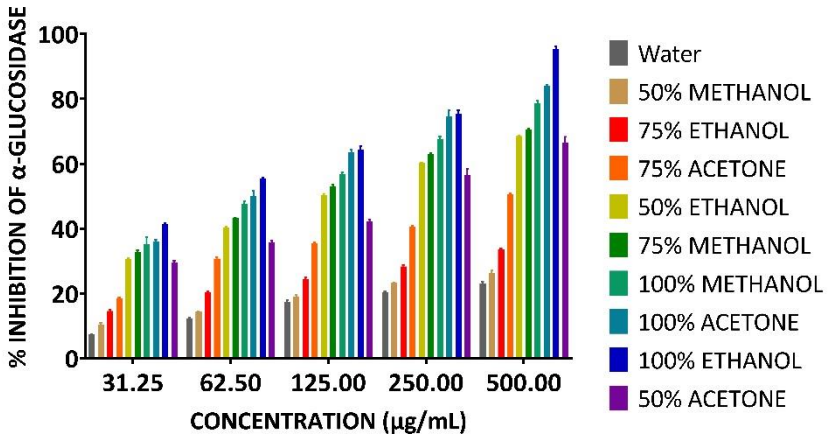

Fig. 4. Inhibitory activity of Lansium domesticum leaf extracts against α-glucosidase enzyme at various concentrations (31.25–500 μg/mL)

Figure 4 demonstrates the effect of extracts at 500 µg/mL, that the most potent α-glucosidase inhibition was observed in the extract obtained with 100% ethanol (95.31 ± 0.88%), followed by 100% acetone (83.97 ± 0.45%), 100% methanol (78.74 ± 0.72%), and 75% methanol (70.55 ± 0.26%). These findings highlight the superior performance of pure organic solvents in extracting bioactive compounds capable of disrupting α-glucosidase activity, an enzyme involved in the final step of carbohydrate digestion [43]. Conversely, the water extract exhibited the weakest inhibitory activity (23.08 ± 0.64%), emphasizing water's limited ability to solubilize non-polar or moderately polar enzyme inhibitors [44]. Moderate inhibition was also observed in aqueous-organic solvent mixtures, particularly 50% ethanol (68.54%) and 50% acetone (66.40%), suggesting that mixed-polarity solvents enhance the co-extraction of both hydrophilic and lipophilic constituents. These trends were further confirmed by IC_{50} values (Table 2), where 100% methanol showed the lowest IC_{50} (70.64 µg/mL), followed by 75% methanol (118.19 µg/mL), while water had the highest IC_{50} (706.37 µg/mL). This inverse relationship between IC_{50} and inhibitory potency reinforces the role of solvent polarity in maximizing the yield of α-glucosidase inhibitors, likely flavonoids and phenolic acids exhibiting competitive or mixed-mode inhibition [45].

A similar pattern was observed in the α-amylase inhibition assay (Figure 5). At 500 µg/mL, the highest inhibition was recorded in 100% ethanol extract (94.07 ± 0.99%), followed by 100% acetone (80.74 ± 0.52%), 100% methanol (73.24 ± 1.20%), and 75% methanol (68.18 ± 0.46%). Once again, the water extract displayed the weakest inhibition (20.71 ± 0.61%). These results corroborate the notion that highly organic solvents are more effective in extracting enzyme-inhibitory compounds [46]. Aqueous-organic solvents showed intermediate activity, particularly 50% ethanol (64.50 ± 0.83%), consistent with their capacity to extract a broader range of phytochemicals. The IC_{50} values for α-amylase inhibition support this trend (Table 2), 100% methanol had the lowest IC_{50} (105.13 µg/mL), while 75% methanol (180.55 µg/mL) and water (720.45 µg/mL) were less effective. These results suggest that similar classes of bioactive compounds may inhibit both α-glucosidase and α-amylase, possibly through shared mechanisms such as substrate binding interference or active site occupancy [47–49].

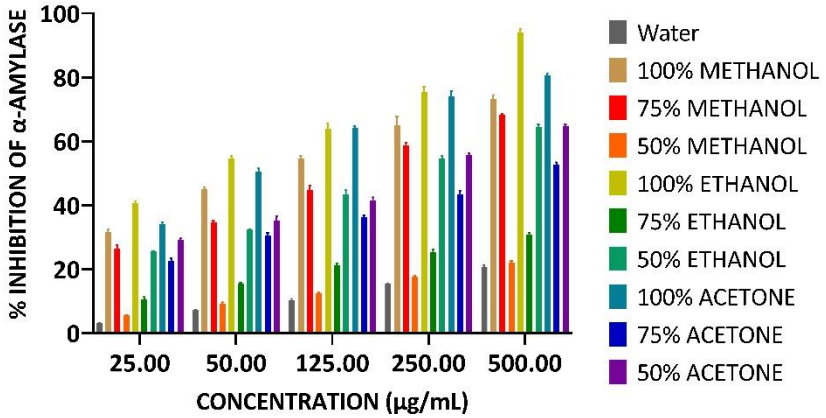

Fig. 5. Inhibitory activity of *Lansium domesticum* leaf extracts against α-amylase enzyme at various concentrations (25–500 µg/mL)

Taken together, the data clearly demonstrate that solvent polarity is a critical determinant in the extraction of antidiabetic compounds. Pure ethanol and methanol consistently yielded extracts with the highest inhibitory activity across both enzyme assays, as well as in antioxidant evaluations (TAA, DPPH, FRAP). These solvents likely promote the extraction of phenolic and flavonoid-rich compounds with multifunctional bioactivity. The dual inhibitory effects observed suggest that *L. domesticum* leaves possess promising therapeutic potential for managing postprandial hyperglycemia. Future research should focus on the isolation, identification, and mechanistic evaluation of the active compounds within these high-performing extracts, with a particular emphasis on ethanol and methanol-based systems for their broad-spectrum bioactivity.

Correlation between phytochemical content with biological activities

To explore the linear associations between phytochemical composition and bioactivities, Pearson correlation analysis was conducted for TPC, TFC, DPPH, FRAP, and IC_{50} values of α-amylase and α-glucosidase. The outcomes are summarized in Table 3. TPC demonstrated a very strong positive correlation with TFC (r = 0.929), suggesting that flavonoids are major contributors to total phenolics. A strong positive correlation was also found between TPC and FRAP (r = 0.796), confirming the role of phenolics in antioxidant reducing power. By contrast, TPC showed strong negative correlations with DPPH IC_{50} (r = -0.710), α-amylase IC_{50} (r = -0.745), and α-glucosidase IC_{50} (r = -0.657). Although these correlations are negative, this reflects a favorable biological relationship: as TPC increases, the IC_{50} values of antioxidant and enzyme inhibitory activities decrease, indicating stronger bioactivityPut differently, extracts with elevated phenolic concentrations tended to show stronger antioxidant and antidiabetic activities. Similarly, TFC was positively linked with FRAP (r = 0.646) and negatively linked with DPPH (r = -0.529), α-amylase (r = -0.617), and α-glucosidase (r = -0.557) IC_{50} values, confirming the functional role of flavonoids in enhancing both antioxidant and enzyme inhibitory activities. Notably, FRAP exhibited a very strong negative correlation with α-amylase (r = -0.940) and α-glucosidase (r = -0.903) IC_{50} values, reinforcing the idea that the antioxidant power of the extract is closely linked to its capacity to inhibit carbohydrate-hydrolyzing enzymes. A near-perfect positive correlation was observed between α-amylase and α-glucosidase IC_{50} values (r = 0.988), suggesting a consistent inhibitory trend across both enzymes. Overall, the negative correlations between phytochemical content and IC_{50} values of antioxidant and antidiabetic activities indicate that the higher the concentration of bioactive compounds, the stronger the biological activity. These outcomes reinforce the notion that phenolic and flavonoid compounds are key contributors to the extracts' antioxidant activity and their effectiveness in enzyme inhibition.

Table 3. Relationships (Pearson correlation coefficients, r) between phytochemical levels (TPC, TFC), antioxidant activities (DPPH, FRAP), and enzyme inhibition (α-amylase, α-glucosidase) in *Lansium domesticum* leaf extracts

Assay	Pearson correlation (r)					
	TPC	**TFC**	**DPPH**	**FRAP**	**α-Amylase inhibition**	**α-Glucosidase inhibition**
TPC		0.929	-0.710	0.796	-0.745	-0.657
TFC	0.929		-0.529	0.646	-0.617	-0.557
DPPH	-0.710	-0.529		-0.808	0.665	0.595
FRAP	0.796	0.646	-0.808		-0.940	-0.903
α-Amylase inhibition	-0.745	-0.617	0.665	-0.940		0.988
α-Glucosidase inhibition	-0.697	-0.557	0.595	-0.903	0.988	

Direct relationships are represented by positive values, and inverse relationships by negative values. Strong negative associations between IC_{50} and TPC/TFC indicate that increased phytochemical content leads to improved biological performance. Significant results ($p < 0.05$) are emphasized in bold type.

CONCLUSION

This investigation revealed that solvent type markedly affects both phytochemical composition and biological activities of *L. domesticum* extracts. Pure organic solvents, especially ethanol and acetone, yielded superior levels of phenolic and flavonoid compounds, which were linked to pronounced antioxidant and antidiabetic enzyme inhibitory effects. The inverse correlations between phytochemical content and IC_{50} values emphasize the therapeutic significance of *L. domesticum* leaves as a natural strategy to combat oxidative stress and regulate postprandial glucose. These outcomes provide valuable scientific support for the potential application of *L. domesticum* in nutraceuticals and phytopharmaceuticals.