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Research article

Jackfruit (*Artocarpus heterophyllus* Lam.) waste extracts as rich source of flavonoids with potential antioxidant and α-glucosidase inhibitory activities

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Abstract

Importance of the work: Agricultural waste from the food industry presents a serious disposal challenge, yet it can serve as a valuable source of bioactive compounds. Jackfruit (*Artocarpus heterophyllus* Lam.) waste, often discarded, has potential to be repurposed into high-value products for food and pharmaceutical applications.

Objectives: To investigate the antioxidant and α-glucosidase inhibitory activities of jackfruit waste extracts and to identify their metabolite composition using liquid chromatography combined with tandem mass spectrometry (LC-MS/MS).

Materials and Methods: Jackfruit waste was extracted using different ethanol concentrations and the extracts were evaluated for total phenolic content (TPC), 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity, nitric oxide radical inhibition and α-glucosidase inhibitory activity. Then, the most active extract was analyzed further using LC-MS/MS coupled with a spectral library search through Global Natural Products Social Molecular Networking for compound identification.

Results: The 50% ethanolic extract had the highest TPC (mean ± SD, 73.76±2.19 mg gallic acid equivalents per gram of extract), with strong bioactivities, including DPPH radical scavenging (concentration of sample required to scavenge 50% of the DPPH free radicals = 85.83±3.14 µg/mL), nitric oxide radical inhibition (37.49±1.83% at 250 µg/mL) and potent α-glucosidase inhibition (half maximal inhibitory concentration = 3.75±0.15 µg/mL). The LC-MS/MS analysis identified 28 compounds, including 12 flavonoids with documented biological activities.

Main finding: Jackfruit waste is a rich source of natural antioxidants and α-glucosidase inhibitors, which collectively highlight their prospective applications in food and pharmaceutical industries and contribute to the sustainable valorization of agro-industrial waste streams.

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Introduction

Food waste is a critical global issue, particularly in tropical regions where fruit production is abundant (Lee et al., 2024). The rapid expansion of fruit processing industries has led to an increased accumulation of byproducts, including peels, seeds and pomace, which contribute greatly to municipal solid waste (MSW; Cheok et al., 2016). In Malaysia, a major tropical fruit producer, the food industry plays a crucial role in both local consumption and export, with a large portion of its production comprising processed fruit products such as juices, jams, dried fruits and concentrates (Dardak, 2019). However, the large-scale processing of fruits generates substantial amounts of waste, which, if not efficiently managed, poses serious environmental and economic concerns (Govindaraj et al., 2018). In urban centers such as Kuala Lumpur, fruit processing residues, including mango peels, watermelon rinds and rambutan skins, constitute a considerable fraction of MSW, leading to waste management challenges and environmental degradation (Ibrahim et al., 2017).

Among the many tropical fruits cultivated in Malaysia, jackfruit (*Artocarpus heterophyllus* Lam.) is consumed widely, as well as being processed into various food products, with jackfruit being regarded as one of the most important tropical fruit crops being cultivated predominantly in countries such as India, Bangladesh and Indonesia (Lin et al., 2022). Typically, this fruit is consumed fresh or processed into products such as jackfruit juice, canned jackfruit and jackfruit-based desserts (Ramli et al., 2016). However, because of its popularity, jackfruit processing generates a very large quantity of waste, primarily in the form of rinds and seeds, which are either discarded or repurposed as animal feed (Govindaraj et al., 2018). In fact, only 30–35% of the entire fruit weight consists of edible flesh, with the remaining 63–72% (including the peel and seeds) being considered waste (Saxena et al., 2011). This disproportionate waste-to-edible ratio highlights the pressing need to develop sustainable utilization strategies for jackfruit byproducts.

Studies have demonstrated that fruit and vegetable byproducts are rich sources of bioactive compounds, particularly phenolic compounds and flavonoids, which have strong antioxidant properties (Sagar et al., 2018; Trigo et al., 2019). Phenolic compounds, which serve as secondary metabolites in plants, play a crucial role in plant defense mechanisms and contribute to the nutritional quality of fruits and vegetables (Kumar et al., 2023). The presence of these bioactive constituents in fruit waste suggests potential applications in nutraceuticals, functional foods and pharmaceutical formulations (Deng et al., 2012; Sagar et al., 2018). Given the high proportion of discarded jackfruit biomass, its phenolic-rich composition presents a presently untapped opportunity for developing value-added products that promote health benefits while reducing food waste.

One of the most compelling health applications of phenolic-rich fruit byproducts is their antioxidant potential, which has been linked to the prevention of various oxidative stress-related disorders, including cardiovascular diseases, neurodegenerative diseases and diabetes (Jideani et al., 2021). Oxidative stress arises from an imbalance between the production of reactive oxygen species (ROS) and the body's ability to neutralize them through antioxidant defense systems (Pizzino et al., 2017). While ROS are inevitable byproducts of oxygen metabolism, their excessive accumulation leads to cellular damage, inflammation and metabolic dysfunction (Di Meo et al., 2016). Notably, oxidative stress plays a substantial role in the progression of diabetes and its complications (Asmat et al., 2015; Caturano et al., 2023). Elevated ROS levels have been shown to impair insulin signaling, promote β-cell dysfunction and induce lipid peroxidation, ultimately contributing to the onset and progression of type 2 diabetes mellitus (Singh et al., 2022). Natural antioxidants, particularly phenolic compounds, have been recognized for their ability to scavenge free radicals, inhibit lipid peroxidation and enhance endogenous antioxidant enzyme activity, thereby mitigating oxidative damage (Bajaj and Khan, 2012). Given this, the exploration of phenolic-rich fruit byproducts (such as jackfruit waste) holds great potential for the development of natural antioxidant sources that could aid in the prevention of oxidative stress-related metabolic disorders.

Despite growing interest in food byproduct valorization, there has been limited research on the bioactive potential of jackfruit waste. While some studies have reported the presence of phenolic compounds in jackfruit peel and seeds (Alibekov et al., 2023; Zhang et al., 2017), there remains a lack of comprehensive identification of their bioactive potential, particularly in relation to antioxidant and anti-diabetic activities. Furthermore, no systematic evaluation has been conducted of the impact of extraction parameters, such as ethanol content, on the bioactivity and recovery of phenolic compounds. Addressing these knowledge gaps is essential for the establishment of jackfruit waste as a viable source of health-promoting bioactive compounds and the advancement of sustainable food waste management strategies.

Therefore, the current study aimed to evaluate the antioxidant and anti-diabetic potential of jackfruit waste extracts under different ethanol extractions and to profile the metabolites of the most bioactive extract using liquid chromatography combined with tandem mass spectrometry (LC-MS/MS) analysis. By elucidating the functional properties of the metabolites derived from jackfruit waste, this study aims to establish a scientific basis for the valorization of fruit byproducts as sources of health-promoting bioactive compounds. These findings should contribute to sustainable food waste management while supporting the potential development of jackfruit waste-derived antioxidants and anti-diabetics for applications in functional foods and nutraceuticals applications.

Materials and Methods

Chemicals and reagents

Dimethyl sulfoxide (DMSO), gallic acid, ethanol were supplied by Systerm (Shah Alam, Malaysia), 2,2-diphenyl-1-picrylhydrazyl (DPPH) reagent, N-(1-naphthyl) ethylenediamine dihydrochloride (Griess reagent), quercetin, 10 mM phosphate buffer saline (PBS), 4-nitrophenyl-α-D-glucopyranoside (PNPG), phosphoric acid, sodium phosphate monobasic, sodium phosphate dibasic dihydrate were supplied by Sigma-Aldrich (St. Louis, MA, USA), 10 mM sodium nitroprusside (SNP) was supplied by Bendosen (Shah Alam, Malaysia), sulfanilamide was supplied by BDH (Poole, UK), glycine was supplied by R&M Chemicals (Semenyih, Malaysia), α-glucosidase (maltase) was supplied by Megazyme (Bray, Ireland), Folin-Ciocalteu reagent was supplied by Merck (Darmstadt, Germany), sodium carbonate was supplied by Nacalai Tesque (Kyoto, Japan). Deionized water was purified using a MiliQ system (supplied by Milipore; Bedford, MA, USA).

Sample preparation and extraction

Jackfruit waste (5.5 kg) was collected from a stall selling jackfruit at the Serdang night market, Malaysia. The jackfruit waste was cut into smaller pieces and then oven-dried at 40°C for 72 hr, until a constant weight was achieved. Then, the dried sample was ground into powder form. Subsequently, the dried ground powder was divided into three samples, each subjected to a different type of solvent extraction. Each weighed ground sample (10 g) was mixed with 100 mL of distilled water, 50% aqueous ethanol (volume per volume, v/v), or absolute ethanol and then subjected to ultrasound-assisted extraction at a controlled temperature (<40°C) using a Thermo-10D Ultrasonic Cleaner (Fisher Scientific; Waltham, MA, USA) at 35 kHz for 1 hr. The extract was passed through Whatman No. 1 filter paper before being concentrated in a rotary evaporator under controlled temperature (40°C) to yield the concentrated crude extract. Each extraction was repeated twice for the remaining residues by adding the same volume of solvents. The extracted samples were dried in a freeze dryer (LabConco; Kansas City, MO, USA) and kept for further analysis. All the extractions were done in triplicate for each type of extraction solvent used.

Determination of total phenolic content

The total phenolic content (TPC) of the jackfruit waste extract was examined using the Folin-Ciocalteu method in a 96-well microplate, following the procedure reported by Lee et al. (2014), with some modifications. Each sample extract (1 mg) was dissolved in 1 mL of DMSO. Then, 20 µL of each sample and 100 µL of Folin-Ciocalteu reagent were added to each well and allowed to stand for 5 min. Next, 80 µL of 7.5% sodium carbonate were added to each well and the plate was incubated for 30 min in the dark. The absorbance was measured at 750 nm using a microplate reader (Tecan Group Ltd.; Männedorf, Switzerland). The analysis was performed in triplicate. The same procedure was used for gallic acid as a standard. A standard curve was created using gallic acid and the results were expressed in milligrams of gallic acid equivalents (GAE) per gram of extract.

Determination of 2,2-diphenyl-1-picrylhydrazyl free radical scavenging activity

The antioxidant potential of jackfruit waste extracts was determined using the DPPH free radical scavenging assay, as described by Lee et al. (2014). The assay was performed in triplicate (n = 3) using a 96-well microplate, with each well containing 50 µL of jackfruit extract prepared in two-fold serial dilutions in the range 1,000–15.63 µg/mL. Then, 100 µL of the DPPH solution was added to each well and incubated for 30 min in the dark. The absorbance was measured at 515 nm against a reagent blank using the microplate reader. The same procedure was applied to quercetin, which served as positive control and was prepared within the same concentration range.

This approach ensured comparability between the test compounds and the positive control, which facilitated a robust evaluation of their effects. The scavenging capacity (SC) was calculated using Equation 1:

$$SC\% = [(Ao - As)/Ao] \times 100 \quad (1)$$

where Ao is the absorbance of the reagent blank and As is the absorbance of the test samples.

The results were expressed as the concentration of sample required to scavenge 50% of the DPPH free radicals (SC_{50}).

Determination of nitric oxide scavenging activity

The nitric oxide (NO) scavenging activity of jackfruit waste was conducted following the method described by Kim et al. (2022), with modifications. Two-fold serial dilutions of the sample extracts in the range 1,000–15.63 µg/mL were prepared and 60 µL of each concentration was transferred into a 96-well microplate. Subsequently, 60 µL of 10 mM SNP in PBS were added to each well containing the sample extracts. The reaction mixture was incubated at 25°C for 150 min. Following incubation, 60 µL of Griess reagent (a mixture of 0.1 g sulfanilamide and 0.01 g naphthylethylenediamine dichloride in 10 mL of 2.5% phosphoric acid) was introduced to facilitate the diazotization of nitrite with sulfanilamide, followed by coupling with naphthylethylenediamine dichloride, leading to the formation of chromophores. The absorbance of the resulting chromophores was measured at 550 nm using the microplate reader. All measurements were performed in triplicate (n = 3) and the mean values were calculated. Quercetin was used as a positive control and subjected to the same treatment with Griess reagent. The percentage inhibition of NO generated was calculated using Equation 2:

$$\text{Percentage inhibition of NO} = [(A_{control} - A_{test})/A_{control}] \times 100 \quad (2)$$

where $A_{control}$ is the absorbance of the control reaction and A_{test} is the absorbance in the presence of the extract sample.

Determination of in vitro α-glucosidase inhibition activity

The α-glucosidase inhibition activity was performed, as described by Lee et al. (2014). A sample (3 mmol/L) of PNPG and 1 U of α-glucosidase (*Saccharomyces cerevisiae*; Sigma-Aldrich; MAn, USA) were dissolved in 50 mM phosphate buffer (pH 6.5) to simulate the conditions of intestinal fluid. The jackfruit waste extracts were prepared in two-fold serial dilutions in the ranges 1,000–15.625 µg/mL for the absolute ethanol extract and 125–1.953 µg/mL for the 50% and aqueous extracts. Each extract was mixed in a 96-well microplate with the addition of 30 mM phosphate buffer and 5% DMSO. Then, 10 µL of the enzyme α-glucosidase were added to each sample well and the negative and positive controls, followed by incubation at 37°C for 5 min. Next, 50 µL of PNPG were added to each sample well and to the negative control and the positive control (quercetin), while the remaining wells were filled with 50 µL of 30 mM phosphate buffer. The wells were incubated at 37°C for 15 min. All well reactions were halted using a stopping agent (50 µL of 2 M glycine at pH 10). The absorbance readings were measured using the microplate reader at a wavelength of 405 nm. The α-glucosidase inhibition activity of the test sample was expressed as a percentage of inhibition using Equation 3:

$$\text{Percentage inhibition of sample} = [(An - As)/An] \times 100\% \quad (3)$$

where An is the difference in absorbance of the negative control and all the blanks, while As is the difference in absorbance of the sample and all the blanks.

Data acquisition using liquid chromatography combined with tandem mass spectrometry

The LC-MS procedure was conducted according to Sajak et al. (2017). A 5 µL aliquot of a 5 mg/mL solution of jackfruit waste extract was injected into a Waters C18 reversed-phase ACQUITY UPLC HSS T3 column (Waters Corp.; Dublin, Ireland), which had a length of 150 mm, an internal diameter of 2.1 mm and a particle size of 1.8 µm. The chromatographic separation was performed at a flow rate of 0.3 mL/min at a column temperature of 40°C, utilizing a gradient elution with water (solvent A) and acetonitrile (solvent B), both containing 0.1% formic acid. The gradient profile was: 15–35% B from 0.00 to 15.00 min, 35–60% B from 15.00 to 30.00 min, 60–80% B from 30.00 to 40.00 min and 80–15% B from 40.00 to 45.00 min. To ensure system stability, LC-MS-grade methanol was injected as a solvent blank at the beginning of the run sequence and after each extract injection. Data acquisition was conducted using liquid chromatography-tandem mass spectrometry in both positive and negative electrospray ionization (ESI) modes. The ion source parameters were optimized using spray voltages of 4.0 kV and 3.0 kV for the positive and negative modes, respectively, a sheath gas flow rate of 70.0 units,

an auxiliary gas flow rate of 30.0 units and a capillary temperature of 350.0°C. The mass spectrometer operated in Full MS/dd-MS² Discovery mode with a resolution of 70,000, a scan range of 150–1500 *m/z*, an automatic gain control (AGC) target of 3.0×10^6 and a maximum injection time of 200 ms. Data-dependent MS/MS events were defined with a resolution of 17,500, an isolation window of 1.5 *m/z*, stepped normalized collision energy of 15, 30 and 45, a default charge state of 1, AGC target of 1.0×10^5, a minimum AGC target of 5.0×10^3, a maximum injection time of 60 ms, a loop scan of 3 scans, an intensity threshold of 8.3×10^4 and dynamic exclusion of 3.0 s. Profile MS and MS/MS spectra were obtained for all extracts and blanks. Finally, the chromatogram and spectra were visualized using the Qual Browser Thermo Xcalibur 2.2 SP1 software (Thermo Fisher Scientific; MA, USA) and the MZmine 4.5.0 package (Heuckeroth et al., 2024).

Mass spectrometry data processing and spectral library search on Global Natural Products Social Molecular Networking

The primary objective of MS data processing is to transform raw spectral data into a list of detected ions, estimate their abundance and assign chemical annotations based on multiple criteria (Heuckeroth et al., 2024). In the current study, data processing was conducted using methods proposed by Schmid et al. (2023) with the MZmine version 4.5.0 package. Detailed raw data processing parameters are provided in Supplementary Fig. S1–Fig. S6. Notably, these parameters are dataset-specific and require an understanding of the raw spectral data, as they are heavily influenced by the instrument setup, including chromatographic conditions and mass analyzer performance. However, the raw data processing steps outlined in the current study could serve as a basic guide for processing other datasets.

Fig. 1 illustrates the general workflow for processing and annotating raw LC-MS data, which is divided into three primary stages. Initially, the raw spectral data are imported into MZmine, where they undergo centroiding and mass detection with predefined intensity thresholds to eliminate low-intensity noise. The second stage involves feature detection, also known as peak picking, which identifies *m/z* signals corresponding to metabolites based on their retention time in LC-MS. This step also aligns features across samples to facilitate statistical comparisons. Finally, feature annotation assigns chemical identities by comparing isotope patterns and MS² spectra using tools such as SIRIUS (Dührkop et al., 2019), as well as spectral library searches on the GNPS platform to enhance metabolite identification. The results from the spectral library search can be visualized using the Cytoscape software (Shannon et al., 2003).

In the current study, the processed spectra were subjected to a library search using the GNPS platform, adhering to the feature-based molecular networking workflow (Horai et al., 2010; Wang et al., 2016). The library spectra were filtered by excluding MS/MS fragment ions within ±17 Da of the precursor ion's *m/z* value. Additionally, MS/MS spectra were window-filtered to include only the top-six fragment ions within a ±50 Da window across the spectrum. The mass tolerance for both the precursor and MS/MS fragment ions was set at 0.05 Da. Library spectra were required to have a score above 0.7 and at least three matched peaks to ensure reliable matches. The DEREPLICATOR tool was used for annotating MS/MS spectra (Mohimani et al., 2018). Finally, the results were visualized using the Cytoscape software version 3.10.2 (Shannon et al., 2003).

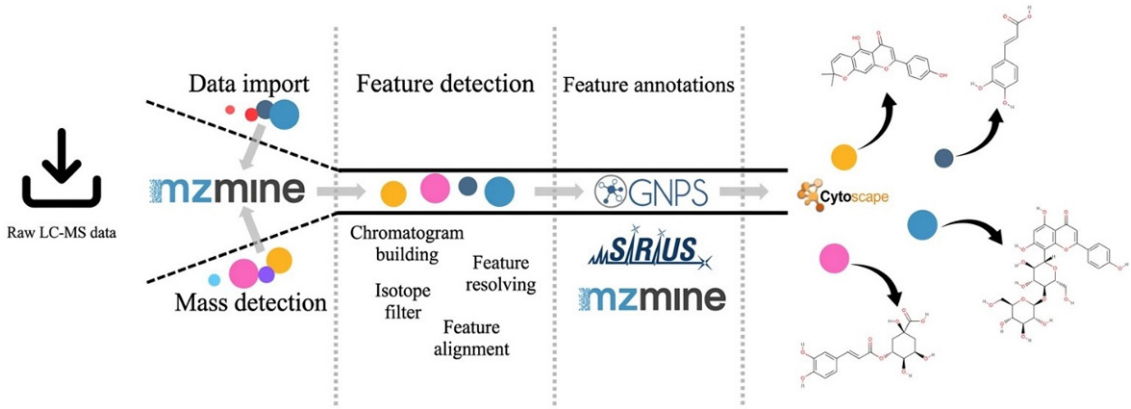

Fig. 1 Basic workflow for feature detection and annotation of raw liquid chromatography combined with tandem mass spectrometry (LC-MS/MS) data using Mzmine

Data analysis

The Minitab software version 14 (Minitab Inc.; State College, PA, USA) was used for the statistical analysis of the TPC, DPPH radical scavenging activity, NO radical scavenging activity and α-glucosidase inhibitory activity data. Results were expressed as mean ± SD values for three replicates. One-way analysis of variance followed by Tukey-honestly significant difference multiple comparison was applied to determine the significance of differences between the different samples at a confidence level of 95%. Pearson's correlation coefficient (r) analysis was performed to examine the relationships between the TPC and biological activities of the extracts. For antioxidant and enzyme inhibition assays, IC_{50} values were transformed to $1/IC_{50}$ to ensure that higher values reflected greater biological activity. Correlation analysis was conducted using mean values for each extract. Due to the limited number of experimental conditions, correlation results were interpreted descriptively as indicative of trends or associations.

Results and Discussion

Yield of extraction of jackfruit waste

The extraction of 10 g of dried jackfruit waste using ethanol-water mixtures (v/v) at ratios of 0%, 50% and 100% yielded 25.31±1.97%, 23.07±1.98% and 7.97±0.47% of crude extract, respectively. The highest extraction yield was obtained with aqueous solvent, which was not significantly different from the yield achieved with 50% ethanol but was significantly (n = 3) higher than that observed with absolute ethanol. These variations in extraction efficiency could be attributed to differences in solvent polarity, which directly influences the solubility of bioactive compounds. Water, as a highly polar solvent, achieved the greatest extraction yield, likely due to its ability to dissolve a broad range of polar secondary metabolites, proteins and carbohydrates (Plaskova and Mlcek, 2023; Ji et al., 2024). This finding aligned with other published studies on fruits within the Moraceae family, such as *Artocarpus chaplasha* Roxb. and *Carissa carandas* L., which also reported enhanced extraction efficiency with solvents of higher polarity (Dhar et al., 2017). In contrast, the significantly lower yield observed with absolute ethanol suggests that high ethanol concentrations may disrupt cellular structures, thereby reducing the solubility of certain bioactive compounds (Zhang et al., 2007). Furthermore, ethanol concentrations exceeding 75% have been shown to decrease extraction efficiency due to their limited capacity to extract polar compounds (Khan et al., 2018).

The extraction yield obtained with 50% ethanol was significantly higher than that with absolute ethanol. This result was consistent with other findings indicating that aqueous ethanol solvents at concentrations of 50–60% were particularly effective for recovering polyphenolic compounds from plant matrices (Jiménez-Moreno et al., 2019; Klongdee and Klinkesorn, 2022; Nga et al., 2024). The superior performance of 50% ethanol could be attributed to its intermediate polarity, which facilitates the extraction of both polar and nonpolar compounds, thereby improving the overall yield (Do et al., 2013). Given that polyphenolic compounds are key contributors to antioxidant activity, optimizing their extraction is critical for assessing the antioxidant properties of edible plants. As such, aqueous ethanol at a concentration of 50% represents a more effective solvent for polyphenol extraction compared to absolute ethanol. In conclusion, based on these results, solvent polarity played a critical role in determining extraction efficiency. Among the tested solvents, the aqueous one produced the highest yield, followed by 50% ethanol, while absolute ethanol (100%) resulted in the lowest yield. These findings highlight the importance of selecting an appropriate solvent system for maximizing the recovery of bioactive compounds from plant-based materials.

Total phenolic content of jackfruit waste extract

The TPC in the 50% ethanolic extract of jackfruit waste was significantly higher (73.76±2.19 mg GAE/ g of extract) than the extracts prepared with aqueous (35.41±1.20 mg GAE/g of extract) and absolute ethanol (45.69±1.73 mg GAE/g of extract), as shown in Table 1. This variation in the TPC could be attributed to differences in the solubility of phenolic compounds in various ethanol-water mixtures. Ethanol concentrations between 40% and 50% have been reported to enhance polyphenol extraction efficiency by improving the solubility of phenolic compounds, flavonoids, polysaccharides and hydrolyzable tannins (Jayaprakasha et al., 2008; Prasad et al., 2008). The presence of water in the 50% ethanol mixture facilitated greater solvent penetration into plant cells, thereby promoting the release of phenolic compounds from the jackfruit waste matrix (Prasad et al., 2008). The TPC values obtained in the current study differed from those reported by Sharma et al. (2013) for jackfruit shell powder (1.58±0.00 mg GAE/g of extract),

Table 1 Yield, total phenolic content (TPC), 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity, nitric oxide (NO) radical scavenging activity and α-glucosidase inhibitory activity for different extraction solvent samples

Sample	Percentage yield (%)	TPC (mg GAE/g extract)	DPPH radical scavenging (SC_{50}) (μg/mL)	NO radical scavenging (%) (250 μg/mL)	α-Glucosidase inhibitory (IC_{50}) (μg/mL)
Absolute ethanol	7.97±0.47[b]	45.69±1.73[b]	122.49±5.19[b]	33.67±1.29[b]	5.26±0.16[b]
50% ethanol (v/v)	23.07±1.98[a]	73.76±2.19[a]	85.83±3.14[c]	37.49±1.83[a]	3.75±0.15[b]
Aqueous	25.31±1.97[a]	35.41±1.20[c]	165.53±3.97[a]	23.18±0.51[c]	1131.01±53.52[a]
Quercetin	-	-	9.53±0.09	8.44±0.37	6.15±0.18

GAE = gallic acid equivalents; SC_{50} = 50% scavenging capacity; v/v = volume per volume.
Result shown as mean ± SD of three replicates. [a, b] = different superscript letters within same column indicate significant differences ($p < 0.05$).

which may have been due to differences in extraction methods, analytical techniques and the complexity of phenolic compounds (Kalt et al., 2001). Additionally, variations in intrinsic factors, such as species, genus and cultivar, as well as extrinsic factors, including agronomic practices, environmental conditions, handling and storage, can influence the phenolic content in plant materials (Tomás-Barberán and Espin, 2001; Jagtap et al., 2010). Since phenolic compounds largely drive antioxidant activity, the extracts' free radical scavenging ability was subsequently evaluated using the DPPH assay.

2,2-Diphenyl-1-picrylhydrazyl free radical scavenging activity of jackfruit waste extract

The DPPH radical scavenging activity of the jackfruit waste extracts varied depending on the ethanol ratio, as reflected by their IC_{50} values. The 50% ethanolic extract exhibited the lowest IC_{50} value (85.83±3.14 μg/mL), indicating significantly greater antioxidant activity than the aqueous extract (165.53±3.97 μg/mL) and the absolute ethanol extract (122.49±5.19 μg/mL) (Table 1). The superior antioxidant capacity of the 50% ethanolic extract could be attributed to the higher solubility of polyphenolic compounds in solvents containing 40–80% ethanol, as reported by Jiménez-Moreno et al. (2019). Similarly, Thavamoney et al. (2018) highlighted that intermediate-polarity solvents, such as 50% ethanol, were more efficient at extracting phenolic compounds from plant materials. Since phenolic compounds contribute significantly to antioxidant activity, their higher concentration in the 50% ethanolic extract likely enhanced DPPH radical scavenging efficiency.

Although other studies have reported that solvents that are more polar generally yield extracts with higher antioxidant activity (Kothari and Seshadri, 2010), the findings of the current study suggested that ethanol was a more effective solvent for extracting phenolic compounds from jackfruit waste. However, while absolute ethanol extracted a higher concentration of phenolic compounds than water, the results indicated that 50% ethanol was the most efficient tested solvent for maximizing the DPPH radical scavenging activity. This observation aligned with other reported findings that intermediate-polarity solvents enhanced the extraction of phenolic compounds with varying solubility profiles (Muhamad et al., 2014; Thavamoney et al., 2018). The lower antioxidant activity observed in the absolute ethanol extract than in the 50% ethanol extract could be attributed to the reduced solubility of certain hydrophilic antioxidants in absolute ethanol.

A comparison with the published literature revealed variations in DPPH radical scavenging efficiency. For example, Shrikanta et al. (2013) reported an SC_{50} value of 430 ± 0.00 μg/mL for jackfruit peel extracted using 80% ethanol, which differed from the values obtained in the current study. The variation in SC_{50} values could be attributed to differences in ethanol ratios, extraction methodologies and sample processing techniques. Notably, Shrikanta et al. (2013) used a shaking water bath, whereas the current study utilized ultrasonic extraction. Ultrasonic cavitation enhances the recovery of bioactive compounds by generating microbubbles that facilitate solvent penetration, thereby improving compound solubility and extraction efficiency (Quiroz et al., 2019). This may explain the enhanced antioxidant activity observed in the jackfruit waste extracts in the current study. Overall, these findings highlight the influence of solvent composition on the extraction efficiency of phenolic compounds and their associated antioxidant activity. Based on the results, 50% ethanol provided an optimal balance for maximizing the DPPH radical scavenging capacity of the jackfruit waste extracts. This knowledge could inform future extraction strategies aimed at enhancing the recovery of bioactive compounds from plant materials. Since antioxidants have diverse mechanisms of action, the current study further investigated using the NO free radical scavenging assay to assess the extracts' ability to neutralize reactive nitrogen species. Given the variations observed in DPPH activity, it was important to determine whether a similar trend occurred in NO radical scavenging efficacy.

Nitrogen oxide free radicals scavenging activity of jackfruit waste extract

The NO scavenging activity of jackfruit waste extracts varied significantly depending on the ethanol ratio, as indicated by their percentage inhibition values at 250 µg/mL (Table 1). The 50% ethanolic extract had the highest NO scavenging activity (37.49±1.83%), followed by the absolute ethanol extract (33.67±1.29%), while the aqueous extract had the lowest activity (23.18±0.51%). These findings indicated that the solvent system influenced the extract's ability to neutralize reactive nitrogen species (RNS), similar to its impact on DPPH radical scavenging. Although NO scavenging followed a similar trend to DPPH activity, the underlying mechanism differed. The DPPH assay primarily evaluates an extract's ability to neutralize free radicals through hydrogen atom transfer (HAT) and single electron transfer mechanisms (Rana et al., 2024; Theofanous et al., 2024), whereas the NO scavenging assay assesses its capacity to interact with RNS, which may involve electron transfer (ET; Apak et al., 2016; Apak et al., 2021) and, in some cases, metal ion chelation mechanisms (Gulcin and Alwasel, 2022).

Notably, the relative difference in NO scavenging between the extracts was less pronounced than the DPPH activity. While the 50% ethanolic extract exhibited had twice the DPPH scavenging efficiency of the 0% extract, the difference in NO scavenging activity was comparatively smaller, suggesting that in addition to phenolic compounds, other compounds, such as organic acids and nitrogen-containing metabolites, might have contributed to NO scavenging, as reported by Eshwarappa et al. (2015) in their plant study. Additionally, that study reported that an aqueous extract of *Ficus glomerata* Roxb. (172.37±0.2 µg/mL) had an IC_{50} for NO scavenging that was significantly lower than that observed for jackfruit waste extracts in the current study, which required concentrations exceeding 250 µg/mL to inhibit 50% of the NO radicals. Since both species belong to the Moraceae family, differences in secondary metabolite composition may explain this discrepancy. The presence of tannins, flavonoids and other antioxidant compounds unique to *F. glomerata* may enhance NO scavenging efficiency. Furthermore, potential antagonistic interactions among bioactive compounds in the jackfruit waste could have reduced the overall scavenging efficiency, despite the presence of high amounts of phenolic compounds (Fernandes et al., 2017). Differences in extraction methodologies and solvent compositions across studies may also contribute to the observed variations (Kalt, 2005).

These findings suggested that NO scavenging activity in the jackfruit waste extracts followed a solvent-dependent trend, similar to that of DPPH radical scavenging, likely due to the influence of phenolic compounds. However, since NO radical neutralization involves mechanisms beyond HAT (such as electron donation and metal ion chelation), additional compounds may have contributed to this activity. The ability of 50% ethanol to optimize NO scavenging efficiency highlights its potential as an effective extraction solvent for bioactive compounds with activity against RNS. Since oxidative stress is a major contributor to metabolic disorders, including diabetes (Caturano et al., 2023), antioxidants that can neutralize RNS may also play a role in modulating glucose metabolism. To further assess the current study evaluated the potential health benefits of jackfruit waste extracts based on their ability to inhibit α-glucosidase. Natural inhibitors of α-glucosidase not only reduce postprandial glucose levels but may also mitigate oxidative stress, offering potential therapeutic applications (Zhong et al., 2025). Therefore, the inhibitory activity of jackfruit waste extracts against α-glucosidase was assessed to determine their potential as functional food ingredients or natural therapeutic agents.

In vitro α-glucosidase inhibitory activity

The ethanol concentration of the ethanolic extracts of jackfruit waste had a significant influence on the α-glucosidase inhibitory potential (Table 1). Specifically, the IC_{50} values indicated that extracts prepared using 50% ethanol (3.75±0.15 µg/mL) and absolute ethanol (5.26±0.16 µg/mL) produced substantially higher enzyme inhibition efficacy than the aqueous extract (1,131.01±53.52 µg/mL). These findings highlight the essential influence of solvent polarity on the extraction of phytochemicals exhibiting significant inhibitory effects against α-glucosidase. The enhanced inhibition observed in the 50% ethanol extract could be attributed to its optimal extraction efficiency for flavonoids and other phenolic compounds, which have been reported widely as effective natural α-glucosidase inhibitors through competitive binding at the enzyme's active sites (He et al., 2019). The strong α-glucosidase inhibitory activity of the jackfruit waste extracts, particularly at moderate ethanol concentrations, suggests their promising potential for managing hyperglycemia by reducing postprandial glucose absorption. These findings were consistent with Kashtoh and Baek (2022), where plant extracts rich in flavonoids and tannins had reported robust α-glucosidase inhibitory effects. Furthermore, the considerably lower inhibitory potency of the aqueous extract in the current study aligned with observations by Thavamoney et al. (2018) that non-polar or intermediate-polar solvents typically enhanced the extraction of

specific phenolics that are crucial for α-glucosidase inhibition. Subsequently, Pearson's correlation analysis was performed to investigate the relationship between phenolic content and the observed biological activities.

Pearson's correlation analysis between total phenolic compound contents and biological activities

Pearson's correlation analysis was used to explore the associations between the TPC and the biological activities of the jackfruit waste extracts (Table 2). Strong positive associations were observed between the TPC and antioxidant assays, particularly DPPH radical scavenging activity (r = 0.92) and NO radical scavenging activity (r = 0.85), suggesting that phenolic compounds played a major role in mediating the antioxidant properties of the extracts. These observations were consistent with other studies that reported close relationships between the TPC and antioxidant capacity, where phenolic compounds, such as flavonoids and phenolic acids, acted as key contributors (Osman et al., 2020; Muflihah et al., 2021). In addition, there was a moderately strong association between the TPC and α-glucosidase inhibitory activity (r = 0.79), indicating that phenolic constituents may have contributed to enzyme inhibition, although other bioactive compounds, such as specific flavonoids or tannins, also may have played distinct inhibitory roles. Given the limited number of experimental conditions used for the current correlation analysis, these relationships should be interpreted as associative trends rather than statistically definitive correlations. Overall, based on these results, the biological activity profile of the jackfruit waste extracts was multifactorial, involving both phenolic and potentially non-phenolic metabolites. Subsequently, LC-MS/MS analysis was performed for comprehensive metabolite profiling to further elucidate the compounds responsible for these associations.

Metabolite profiling of 50% ethanolic extract of jackfruit waste via spectral library search in Global Natural Products Social Molecular Networking and their potential biological activities

The LC-MS/MS analysis of the jackfruit waste extracts (Fig. 2) revealed a diverse array of 28 bioactive metabolites, primarily comprising flavonoids, phenolic acids, phenylpropanoids, xanthones, coumarins, octadecanoids and secondary alcohol (Table 3). Among these, flavonoids were the most abundant class, highlighting their potential as key contributors to the biological activities observed in the current study. The presence of multiple flavonoid glycosides suggested that glycosylation enhanced the solubility and stability of these compounds, potentially influencing their bioactivity (Tang et al., 2024). Unlike other studies that focused on the phytochemical composition of jackfruit pulp and seeds (Chandran, 2017; Ojwang et al., 2018), the current study has provided the first comprehensive metabolite profile of jackfruit waste using an automated spectral library search in GNPS via feature-based molecular network workflow. These findings highlight jackfruit waste as a valuable, yet underutilized, source of bioactive compounds with considerable potential for future applications.

Table 2 Pearson's correlation between TPC, DPPH radical scavenging activity, NO radical scavenging activity and α-glucosidase inhibitory activity

Correlation between	Pearsons' correlation coefficient
TPC and DPPH radical scavenging activity	0.92
TPC and NO radical scavenging activity	0.85
TPC and α-glucosidase inhibitory activity	0.79

TPC = total phenolic content; DPPH: = 2,2-diphenyl-1-picrylhydrazyl; NO = nitric oxide.

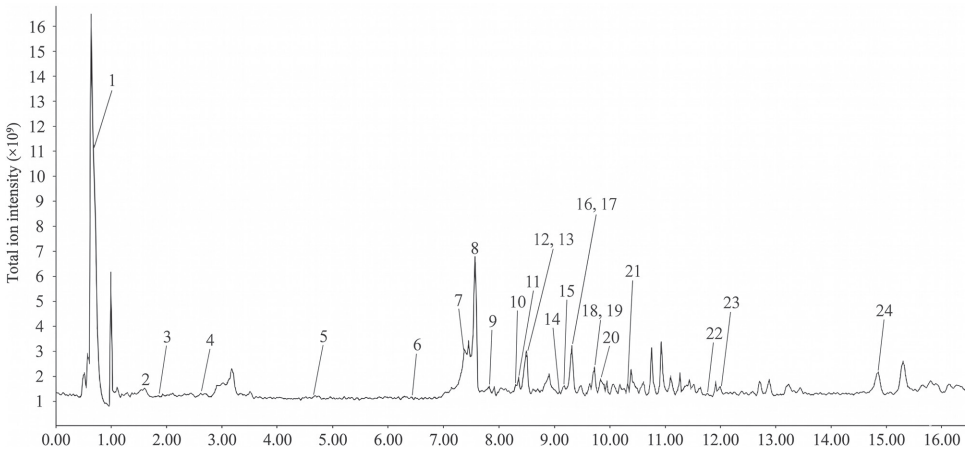

Fig. 2 Representative total ion chromatogram in negative mode of 50% ethanolic jackfruit waste extract, with peak numbering assigned based on metabolites identified in Table 3

Table 3 Metabolites identified from liquid chromatography combined with tandem mass spectrometry analysis of jackfruit waste using spectral library searches in Global Natural Products Social Molecular Networking

Peak No.	Retention time (min)	Compound name	Molecular formula	Precursor mass (*m/z*)	Mass difference (Da)	Adduct	Cosine score	Number of shared peaks	Class
1	0.69	Citric acid	$C_6H_8O_7$	191.0549	0.0349	$[M-H]^-$	0.91	6	Carboxylic acids
2	1.61	Gallic acid	$C_7H_6O_5$	169.0132	0.0008	$[M-H]^-$	0.98	5	Phenolic acids
3	1.85	Hydroxytyrosol 4-*O*-glucoside	$C_{14}H_{20}O_8$	315.0719	0.0371	$[M-H]^-$	0.85	5	Phenylethanoids
4	2.61	Gentisic acid 5-*O*-glucoside	$C_{13}H_{16}O_9$	315.0718	0.0002	$[M-H]^-$	0.92	8	Phenolic acids
5	4.67	Neochlorogenic acid	$C_{16}H_{18}O_9$	353.0873	0.0007	$[M-H]^-$	0.97	5	Phenylpropanoids
6	6.49	Esculin	$C_{15}H_{16}O_9$	339.0717	0.0003	$[M-H]^-$	0.95	4	Coumarins
7	7.35	Caffeic acid 3-glucoside	$C_{15}H_{18}O_9$	341.0873	0.0007	$[M-H]^-$	0.96	4	Phenylpropanoids
8	7.57	Quinic acid	$C_7H_{12}O_6$	191.0551	0.0009	$[M-H]^-$	0.95	8	Phenolic acids
9	7.80	Caffeate	$C_9H_8O_4$	179.0340	0.0009	$[M-H]^-$	0.93	3	Phenylpropanoids
10	8.31	Chlorogenic acid	$C_{16}H_{18}O_9$	353.0875	0.0005	$[M-H]^-$	0.99	9	Phenylpropanoids
11	8.39	Mangiferin	$C_{19}H_{18}O_{11}$	421.0773	0.0227	$[M-H]^-$	0.94	7	Xanthones
12	8.51	Hovetrichoside C	$C_{21}H_{22}O_{11}$	449.1085	0.0005	$[M-H]^-$	0.90	13	Flavonoids
13	8.51	Vicenin 2	$C_{27}H_{30}O_{15}$	593.1509	0.0001	$[M-H]^-$	0.89	10	Flavonoids
14	9.12	Luteolin 8-*C*-glucoside	$C_{21}H_{20}O_{11}$	447.0929	0.0001	$[M-H]^-$	0.95	16	Flavonoids
15	9.18	Sayaendoside	$C_{19}H_{28}O_{10}$	415.1606	0.0004	$[M-H]^-$	0.97	9	Phenylethanoids
16	9.24	Taxifolin-3-glucoside	$C_{21}H_{22}O_{12}$	465.1034	0.0006	$[M-H]^-$	0.87	13	Flavonoids
17	9.27	Vitexin 4-*O*-glucoside	$C_{27}H_{30}O_{15}$	593.1508	0.0002	$[M-H]^-$	0.94	9	Flavonoids
18	9.73	Luteolin 7-*O*-glucoside	$C_{21}H_{20}O_{11}$	447.0928	0.0192	$[M-H]^-$	0.83	3	Flavonoids
19	9.73	Luteolin 7-glucuronide	$C_{21}H_{18}O_{12}$	461.0722	0.0008	$[M-H]^-$	0.81	7	Flavonoids
20	9.81	Taxifolin 3-*O*-rhamnoside	$C_{21}H_{22}O_{11}$	449.1088	0.0002	$[M-H]^-$	0.96	12	Flavonoids
21	10.33	Luteolin 4'-*O*-glucoside	$C_{21}H_{20}O_{11}$	447.0929	0.0001	$[M-H]^-$	0.71	3	Flavonoids
22	11.77	4H-1-Benzopyran-4-one, 2-(2,6-dihydroxyphenyl)-2, 3-dihydro-5,7-dihydroxy-, (2*S*)-	$C_{15}H_{12}O_6$	287.0557	0.0003	$[M-H]^-$	0.96	7	Flavonoids
23	12.01	Luteolin	$C_{15}H_{10}O_6$	285.0401	0.0001	$[M-H]^-$	0.84	12	Flavonoids
24	14.86	(10*E*,15*E*)-9,12,13-trihydroxyoctadeca-10,15-dienoic acid	$C_{18}H_{32}O_5$	327.2173	0.0007	$[M-H]^-$	0.94	11	Octadecanoids
25	2.71	Pantothenic acid	$C_9H_{17}NO_5$	220.1177	0.0002	$[M+H]^+$	0.96	10	Secondary alcohol
26	3.52	Argaminolic A	$C_{11}H_{11}NO_4$	222.0758	0.0002	$[M+H]^+$	0.74	6	Amines
27	8.17	Ferulic acid	$C_{10}H_{10}O_4$	177.0543	0.0006	$[M+H-H_2O]^+$	0.98	7	Phenylpropanoids
28	13.85	Apigenin	$C_{15}H_{10}O_5$	271.0596	0.0004	$[M+H]^+$	0.88	10	Flavonoids

Shared peaks = number of similar ions fragmentation between experimental and library data. URLs in Supplementary Table S1 provide more detailed views of tandem mass spectrometry (MS/MS) peaks shared between experimental and reference spectra.

Flavonoids, particularly luteolin and its glycosylated derivatives, were among the most abundant metabolites identified in the jackfruit waste extracts. Luteolin, along with its glucosides, such as luteolin 7-*O*-glucoside, luteolin 4'-*O*-glucoside and luteolin 7-glucuronide, is recognized widely for its potent antioxidant and α-glucosidase inhibitory activities (Yan et al., 2013; Xu et al., 2022). The antioxidant properties of luteolin are attributed to its ability to scavenge ROS through hydrogen atom donation from hydroxyl groups located at the 4 and 7 positions of the B and A rings, respectively (Andrés et al., 2023). The presence of luteolin glycosides in jackfruit waste is particularly noteworthy, as glycosylation has been reported to enhance the solubility and stability of flavonoids, potentially improving their pharmacological properties (Dahiya et al., 2023). Additionally, the identification of taxifolin glycosides, including taxifolin 3-*O*-rhamnoside and taxifolin-3-glucoside, broadens the functional potential of the extract. Taxifolin is structurally distinct from luteolin due to its dihydroflavonol core, which enables additional hydrogen bonding interactions, enhancing its inhibitory effect on α-glucosidase (Liu et al., 2017). Furthermore, the detection by the current study of vicenin-2, a stable *C*-glycosyl flavone, is noteworthy since its presence in jackfruit waste had not been previously reported. The inherent stability of *C*-glycosyl flavonoids suggests their suitability for long-term bioactivity and potential applications in nutraceutical formulations.

In addition to flavonoids, phenolic acids and phenylpropanoids were identified as important contributors to the antioxidant and α-glucosidase inhibitory activities of the jackfruit waste extract. Notable compounds included chlorogenic acid, neochlorogenic acid, caffeic acid 3-glucoside, ferulic acid and gallic acid, all of which have potent radical-scavenging properties (Kadoma and Fujisawa, 2008; Sueishi et al., 2014; Hutachok et al., 2021; Vo et al., 2024). Furthermore, chlorogenic acid and its isomer, neochlorogenic acid, are well-documented α-glucosidase and α-amylase inhibitors, primarily due to their ester-linked caffeic acid moieties, which interact with carbohydrate-hydrolyzing enzymes and delay the digestion of complex carbohydrates (Wang et al., 2021). The presence of ferulic acid and gallic acid further strengthened the antioxidant capacity of the extract, as these compounds are known to mitigate lipid peroxidation and oxidative stress-related damage (Srinivasan et al., 2007). Notably, caffeic acid 3-glucoside has been identified as a water-soluble phenylpropanoid (Shimoda et al., 2016), indicating that glycosylation could enhance its bioavailability and facilitate its application in functional beverage formulations. The abundance of these bioactive flavonoids and phenolic acids in the 50% ethanol extract explains its superior antioxidant and α-glucosidase inhibitory performance observed in this study.

Beyond flavonoids and phenolic acids, additional bioactive compounds were detected such as mangiferin and esculin. Mangiferin, a xanthone derivative, is a well-known neuroprotective and anti-inflammatory agent (Tan et al., 2024). Its presence in jackfruit waste suggests metabolic similarities between the *Artocarpus* and *Mangifera* genera, which could be explored for comparative phytochemical studies. Esculin, a coumarin glycoside, is recognized widely for its antioxidant (Ju et al., 2024) and ultraviolet-absorbing properties (Tattini et al., 2014), making it a potential candidate for cosmetic and skincare applications. The functional implications of these findings highlight the potential industrial applications of jackfruit waste extracts. Given their rich flavonoid and phenolic acid content, these extracts could serve as natural antioxidants in nutraceutical and pharmaceutical formulations. The observed α-glucosidase inhibitory activity suggests their potential for diabetes management, particularly as a natural alternative to synthetic postprandial glucose-lowering agents. Furthermore, the presence of phenolic acids and coumarins with known skin-protective properties indicates that jackfruit waste extracts could be incorporated into cosmetic formulations for anti-aging and UV-protection benefits. Additionally, the extract's phenolic profile suggests its suitability as a natural preservative in food systems, reducing the need for synthetic antioxidants.

Despite the promising bioactive potential of jackfruit waste, several limitations should be acknowledged. Although the present study provided a comprehensive metabolite profile, further *in vivo* studies are necessary to confirm the bioavailability and pharmacokinetics of the identified compounds. Additionally, enzyme kinetics studies could provide deeper insights into the mechanism of α-glucosidase inhibition, distinguishing between competitive and non-competitive inhibition patterns. Furthermore, large-scale extraction and purification strategies should be optimized to facilitate the commercialization of jackfruit waste extracts for functional applications. Overall, this study provides compelling evidence that jackfruit waste is a rich and underutilized source of bioactive flavonoids, phenolic acids and other phytochemicals with considerable antioxidant and α-glucosidase inhibitory activities. The identification of flavonoid glycosides, phenylpropanoids and xanthones highlights the functional diversity of these extracts, positioning them as potential candidates for nutraceutical, pharmaceutical

and cosmetic applications. These findings reinforce the importance of valorizing agricultural byproducts and suggest that jackfruit waste represents a sustainable resource for the development of health-promoting natural products.

Conclusion

This study demonstrated that jackfruit waste extracts have considerable antioxidant and α-glucosidase inhibitory activities, strongly influenced by the ethanol ratio used during extraction. Specifically, the 50% ethanol extract had the highest TPC, significant DPPH and NO radical scavenging activity and superior α-glucosidase inhibition, indicating that balanced solvent polarity had optimized the recovery of the key bioactive compounds. Metabolite profiling using LC-MS/MS further confirmed the presence of flavonoids, phenolic acids and other metabolites that likely contributed to these observed bioactivities. Pearson's correlation analysis reinforced a strong association between the TPC and antioxidant activities, alongside a moderate correlation with α-glucosidase inhibition, suggesting additional bioactive compounds may also play a role. Based on these results, there is promising potential for jackfruit waste as a sustainable source of natural antioxidants and antidiabetic agents. Furthermore, this study provided the first comprehensive LC-MS/MS-based metabolite profiling of, that should be a solid foundation for future valorization strategies. Further research is required to fully realize the potential of jackfruit waste, including *in vivo* bioactivity validation, detailed bioavailability studies and isolation of specific active compounds, thereby advancing sustainable agricultural practices and supporting the development of novel functional products in food, pharmaceutical and nutraceutical applications.

Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

Alibekov, R.S., Kamal, S.M.M., Taip, F.S., Sulaiman, A., Azimov, A.M., Urazbayeva, K.A., 2023. Recovery of phenolic compounds from jackfruit seeds using subcritical water extraction. Foods. 12, 3296. https://doi.org/10.3390/foods1217

Andrés, C.M.C., De La Lastra, J.M.P., Juan, C.A., Plou, F.J., Pérez-Lebeña, E. 2023. Polyphenols as antioxidant/pro-oxidant compounds and donors of reducing species: relationship with human antioxidant metabolism. Processes 11: 2771. doi.org/10.3390/pr11092771

Apak, R., Calokerinos, A., Gorinstein, S., et al. 2021. Methods to evaluate the scavenging activity of antioxidants toward reactive oxygen and nitrogen species (IUPAC Technical Report). Pure Appl. Chem. 94: 87–144. doi.org/10.1515/pac-2020-0902

Apak, R., Özyürek, M., Güçlü, K., Çapanoğlu, E. 2016. Antioxidant activity/capacity measurement. 1. classification, physicochemical principles, mechanisms and electron transfer (ET)-based assays. J. Agric. Food Chem. 64: 997–1027. doi.org/10.1021/acs.jafc.5b04739

Asmat, U., Abad, K., Ismail, K. 2015. Diabetes mellitus and oxidative stress—a concise review. Saudi Pharm. J. 24: 547–553. doi.org/10.1016/j.jsps.2015.03.013

Bajaj, S., Khan, A. 2012. Antioxidants and diabetes. Indian J. Endocrinol. Metab. 16: 267–271. doi.org/10.4103/2230-8210.104057

Caturano, A., D'Angelo, M., Mormone, A., et al. 2023. Oxidative stress in type 2 diabetes: impacts from pathogenesis to lifestyle modifications. Curr. Issues Mol. Biol. 45: 6651–6666. doi.org/10.3390/cimb45080420

Chandran, P. 2017. Phytochemical, proximate, antimicrobial, antioxidant and FTIR analyses of seeds of *Artocarpus heterophyllus* Lam. Adv. Biotechnol. Microbiol. 5: 1–9. doi.org/10.19080/aibm.2017.05.555653

Cheok, C.Y., Adzahan, N.M., Rahman, R.A., Abedin, N.H.Z., Hussain, N., Sulaiman, R., Chong, G.H. 2016. Current trends of tropical fruit waste utilization. Crit. Rev. Food Sci. Nutr. 58: 1–27. doi.org/10.1080/10408398.2016.1176009

Dahiya, A., Majee, C., Mazumder, R., Priya, N., Salahauddin, S., Atriya, A. 2023. Insight into the glycosylation methods of the flavonoids as an approach to enhance its bioavailability and pharmacological activities. Indian J. Pharm. Educ. Res. 57: 354–371. doi.org/10.5530/ijper.57.2.45

Dardak, R.A. 2019. Trends in production, trade and consumption of tropical fruit in Malaysia. FFTC Agric. Policy Platf. (FFTC-AP). https://ap.fftc.org.tw/article/1381, 4 March 2025.

Deng, G., Shen, C., Xu, X., et al. 2012. Potential of fruit wastes as natural resources of bioactive compounds. Int. J. Mol. Sci. 13: 8308–8323. doi.org/10.3390/ijms13078308

Dhar, G., Akther, S., Sultana, A., May, U., Islam, M., Dhali, M., Sikdar, D. 2017. Effect of extraction solvents on phenolic contents and antioxidant capacities of *Artocarpus chaplasha* and *Carissa carandas* fruits from Bangladesh. J. Appl. Biol. Biotechnol. 5: 39–44. doi.org/10.7324/jabb.2017.50307

Dührkop, K., Fleischauer, M., Ludwig, M., et al. 2019. SIRIUS 4: a rapid tool for turning tandem mass spectra into metabolite structure information. Nat. Methods. 16, 299–302. https://doi.org/10.1038/s41592-019-0344-8

Di Meo, S., Reed, T.T., Venditti, P., Victor, V.M. 2016. Harmful and beneficial role of ROS. Oxid. Med. Cell. Longev. 2016: 7909186. doi.org/10.1155/2016/7909186

Do, Q.D., Angkawijaya, A.E., Tran-Nguyen, P.L., Huynh, L.H., Soetaredjo, F.E., Ismadji, S., Ju, Y. 2013. Effect of extraction solvent on total phenol content, total flavonoid content and antioxidant activity of *Limnophila aromatica*. J. Food Drug Anal. 22: 296–302. doi.org/10.1016/j.jfda.2013.11.001

Eshwarappa, R.S.B., Iyer, S., Subaramaihha, S.R., Richard, S.A., Dhananjaya, B.L. 2015. Antioxidant activities of *Ficus glomerata* (Moraceae [*sic*]) leaf gall extracts. Pharmacogn. Res. 7: 114–120. doi.org/10.4103/0974-8490.147225

Fernandes, F., Ferreres, F., Gil-Izquierdo, A., Oliveira, A.P., Valentão, P. andrade, P.B. 2017. Accumulation of primary and secondary metabolites in edible jackfruit seed tissues and scavenging of reactive nitrogen species. Food Chem. 233: 85–95. doi.org/10.1016/j.foodchem.2017.04.068

Govindaraj, D., Rajan, M., Hatamleh, A.A., Munusamy, M.A. 2018. From waste to high-value product: Jackfruit peel derived pectin/apatite bionanocomposites for bone healing applications. Int. J. Biol. Macromol. 106: 293–301. doi.org/10.1016/j.ijbiomac.2017.08.017

Gulcin, İ., Alwasel, S.H. 2022. Metal ions, metal chelators and metal chelating assay as antioxidant method. Processes 10: 1–16. doi.org/10.3390/pr10010132

He, C., Liu, X., Jiang, Z., Geng, S., Ma, H., Liu, B. 2019. Interaction mechanism of flavonoids and α-glucosidase: experimental and molecular modelling studies. Foods 8: 355. doi.org/10.3390/foods8090355

Heuckeroth, S., Damiani, T., Smirnov, A., et al. 2024. Reproducible mass spectrometry data processing and compound annotation in MZmine 3. Nat. Protoc. 19: 2597–2641. doi.org/10.1038/s41596-024-00996-y

Horai, H., Arita, M., Kanaya, S., et al. 2010. MassBank: A public repository for sharing mass spectral data for life sciences. J. Mass Spectrom. 45: 703–714. doi.org/10.1002/jms.1777

Hutachok, N., Koonyosying, P., Pankasemsuk, T., Angkasith, P., Chumpun, C., Fucharoen, S., Srichairatanakool, S. 2021. Chemical analysis, toxicity study and free-radical scavenging and iron-binding assays involving coffee (*Coffea arabica*) extracts. Molecules 26: 4169. doi.org/10.3390/molecules26144169

Ibrahim, U.K., Kamarrudin, N., Suzihaque, M.U.H., Hashib, S.A. 2017. Local fruit wastes as a potential source of natural antioxidant: an overview. IOP Conf. Ser. Mater. Sci. Eng. 206: 012040. doi.org/10.1088/1757-899x/206/1/012040

Jagtap, U.B., Panaskar, S.N., Bapat, V.A. 2010. Evaluation of antioxidant capacity and phenol content in jackfruit (*Artocarpus heterophyllus* Lam.) fruit pulp. Plant Foods Hum. Nutr. 65: 99–104. doi.org/10.1007/s11130-010-0155-7

Jayaprakasha, G., Girennavar, B., Patil, B.S. 2008. Radical scavenging activities of Rio red grapefruits and sour orange fruit extracts in different in vitro model systems. Bioresour. Technol. 99: 4484–4494. doi.org/10.1016/j.biortech.2007.07.067

Ji, C., Ma, Y., Xie, Y., et al. 2024. Isolation and purification of carbohydrate components in functional food: A review. RSC Adv. 14: 23204–23214. doi.org/10.1039/d4ra02748e

Jideani, A.I.O., Silungwe, H., Takalani, T., Omolola, A.O., Udeh, H.O., Anyasi, T.A. 2021. Antioxidant-rich natural fruit and vegetable products and human health. Int. J. Food Prop. 24: 41–67. doi.org/10.1080/10942912.2020.1866597

Jiménez-Moreno, N., Volpe, F., Moler, J.A., Esparza, I., Ancín-Azpilicueta, C. 2019. Impact of extraction conditions on the phenolic composition and antioxidant capacity of grape stem extracts. Antioxidants 8: 597. doi.org/10.3390/antiox8120597

Ju, S., Tan, Y., Wang, Q., Zhou, L., Wang, K., Wen, C., Wang, M. 2024. Antioxidant and anti-inflammatory effects of esculin and esculetin (review). Exp. Ther. Med. 27: 248. doi.org/10.3892/etm.2024.12536

Kadoma, Y., Fujisawa, S. 2008. A comparative study of the radical-scavenging activity of the phenolcarboxylic acids caffeic acid, p-coumaric acid, chlorogenic acid and ferulic acid, with or without 2-mercaptoethanol, a thiol, using the induction period method. Molecules 13: 2488–2499. doi.org/10.3390/molecules13102488

Kalt, W. 2005. Effects of production and processing factors on major fruit and vegetable antioxidants. J. Food Sci. 70: R11–R19. doi.org/10.1111/j.1365-2621.2005.tb09053.x

Kalt, W., Ryan, D.A.J., Duy, J.C., Prior, R.L., Ehlenfeldt, M.K., Kloet, S.P.V. 2001. Interspecific variation in anthocyanins, phenolics and antioxidant capacity among genotypes of highbush and lowbush blueberries (*Vaccinium* Section *cyanococcus* spp.). J. Agric. Food Chem. 49: 4761–4767. doi.org/10.1021/jf010653e

Kashtoh, H., Baek, K. 2022. Recent updates on phytoconstituent alpha-glucosidase inhibitors: an approach towards the treatment of type two diabetes. Plants 11: 2722. doi.org/10.3390/plants11202722

Khan, S.A., Aslam, R., Makroo, H.A. 2018. High pressure extraction and its application in the extraction of bio-active compounds: A review. J. Food Process Eng. 42: 1–15. doi.org/10.1111/jfpe.12896

Kim, S., Lee, J.Y., Jeong, Y., Kang, C. 2022. Antioxidant activity and probiotic properties of lactic acid bacteria. Fermentation 8: 29. doi.org/10.3390/fermentation8010029

Klongdee, S., Klinkesorn, U. 2022. Optimization of accelerated aqueous ethanol extraction to obtain a polyphenol-rich crude extract from rambutan (*Nephelium lappaceum* L.) peel as natural antioxidant. Sci. Rep. 12: 21153. doi.org/10.1038/s41598-022-25818-7

Kothari, V., Seshadri, S. 2010. Antioxidant activity of seed extracts of *Annona squamosa* and *Carica papaya*. Nutr. Food Sci. 40: 403–408. doi.org/10.1108/00346651011062050

Kumar, K., Debnath, P., Singh, S., Kumar, N. 2023. An overview of plant phenolics and their involvement in abiotic stress tolerance. Stresses 3: 570–585. doi.org/10.3390/stresses3030040

Lee, A., Lan, J.C.W., Jambrak, A.R., Chang, J.S., Lim, J.W., Khoo, K.S., 2024. Upcycling fruit waste into microalgae biotechnology: Perspective views and way forward. Food Chem. Mol. Sci. 8, 100203. https://doi.org/10.1016/j.fochms.2024.100203

Lee, S.Y., Mediani, A., Nur Ashikin, A.H., Azliana, A.B.S., Abas, F., 2014. Antioxidant and α-glucosidase inhibitory activities of the leaf and stem of selected traditional medicinal plants. Int. Food Res. J. 21: 165–172.

Lin, X., Feng, C., Lin, T., Harris, A.J., Li, Y., Kang, M. 2022. Jackfruit genome and population genomics provide insights into fruit evolution and domestication history in China. Hortic. Res. 9: uhac173. doi.org/10.1093/hr/uhac173

Liu, J., Wang, X., Geng, S., Liu, B., Liang, G. 2017. Inhibitory mechanism of taxifolin against α-glucosidase based on spectrofluorimetry and molecular docking. Nat. Prod. Commun. 12: 1934578X1701201. doi.org/10.1177/1934578x1701201116

Mohimani, H., Gurevich, A., Shlemov, A., et. al. 2018. Dereplication of microbial metabolites through database search of mass spectra. Nat. Commun. 9: 4035. doi.org/10.1038/s41467-018-06082-8

Muflihah, Y.M., Gollavelli, G., Ling, Y. 2021. Correlation study of antioxidant activity with phenolic and flavonoid compounds in 12 Indonesian indigenous herbs. Antioxidants 10: 1530. doi.org/10.3390/antiox10101530

Muhamad, N., Muhmed, S.A., Yusof, M.M., Gimbun, J. 2014. Influence of solvent polarity and conditions on extraction of antioxidant, flavonoids and phenolic content from *Averrhoa bilimbi*. J. Food Sci. Eng. 4: 255–260. doi.org/10.17265/2159-5828

Nga, N.T.T., Bac, N.X., Hanh, V.T., Ha, L.T.N. 2024. Polyphenols from tropical almond leaves (*Terminalia catappa* L.): optimized extraction conditions and α-glucosidase inhibitory activity. Vietnam J. Agric. Sci. 7: 2064–2075. doi.org/10.31817/vjas.2024.7.1.05

Ojwang, R., Muge, E., Mbatia, B., Mwanza, B., Ogoyi, D. 2018. Compositional, elemental, phytochemical and antioxidant characterization of jackfruit (*Artocarpus heterophyllus*) pulps and seeds from selected regions in Kenya and Uganda. Eur. J. Med. Plants 23: 1–12. doi.org/10.9734/ejmp/2018/40967

Osman, M., Mahmoud, G., Shoman, S. 2020. Correlation between total phenols content, antioxidant power and cytotoxicity. Biointerface Res. Appl. Chem. 11: 10640–10653. doi.org/10.33263/briac113.1064010653

Pizzino, G., Irrera, N., Cucinotta, M., et al. 2017. Oxidative stress: harms and benefits for human health. Oxid. Med. Cell. Longev. 2017: 8416763. doi.org/10.1155/2017/8416763

Plaskova, A., Mlcek, J. 2023. New insights of the application of water or ethanol-water plant extract rich in active compounds in food. Front. Nutr. 10: 1118761. doi.org/10.3389/fnut.2023.1118761

Prasad, K.N., Yang, E., Yi, C., Zhao, M., Jiang, Y. 2008. Effects of high pressure extraction on the extraction yield, total phenolic content and antioxidant activity of longan fruit pericarp. Innov. Food Sci. Emerg. Technol. 10: 155–159. doi.org/10.1016/j.ifset.2008.11.007

Quiroz, J.Q., Duran, A.M.N., Garcia, M.S., Gomez, G.L.C., Camargo, J.J.R. 2019. Ultrasound-assisted extraction of bioactive compounds from annatto seeds, evaluation of their antimicrobial and antioxidant activity and identification of main compounds by LC/ESI-MS analysis. Int. J. Food Sci. 2019: 1–9. doi.org/10.1155/2019/3721828

Ramli, R.A., Azmi, A., Johari, N.R., Noor, S.M. 2016. Minimally processed jackfruit: opportunity for the foodservice industry. J. Food Res. 6: 1–6. doi.org/10.5539/jfr.v6n1p1

Rana, M.S., Rayhan, N.M.A., Emon, M.S.H., et al. 2024. Antioxidant activity of Schiff base ligands using the DPPH scavenging assay: an updated review. RSC Adv. 14: 33094–33123. doi.org/10.1039/d4ra04375h

Sagar, N.A., Pareek, S., Sharma, S., Yahia, E.M., Lobo, M.G. 2018. Fruit and vegetable waste: bioactive compounds, their extraction and possible utilization. Compr. Rev. Food Sci. Food Saf. 17: 512–531. doi.org/10.1111/1541-4337.12330

Sajak, A.A.B., Mediani, A., Maulidiani, N., et al. 2017. Effect of *Ipomoea aquatica* ethanolic extract in streptozotocin (STZ) induced diabetic rats via ^{1}H NMR-based metabolomics approach. Phytomedicine 36: 201–209. doi.org/10.1016/j.phymed.2017.10.011

Saxena, A., Bawa, A., Raju, P. 2011. In: Yahia, E. (Ed.). Postharvest biology and technology of tropical and subtropical fruits: jackfruit (*Artocarpus heterophyllus* Lam.). Woodhead Publishing. pp. 275–299e.

Schmid, R., Heuckeroth, S., Korf, A. et al. 2023. Integrative analysis of multimodal mass spectrometry data in MZmine 3. Nat. Biotechnol. 41: 447–449. doi.org/10.1038/s41587-023-01690-2

Shannon, P., Markiel, A., Ozier, O., et al. 2003. Cytoscape: A software environment for integrated models of biomolecular interaction networks. Genome Res. 13: 2498–2504. doi.org/10.1101/gr.1239303

Sharma, A., Gupta, P., Verma, A.K. 2013. Preliminary nutritional and biological potential of *Artocarpus heterophyllus* L. shell powder. J. Food Sci. Technol. 52: 1339–1349. doi.org/10.1007/s13197-013-1130-8

Shimoda, K., Kubota, N., Uesugi, D., Tanigawa, M., Hamada, H. 2016. Hydroxylation and glycosylation of phenylpropanoids by cultured cells of *Phytolacca americana*. Nat. Prod. Commun. 11: doi.org/10.1177/1934578x1601100216

Shrikanta, A., Kumar, A., Govindaswamy, V. 2013. Resveratrol content and antioxidant properties of underutilized fruits. J. Food Sci. Technol. 52: 383–390. doi.org/10.1007/s13197-013-0993-z

Singh, A., Kukreti, R., Saso, L., Kukreti, S. 2022. Mechanistic insight into oxidative stress-triggered signaling pathways and type 2 diabetes. Molecules 27: 950. doi.org/10.3390/molecules27030950

Srinivasan, M., Sudheer, A.R., Menon, V.P., 2007. Ferulic acid: therapeutic potential through its antioxidant property. J. Clin. Biochem. Nutr. 40, 92–100. https://doi.org/10.3164/jcbn.40.92

Sueishi, Y., Hori, M., Ishikawa, M., Matsu-Ura, K., Kamogawa, E., Honda, Y., Kita, M., Ohara, K. 2014. Scavenging rate constants of hydrophilic antioxidants against multiple reactive oxygen species. J. Clin. Biochem. Nutr. 54: 67–74. doi.org/10.3164/jcbn.13-53

Tan, H., Liang, D., Lu, N., Zhang, J., Zhang, S., Tan, G. 2024. Mangiferin attenuates lipopolysaccharide-induced neuronal injuries in primary cultured hippocampal neurons. Aging 16: 8645–8656. doi.org/10.18632/aging.205830

Tang, S., Wang, B., Liu, X., Xi, W., Yue, Y., Tan, X., Bai, J., Huang, L. 2024. Structural insights and biological activities of flavonoids: Implications for novel applications. Food Front 6: 218–247. doi.org/10.1002/fft2.494

Tattini, M., Di Ferdinando, M., Brunetti, C., et al. 2014. Esculetin and esculin (esculetin 6-O-glucoside) occur as inclusions and are differentially distributed in the vacuole of palisade cells in *Fraxinus ornus* leaves: A fluorescence microscopy analysis. J. Photochem. Photobiol. B Biol. 140: 28–35. doi.org/10.1016/j.jphotobiol.2014.06.012.

Thavamoney, N., Sivanadian, L., Tee, L.H., Khoo, H.E., Prasad, K.N., Kong, K.W. 2018. Extraction and recovery of phytochemical components and antioxidative properties in fruit parts of *Dacryodes rostrata* influenced by different solvents. J. Food Sci. Technol. 55: 2523–2532. doi.org/10.1007/s13197-018-3170-6

Theofanous, A., Deligiannakis, Y., Louloudi, M. 2024. Hybrids of gallic acid@SiO2 and {hyaluronic-acid counterpats}@SiO2 against hydroxyl (●OH) radicals studied by EPR: A comparative study vs their antioxidant hydrogen atom transfer activity. Langmuir 40: 26412–26424. doi.org/10.1021/acs.langmuir.4c02760

Tomás-Barberán, F.A., Espín, J.C. 2001. Phenolic compounds and related enzymes as determinants of quality in fruits and vegetables. J. Sci. Food Agric. 81: 853–876. doi.org/10.1002/jsfa.885

Trigo, J.P., Alexandre, E.M.C., Saraiva, J.A., Pintado, M.E. 2019. High value-added compounds from fruit and vegetable by-products – characterization, bioactivities and application in the development of novel food products. Crit. Rev. Food Sci. Nutr. 60: 1388–1416. doi.org /10.1080/10408398.2019.1572588

Vo, Q.V., Hoa, D.T.T., Hoa, N.T., Tran, M.D., Mechler, A. 2024. The radical scavenging activity of monocaffeoylquinic acids: the role of neighboring hydroxyl groups and pH levels. RSC Adv. 14: 4179–4187. doi.org/10.1039/d3ra08460d

Wang, M., Carver, J.J., Phelan, V.V., et al. 2016. Sharing and community curation of mass spectrometry data with Global Natural Products Social Molecular Networking. Nat. Biotechnol. 34: 828–837. doi.org/10.1038/nbt.3597

Wang, S., Li, Y., Huang, D., Chen, S., Xia, Y., Zhu, S. 2021. The inhibitory mechanism of chlorogenic acid and its acylated derivatives on α-amylase and α-glucosidase. Food Chem. 372: 131334. doi.org/10.1016/j.foodchem.2021.131334

Xu, T., Wang, C., Jiang, S., Yang, T., Wu, X. 2022. Glycosylation of luteolin in hydrophilic organic solvents and structure–antioxidant relationships of luteolin glycosides. RSC Adv. 12: 18232–18237. doi.org/10.1039/d2ra03300c

Yan, J., Zhang, G., Pan, J., Wang, Y. 2013. α-Glucosidase inhibition by luteolin: kinetics, interaction and molecular docking. Int. J. Biol. Macromol. 64: 213–223. doi.org/10.1016/j.ijbiomac.2013.12.007

Zhang, S., Bi, H., Liu, C. 2007. Extraction of bio-active components from *Rhodiola sachalinensis* under ultrahigh hydrostatic pressure. Sep. Purif. Technol. 57: 277–282. doi.org/10.1016/j.seppur.2007.04.022

Zhang, L., Tu, Z.C., Xie, X., Wang, H., Wang, H., Wang, Z.X., Sha, X.M., Lu, Y. 2017. Jackfruit (*Artocarpus heterophyllus* Lam.) peel: A better source of antioxidants and α-glucosidase inhibitors than pulp, flake and seed, and phytochemical profile by HPLC-QTOF-MS/MS. Food Chem. 234: 303–313. doi.org/10.1016/j.foodchem.2017.05.003

Zhong, L., Yang, J., Syed, J.N., Zhang, Y., Tian, Y., Fu, X., 2025. Alpha-glucosidase inhibitors in aging and aging-related diseases: Clinical applications and relevant mechanisms. Aging Dis.16, 0. https://doi.org/10.14336/ad.2024.1477