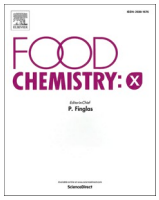
Food Chemistry: X 21 (2024) 101164

Contents lists available at ScienceDirect

Food Chemistry: X

journal homepage: www.sciencedirect.com/journal/food-chemistry-x



Waste to Wealth: Dynamics and metabolic profiles of the conversion of jackfruit flake into value-added products by different fermentation methods

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ARTICLE INFO

Keywords:
Jackfruit flake
Fermentation
Value-added products
Lactic acid bacteria
HS-SPME-GC–MS
Untargeted metabolite profile

ABSTRACT

Thus far, little is known about whether jackfruit flake, a byproduct of jackfruit, can be used as a fermentation substrate to obtain value-added products through microbial fermentation. Here, jackfruit flake puree was fermented by three different ways: spontaneous fermentation (JF), inoculated with LAB (JFL), inoculated co-fermentation with LAB and yeast (JFC). In contrast to JF, the total polyphenol and flavonoid content and syndrome-associated enzyme inhibition are significantly increased in JFC at the end of fermentation. Electronic tongue analysis revealed that the JFC was significantly lower in astringency and higher in bitterness. 41 volatile compounds were identified during fermentation by HS-SPME-GC–MS, and JFC was richer in honey, rose, and fruity flavors. A total of 290 compounds were screened for discriminative pre- and post-fermentation differential metabolites by non-target metabolomics analysis. These results provide a potential reference for the conversion of jackfruit waste into functional products using fermentation.

Introduction

Jackfruit (*Artocarpus heterophyllus Lam.*), commonly known as the largest tree-borne fruits in the world, is rich in nutrients including proteins, carbohydrates, fat, vitamins, minerals, fiber, as well as phytochemicals. Moderate consumption of jackfruit has been linked to nutritional and pharmacological benefits such as antioxidant, anti-inflammatory, antibacterial, antifungal, antineoplastic, hypoglycemic, and wound healing effects (Baliga, Shivashankara, Haniadka, Dsouza, & Bhat, 2011).

While jackfruit flesh is a major product for edible purposes, large numbers of jackfruit wastes (e.g., rag, seed, peel, bulb, and central core), accounting for 60 % of jackfruit weight are non-edible, and commonly discarded as bio-waste, remaining underutilized, causing serious environmental issues (Tran, Nguyen, Tran, & Nguyen, 2023). Essentially, these jackfruit bio-waste products can be developed into robust value-added and eco-friendly products. The ripe seeds of jackfruit are edible after boiling and roasting, and may be consumed as a snack (Chai et al., 2021). Besides, jackfruit seed starch (JSS) can be developed as novel gastroretentive nanoparticles loaded with metformin (Jain, Upadhyay, Mishra, & Jain, 2022), as well as pioglitazone-loaded JSS-alginate beads with significant hypoglycemic effect (Nayak, Pal, & Hasnain, 2013). Another work was reported by Le et al. (2023), where seed starch derived from jackfruit waste was used to increase lactic acid production by co-fermentation with *Lactobacillus plantarum* and *Bacillus subtili*. As for the jackfruit peel, which has also been shown to be a source of polyphenol with strong antioxidant activity, as well as a source of polysaccharides with hypoglycemic activity, with potential applications in the food and pharmaceutical industries (Jiang, Shi, Chen, & Wang, 2019; Wang & Jiang, 2022). Therefore, given the high value added properties of jackfruit by-products, it is worth considering whether there are still unexplored parts has not been fully investigated.

Jackfruit flake (rags), the outer packaged part of pulps, regarded as immature pulp, most of which is discarded as waste. However, jackfruit flake is heavy in polyphenol and flavonoid, and exert antioxidant and hypoglycemic activity *in vitro* (Zhang et al., 2017). It can also be served as a source of higher antioxidant and antibacterial biopolymers such as pectin (Tran et al., 2023). As a result, jackfruit flake has a great chance of

Abbreviations: LAB, Lactic acid bacteria; TA, Titratable Acidity; TPC, Total polyphenol content; GAE, Gallic acid equivalent; DW, Dry weight; TFC, Total flavonoid content; RE, Rutin equivalent.

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https://doi.org/10.1016/j.fochx.2024.101164
Received 3 October 2023; Received in revised form 12 January 2024; Accepted 25 January 2024
Available online 30 January 2024

being developed into superior value-added products.

Lactic acid bacteria (LAB), a common probiotic, has been widely applied in the fermented foods including fruit (Lan et al., 2023), vegetables (Zhao et al., 2016), dairy (Peng, Koubaa, Bals, & Vorobiev, 2020), bakery (Daba, Elnahas, & Elkhateeb, 2021), owing to produce metabolites capable of improving some parameters linked to the overall quality of food, such as aroma profile and sensory quality. Compared with monoculture fermentation, mixed fermentation acts as a more complicated system, allowing the exchange of multiple metabolites and provides mutual growth-promoting effects (Lan et al., 2023). Accumulating evidence substantiates that co-fermentation of LAB and yeast may provide additional benefits for food development. It was found that co-fermentation application with *Lactobacillus plantarum* HLJ29L2 and yeast (DN-1) firmly improved the protein digestibility of crackers (Hu et al., 2023). Another work reported by Cassimiro et al. (2023), they developed superior-quality conilon coffee with co-cultivation of LAB and yeasts using the self-induced anaerobic fermentation methodology. However, there is a lack of extensive report on jackfruit and related by-products fermentation by LAB or mixed strains.

Therefore, in this work, autochthonous LAB (*Lactococcus lactis* LA5) and yeast (*Hanseniaspora opuntiae* SA2) isolated from pineapple cores in previous work of our lab were used to co-ferment a mixture of jackfruit flake, and a separate LAB fermentation group and spontaneous group were set as control, and whey protein was added as the nitrogen source. The physicochemical properties, total polyphenol and flavonoid content, two metabolic syndrome-associated enzyme inhibitory ability, taste assessment, and volatile flavor compounds of jackfruit flake puree during fermentation process (0,12,24,36,48 h) were initially investigated. Untargeted metabolomic analysis was employed to reveal the differences in metabolites between different groups. This work provides fresh insight into the co-fermentation of jackfruit flake via LAB and yeast, and serves as a practical reference for the development of jackfruit value-added products via microbial fermentation.

Materials and methods

Materials and chemicals

Fully ripe jackfruits (*Malaysia* No.1) were purchased from a local supermarket, which harvested in June 2023 from Hainan, China. Whey protein (purity: 98 %), α-amylase (≥12 U/mg), lipase (≥30,000 U/g) were purchased from Yuanye-Bio Technology (Shanghai, China). Culture Medium was purchased from Solarbio Science (Beijing, China). All the different reagents used in this study are of analytical grade.

Preparation of fermented jackfruit flake

Lactococcus lactis LA5 and *Hanseniaspora opuntiae* SA2 were endophytic microorganisms isolated in our previous experiment (Luo et al., 2023). The jackfruit flake was pulped with a high-speed blender and mixed at a mass ratio of 1:2.5 (g: mL), then whey protein (2.6 %, *w/w*) was added, and the pH of the system was adjusted to 5.2. Afterward, the mixture of jackfruit flake puree was sterilized in a water bath at 70 °C for 20 min.

The experimental samples were categorized into three groups for comparative analysis: jackfruit flake puree fermented with LA5 (JFL), jackfruit flake puree co-fermented by LA5 and SA2 (JFC), and jackfruit flake puree without LA5 and SA2 (JF) as the control group. For JFC, the starter culture strains were simultaneously inoculated at a volume ratio of 6:1 (LAB: yeast) in an incubator, where the LAB inoculation ratio was 1.6 % (*w/w*), and the cell concentration of LA5 and SA2 was approximately 1×10^6 CFU/mL determined by optical density (OD600). The LA5 inoculation volume for JFL was comparable to that for JFC, while an equal amount of sterile water was added to the jackfruit flake puree. Fermentation was conducted under static conditions at 37 °C, and samples were collected at 0, 12, 24, 36, and 48 h with each sample being replicated three times. The lyophilized samples were stored at −80 °C for additional experimentation.

Determination of pH and titratable acidity

The pH was measured at room temperature with a calibrated pH meter. The value of titratable acidity (TA) was determined by the 0.1 M NaOH and expressed as percentage (*w/w*) of lactic acid.

Measurement of total polyphenol and flavonoid content

The Folin–Ciocalteu method was applied to determine the content of total polyphenol content (TPC). The TPC was expressed in mg of gallic acid equivalent (GAE) per g of dry weight (DW).

Measurement of the total flavonoid content (TFC) was carried out by the method reported in our previous work using sodium nitrite-aluminum chloride colorimetry. The TFC was expressed in mg of rutin equivalent (RE) per g of dry weight (DW).

Enzyme-Inhibitory effects of jackfruit flake puree during fermentation

Pancreatic α-amylase and pancreatic lipase inhibitory activities were assayed according to our previous work with minor modification (Suo et al., 2021). 120 μL of the JF, JFL and JFC fermentation frozen samples and control (sterilized deionized water) sample was mixed with 80 μL starch solution (3 g/L). The enzymatic reaction was initiated by the addition of 100 μL of α-amylase solution (8 U/mL, PBS, 0.1 M, pH 6.9), and the reaction mixture was incubated at 37 °C for 30 min. Then, 250 μL of DNS reagent was added. The mixture was heated at 100 °C in a boiling water bath for 10 min and chilled immediately in an ice-water bath. The absorption was measured at 540 nm. As to pancreatic lipase, 150 μL of fermentation samples were mixed with 50 μL of substrate (pNPB, 10 mM). The reaction was initiated by the addition of 35 μL of pancreatic lipase solution (300 U/mL, PBS, 0.2 M, pH 7.2). After incubation at 37 °C for 30 min, absorbance was measured at 405 nm. Enzymatic inhibitory activity was calculated as follows:

$$\text{Inhibition capacity}\% = \frac{\text{Acontrol-Asample}}{\text{Acontrol}} \times 100 \quad (1)$$

Measurement of taste changes during fermentation by e-tongue

The Insent taste sensing system (SA402B, Atsugi-chi, Japan) was used to evaluate the eight taste features of three groups including sourness, bitterness, astringency, aftertaste-A (astringent aftertaste), aftertaste-B (bitter aftertaste), umami, richness and saltiness. Samples weighing 100 mg from various stages of fermentation were sonicated in 8 mL of distilled water for 10 min before being centrifuged for five minutes at 4000 r/min. Approximately 30 mL of the diluted solution was used for taste value determination. The unfermented sample (JF-0 h) was used as a control.

Headspace solid-phase microextraction (HS-SPME)

300 mg of JF, JFL and JFC samples were weighed and placed into a 20 mL headspace and 3 mL saturated NaCl solution was added. The cyclohexanone solution (10 μL) was used as the internal standard for quantitative determination. An SPME fiber was inserted into the sample headspace for five minutes at 50 °C. After extraction, the fiber was removed from the vial and immediately inserted into the GC–MS sampler for desorption (250 °C for 30 min) and further analysis.

Gas chromatography-mass spectrometer (GC–MS) analysis

A Model 8890 GC system (Agilent, Palo Alto, CA, USA) and a 7000D GC/TQ mass spectrometer (Agilent, Palo Alto, CA, USA) were used to

perform GC–MS analysis. DB-WAX UI (30 m × 0.25 mm, 0.25 μm; Agilent, USA) was employed as column. Chromatographic separations were performed as follow: 35 °C for 0–6 min, increased to 150 °C at a rate of 5 °C /min and held for 2 min, then increased to 250 °C at a rate of 10 °C /min and held for 3 min. The mass spectrometer ion source was 250 °C, and the electron impact ionization was tuned to 70 eV with mass ranges from 50 to 550 *m/z*. The relative concentration (ng/g) of each volatile compound was quantified by calculating the peak area ratio of each compound with that of the internal standard.

Metabolomics analysis

The fermented samples (100 mg) were individually grounded with liquid nitrogen and the homogenate was re-suspended with 80 % methanol. The samples were incubated on ice for 5 min and then were centrifuged at 15,000 g, 4 °C for 20 min. Some of supernatant was diluted to final concentration containing 53 % methanol by LC-MS grade water. The samples were centrifuged at 15,000 g, 4 °C for 20 min, and the supernatant was collected for further analyses. UHPLC-MS/MS analyses were performed using a Vanquish UHPLC system (ThermoFisher, Germany) coupled with an Orbitrap Q Exactive TM HF mass spectrometer or Orbitrap Q Exactive TM HF-X mass spectrometer (Thermo Fisher, Germany).

Statistical analysis

Statistical analysis was performed using SPSS 22.0 software (IBM, USA). Data are presented as mean ± standard error of the mean (SEM). Differences among groups were analyzed by one-way analysis of variance (ANOVA) followed by Turkey's test. Each experiment was replicated three times independently.

Results and discussion

Characteristics of jackfruit flake puree at different fermentation phase

pH and TA changes

In general, as shown in Fig. 1, the pH values of the two groups of inoculated fermented jackfruit flake puree decreased compared with spontaneous fermented jackfruit flake puree at the end of fermentation stage (48 h), while the TA content of two fermented groups increased higher rates than the spontaneous fermented group. The alter pH value was negatively correlated with the variation in TA content, which indicates that additional acids were generated after fermentation with LAB or co-fermentation of LAB and yeast for 48 h. The further acidity of these two fermented groups is potentially due to its elevated efficiency in metabolizing sugar into organic acids (Wang, Wei, Wang, Zhang, & Gong, 2023). As expected, co-fermentation exhibited improved acidification characteristics than monoculture LAB or spontaneous fermentation and this trend was consistent with the results reported by Andeta et al. (2018).

Sugar content

Jackfruit possesses adequate fermentable sugar (Muhialdin, Meor Hussin, Kadum, Abdul Hamid, & Jaafar, 2021). Fig. 2A and B depict sugar content variation of three experiments groups in terms of total sugars and reducing sugars at different fermentation phase. In all fermentation groups, the total and reducing sugar levels decreased throughout the fermentation. At the 48 h of the fermentation, the total sugar content of JFL significantly ($p < 0.05$) decreased from 11.82 ± 0.41 g/100 g to 8.91 ± 0.54 g/100 g, as to JFC, which was significantly ($p < 0.05$) decreased from 12.20 ± 0.44 g/100 g to 9.02 ± 0.52 g/100 g. Despite this, no significant difference in the total sugar content was observed at the end of fermentation in the JF group, although the average value of 48 h was lower than 0 h. The trend of reducing sugar during fermentation was practically the same as for the total soluble sugars. At the end of the fermentation, the reducing sugars of JFL significantly ($p < 0.05$) decreased from 8.77 ± 0.16 g/100 g to 7.30 ± 0.36 g/100 g, while no significant difference was observed in JFC group. Interestingly, as to JFC, reducing sugar content significantly ($p < 0.05$) decreased to 6.96 ± 0.17 g/100 g by the end of the 36 h. LAB fermentation is a process in which sugars are consumed and acids are produced. Due to the reducing sugar content during fermentation, it has been suggested that microorganisms may use these sugars produced from jackfruit itself for cell growth and biotransformation. It is important to note that no additional sugar was added during fermentation in this work, which demonstrates the promising health benefits of low-sugar fermented products that meet consumer demand for healthy foods.

TPC and TFC

The polyphenol and flavonoid in fruits are key functional components due to their positive impact on various physiological processes related to human health, such as antioxidant activity, improving glucose metabolism, as well as regulating gut microbiota balance. As shown in Fig. 2C, D, compared with the initial fermentation, the TPC of fermented samples through monoculture LAB (JFL) and co-fermentation (JFC) were significantly ($p < 0.05$) increased at 12, 24, 36, and 48 h, and the final fermentation TP content were 11.20 ± 0.22 mg GAE/g DM,1.75 ± 0.26 mg GAE/g DM, respectively. Additionally, a similar increased trend in TFC was found in JFL and JFC with the extension of fermentation time. However, there is no significant shift in the TPC and TFC in the JF

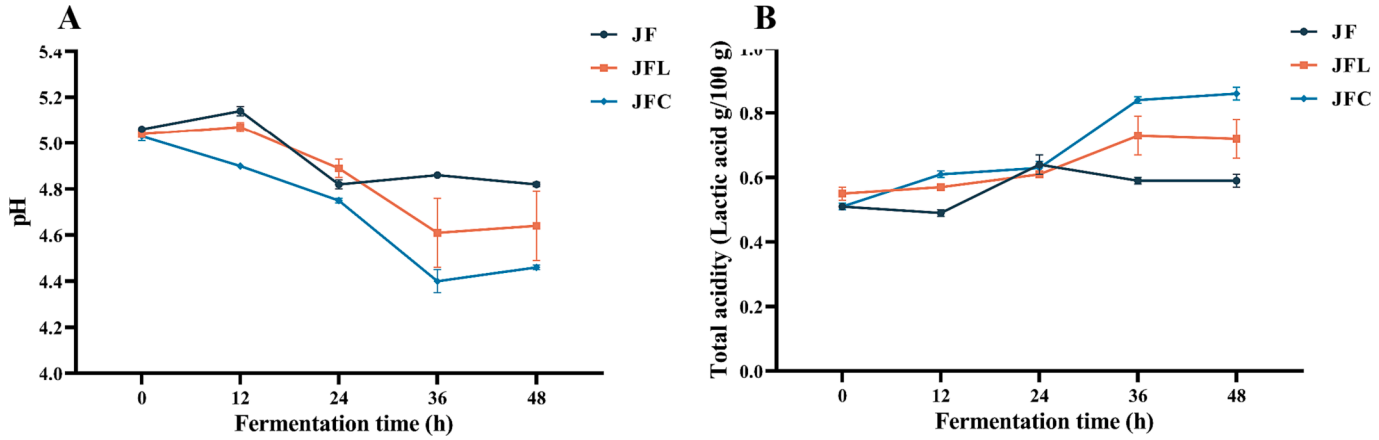

Fig. 1. The values of pH (A) and total acidity (B) of three groups at different fermentation times. JF, spontaneous fermentation on jackfruit flake; JFL, jackfruit flake fermented with lactic acid bacteria; JFC, co-fermented with lactic acid bacteria and yeast on jackfruit flake.

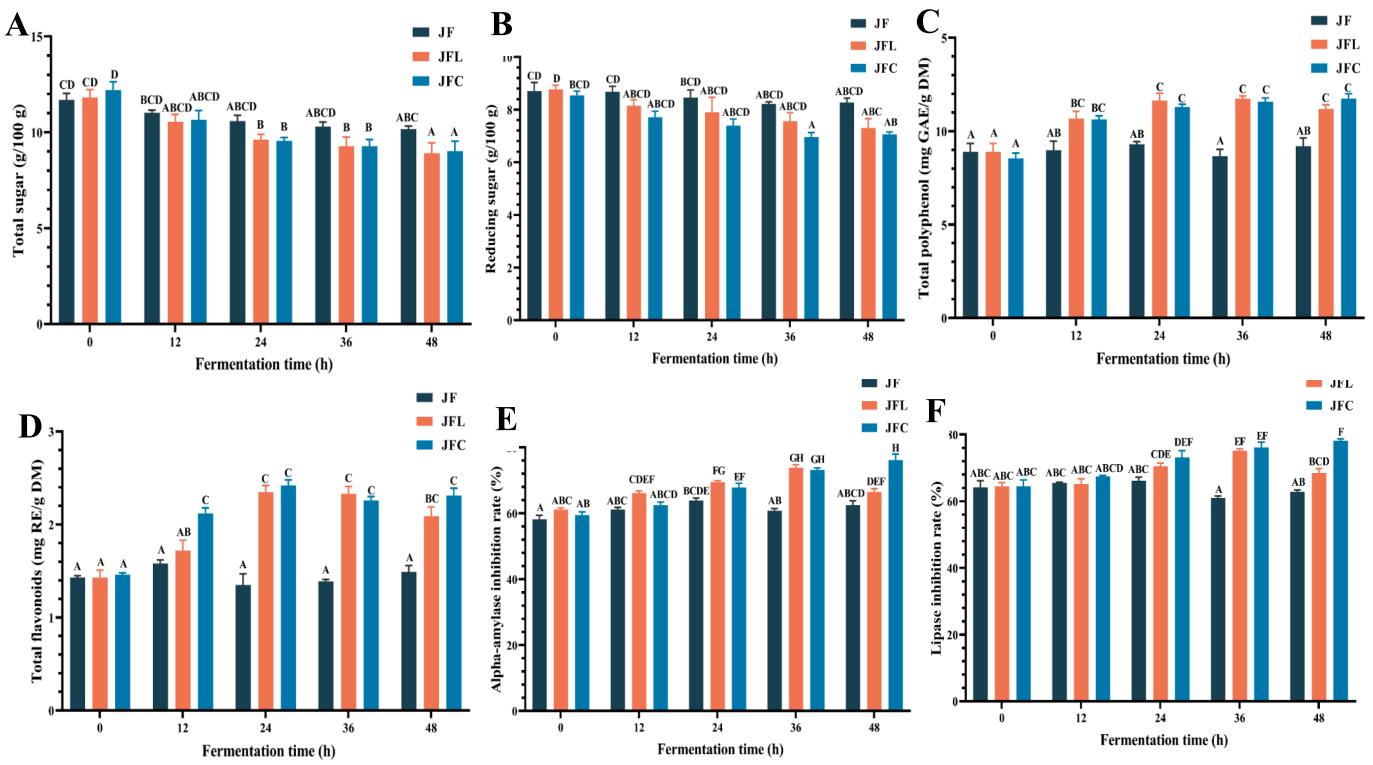

Fig. 2. The total sugar content (A), reducing sugar content (B), total polyphenol content (C), total flavonoids content (D), α-amylase inhibition rate (E), pancreatic lipase inhibition rate (F) of three groups at different fermentation times. JF, spontaneous fermentation on jackfruit flake; JFL, jackfruit flake fermented with lactic acid bacteria; JFC, co-fermented with lactic acid bacteria and yeast on jackfruit flake.

from 0 h to 48 h.

The assessment of the shift in TAC and TFC during the fermentation phase appears to be increasingly significant, as it will allow us to better understand whether monoculture LAB fermentation or co-fermentation of yeast and LAB promotes the release of phenolic compounds from jackfruit flake. The increase in TPC may be due to cell wall of fruit degradation by microbial fermentation (Gao et al., 2022), besides, organic acids produced during the fermentation may prevent the degradation of polyphenol or flavonoid (Sun, Chou, & Yu, 2009).

Similarly, in another study by Vivek et al., they reported that TPC and TFC in Sohiong (*Prunus nepalensis*) juice were increased during fermentation with *Lactobacillus plantarum* MCC 2974 (Vivek, Mishra, Pradhan, & Jayabalan, 2019). However, Wu et al. (2020) found a dramatic decrease in TPC and TFC in apple juice fermented by *Lactobacillus helveticus* 76, which decreased TPC and TFC by 26.9 % and 33.2 %, respectively. Therefore, screening appropriate bacterial strains for their ability to produce additional bioactive compounds in different fruit fermentation processes is something we need to focus on in future work.

Enzyme-Inhibitory assay during fermentation

Spectrophotometric analysis of the JF, JFL and JFC groups on pancreatic α-amylase, pancreatic lipase was conducted, and the results are shown in Fig. 2E – F. For instance, the pancreatic α-amylase inhibition rate of the JFL at 0 h was 61.14 %, it gradually increased to 73.82 % following 36 h, and decreased to 66.53 % at the end of fermentation. As to pancreatic lipase, the inhibition ability of JFL significantly ($p < 0.05$) increased from 64.47 % to 75.15 % (0–36 h), and which significantly ($p < 0.05$) increased from 64.45 to 78.12 from (0–48 h). However, no significant variation was observed in the lipase inhibition ability of JF at different times.

The prevalence of type 2 diabetes mellitus (T2DM) has been on an alarmingly increasing trend worldwide and diet interventions have been shown to delay or prevent the onset of T2DM.Rao et al. (2021) demonstrated that consumption of jackfruit flour can be selected as a medical nutritional therapy in place of equivalent amounts of rice or wheat flour of daily meal in patients with T2DM. Besides, jackfruit extracts has also been proved possess the ability for the management of diabetes mellitus (Ajiboye et al., 2018; Maradesha et al., 2023).Regulation of carbohydrate and fat digestion and/or absorption in the gastrointestinal tract may be another promising strategy for the prevention of T2DM. Recent studies have shown that the consumption of fermentation food is linked to reducing the risks of obesity, and the inhibition of digestive enzyme activities has been regarded as one of the most crucial action mechanisms underlying the beneficial effects (Yoon et al., 2022).

In this work, compared to non-fermented sample, both monoculture fermentation and co-fermentation could enhance the inhibition ability of α-amylase and lipase, which proved that LAB fermentation could improve the inhibition of lipase and α-amylase. This is consistent with the finding reported by Wang et al. (2023). Therefore, we believe that fermented jackfruit flake is a promising dietary ingredient for ameliorating metabolic disease through probiotics. A large number of studies show that TPC of the sample exhibits a significant positive correlation with metabolic disease related enzymes inhibitory activity (Shobana, Sreerama, & Malleshi, 2009). As we discussed above, the TPC was increased by inoculation fermentation, and which may partly explain the typically higher inhibitory activity against the α-amylase and lipase assayed at different fermentation phase.

E-tongue analysis

As shown in Fig. 3A, the fermentation time had more impact on the saltiness of JF with significant ($p < 0.05$) difference from 0 h to 48 h, and the astringency showed an increasing trend with the fermentation time increasing, while aftertaste-A seems no difference shift. As to JFL (Fig. 3B), compared to control (JF-0 h), the value of sourness, astringency, aftertaste-A, aftertaste-B, and richness changed significantly ($p <$

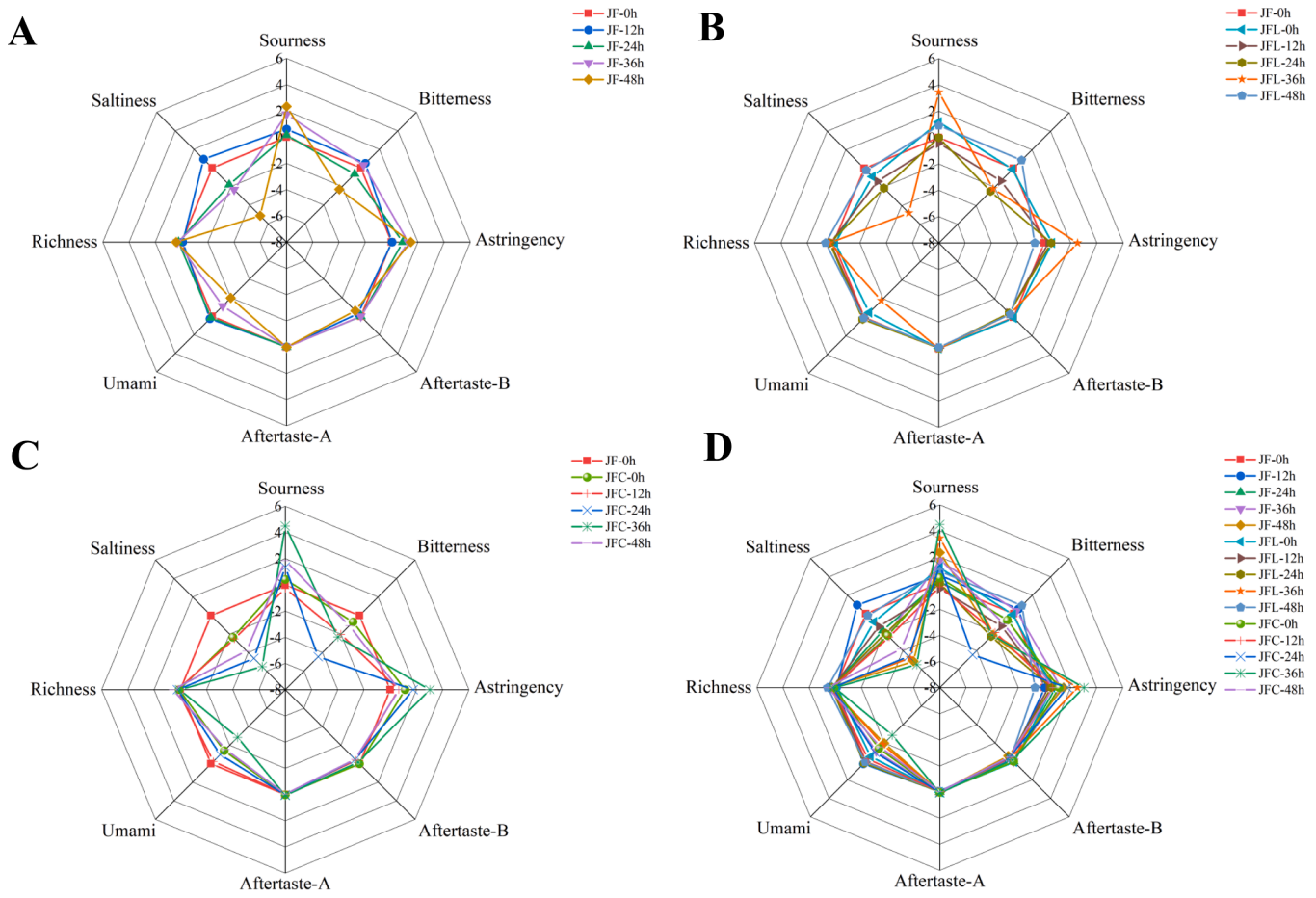

Fig. 3. Radar plot for electronic tongue sensory score of JF(A), JFL(B), JFC (C), and three groups together (D) at different fermentation times. JF, spontaneous fermentation on jackfruit flake; JFL, jackfruit flake fermented with lactic acid bacteria; JFC, co-fermented with lactic acid bacteria and yeast on jackfruit flake.

0.05) at 48 h, while the rest of the three taste values were no significant change. As is obviously shown in Fig. 3C, similarly like JFL, the trend of JFC in bitterness value decreased from 0 h to 24 h, and increased from 24 h to 48 h. In addition, compared to JF-0 h, all the eight taste values changed significantly ($p < 0.05$) at 48 h.

For a closer comparison of the flavor properties of fermented jackfruit flake, Fig. 3D additionally shows the differences across different experimental groups. After fermentation of jackfruit flake with LAB or LAB combined with yeast, the sourness of the fermented samples reached its maximum at 36 h, in agreement with the values in pH and TA. Large amounts of organic acids produced by microorganisms may be responsible for the sourness increase (Luo et al., 2023). Moreover, the reduction of bitterness in JFL and JFC at 36 h may be due to the formation of large amounts of acids masking alternative tastes (Lao, Zhang, Li, & Bhandari, 2020). Popescu et al. (2013) found that yeast can utilize the bitter substances in the beer fermentation process for growth and metabolism, thereby reducing the bitterness of the fermented product. Regarding astringency, the sensor values of JFL, JFC and JF at 36 h are 2.53, 3.02 and 1.27 respectively. Both JFL and JFC were significant ($p < 0.05$) higher than JF, which may attribute to the increasing of TPC (Jöbstl, O'Connell, Fairclough, & Williamson, 2004). From this, we can conclude that inoculation with LAB or LAB combined yeast has a significant effect on the taste of fermented jackfruit flake.

Volatile profiles detected by HS-SPME-GC–MS

Overall, based on the NIST Mass Spectral Database, a total of 41 volatile substances including 12 esters, 7 alcohols, 5 acids, 4 alkanes, 3 alkenes, 2 thiols, 1 ketone, 1 aldehyde, 1 thioether, and 5 other compounds were identified in the three fermenting jackfruit flake. 1-butanol, D-limonene, and butanoic acid were detected in all three groups at different fermentation times. 19 volatile organic compounds were detected in the unfermented jackfruit flake group (JF), and 11 volatile compounds were detected at the end of fermentation. Additionally, only 6 volatile compounds were found in the JFL group at 0 h, and increased to 18 volatile compounds at 12 h, and 5 were detected at 48 h. Similarly, as to JFC, the variety of volatile compounds increased from 10 (0 h) to 20 (24 h), and decreased to 8 at 48 h. Thus, the volatile components of jackfruit flake may be obscured by additional inoculation of LAB or LAB with yeast. However, as the fermentation time lengthened, both sets of inoculated aromatic substances showed a trend of first increasing and then decreasing. Clearly, this is normally associated with microbial metabolism (Liao, Luo, Huang, & Xia, 2023).

As shown in Table 1, acetoin was detected in both the JFL and JFC. Acetoin is an essential physiological metabolite generated through the metabolism of citrate by LAB, which imparts desirable buttery flavor and odor to various foods including cheese (Lo, Ho, Bansal, & Turner, 2018). In contrast to the remaining two groups, 3-methyl-1-butanol and 2-phenylethanol are the two characteristic volatile components of the JFC group. 3-methyl-1-butanol has a fruity and alcohol flavor or caramel odor (Yu et al., 2012), which could be produced from the amino acids catabolism. The increase in this particular aroma is mainly attributed to the addition of yeast (*Hanseniaspora opuntiae* SA2). In addition, 2-phenylethanol, a product of yeast metabolism, imparts honey, rose and fruity aromas (Moreira, Trugo, Pietroluongo, & De Maria, 2002). From this, we can conclude that 3-methyl-1-butanol and 2-phenylethanol can be used as volatile flavor markers by yeast co-fermentation. JFC is likely to exhibit a more pleasing and complex aroma than JFL and JF due to the

Table 1
List of volatile compounds of three groups during fermentation.

No.	RT (min)	Compound	CAS	Formula	Relative content of volatile compounds in JF (ng/g)					Relative content of volatile compounds in JFL (ng/g)					Relative content of volatile compounds in JFC (ng/g)				
					0 h	12 h	24 h	36 h	48 h	0 h	12 h	24 h	36 h	48 h	0 h	12 h	24 h	36 h	48 h
1	10.756	*n*-Butyl acetate	123–86-4	$C_6H_{12}O_2$	130.30 ± 1.74	–	9.23 ± 0.11	–	–	–	99.75 ± 1.46	–	–	–	39.96 ± 0.70	20.25 ± 0.80	–	–	–
2	12.598	lsoamyl acetate	123–92-2	$C_7H_{14}O_2$	28.48 ± 0.27	–	–	–	–	–	19.01 ± 0.20	–	–	–	–	–	–	–	–
3	12.608	3,3′,4,4′-Tetrahydrospirilloxanthin	13833–01-7	$C_{42}H_{64}O_2$	5.81 ± 0.26	–	–	–	–	–	–	–	–	–	–	–	8.67 ± 0.18	–	–
4	13.387	1-Butanol	71–36-3	$C_4H_{10}O$	25.34 ± 0.35	16.69 ± 0.22	27.30 ± 0.35	48.78 ± 0.72	28.42 ± 0.26	6.93 ± 0.10	47.22 ± 0.35	10.01 ± 0.72	11.07 ± 0.35	50.50 ± 1.01	28.64 ± 0.24	19.65 ± 0.24	18.86 ± 0.35	15.41 ± 0.53	10.64 ± 0.38
5	15.095	D-Limonene	5989–27-5	$C_{10}H_{16}$	14.08 ± 0.04	26.63 ± 0.43	13.33 ± 0.06	10.87 ± 0.10	15.43 ± 0.57	14.24 ± 0.33	13.83 ± 0.36	15.70 ± 0.92	9.00 ± 0.53	11.12 ± 0.23	8.51 ± 0.37	8.45 ± 0.50	8.61 ± 0.53	10.00 ± 0.12	6.90 ± 0.15
6	15.460	3-Methyl-1-butanol	123–51-3	$C_5H_{12}O$	–	–	–	–	–	–	–	–	–	–	9.13 ± 0.32	15.39 ± 0.53	64.73 ± 0.87	30.76 ± 0.40	22.29 ± 0.32
7	15.583	3-Ethyl-5-(2′-ethylbutyl) octadecane	55282–12-7	$C_{26}H_{54}$	9.19 ± 0.13	–	8.46 ± 0.04	–	–	–	9.09 ± 0.35	–	8.27 ± 0.28	–	–	15.66 ± 0.55		–	–
8	15.593	Dodecane	112–40-3	$C_{12}H_{26}$	–	–	–	13.88 ± 0.06	–	–	–	–	–	–	–	–	–	–	–
9	15.835	*n*-Butyl butanoate	109–21-7	$C_8H_{16}O_2$	–	–	–	10.81 ± 0.25	–	–	–	–	–	–	–	–	–	–	–
10	16.764	Phenylethylene	100–42-5	C_8H_8	–	16.47 ± 0.04	–	15.10 ± 0.23	8.93 ± 0.11	9.21 ± 0.31	–	8.56 ± 0.21	–	–	–	–	–	–	–
11	16.840	Butyl isovalerate	109–19-3	$C_9H_{18}O_2$	28.47 ± 0.12	–	22.35 ± 0.35	–	–	–	33.67 ± 0.97	–	–	–	–	–	–	–	–
12	17.059	Tetratetracontane	7098–22-8	$C_{44}H_{90}$	–	–	–	8.15 ± 0.33	–	–	–	–	–	–	–	–	–	–	–
13	17.575	Acetoin	513–86-0	$C_4H_8O_2$	–	–	–	–	–		19.80 ± 0.15	–	–	–		8.01 ± 0.17	21.21 ± 0.34	–	–
14	18.284	2-Methylbutyl isovalerate	2445–77-4	$C_{10}H_{20}O_2$	16.92 ± 0.07	–	12.30 ± 0.08	–	–	–	19.35 ± 0.35	–	–	–	–	–	7.56 ± 0.21	–	–
15	19.835	Rhodopin	105–92-0	$C_{40}H_{58}O$	–	–	–	–	–	–	–	–	–	–	–	6.97 ± 0.35		–	–
16	19.835	1-Hexanol	111–27-3	$C_6H_{14}O$	–	–	14.00 ± 0.02	–	–	–	–	–	–	–	–	–	16.55 ± 0.26	–	–
17	20.534	Urea	57–13-6	CH_4N_2O	8.26 ± 0.23	–	–	–	–	–	–	–	–	2.25 ± 0.17	4.82 ± 0.68	–	–	–	–
18	20.888	Caprylic acid methyl ester	111–11-5	$C_9H_{18}O_2$	–	–	11.67 ± 0.09	–	–		8.47 ± 0.53	–	–	–	–	–	–	–	–
19	21.903	4-Heptanol	589–55-9	$C_7H_{16}O$	–	–	–	–	–	–	8.61 ± 0.21	–	–	–	–	–	–	–	–
20	22.128	Methyl formate	107–31-3	$C_2H_4O_2$	–	–	45.43 ± 0.53	–	–	10.93 ± 0.25	–	–	–	–	–	–	–	49.76 ± 0.61	–
21	22.155	Ethyl caprylate	106–32-1	$C_{10}H_{20}O_2$	–	–	–	–	–	–	–	–	–	–	–	–	69.42 ± 0.84	–	–
22	22.199	Acetic acid	64–19-7	$C_2H_4O_2$	10.40 ± 0.27	–	–	–	–	–	40.83 ± 0.99	30.50 ± 0.46	115.16 ± 1.53	–	35.29 ± 0.57	–	–	–	74.41 ± 0.72
23	22.569	1,1-Bis(dodecyloxy) hexadecane	56554–64-4	$C_{40}H_{82}O_2$	6.10 ± 0.05	–	–	–	–	–	–	–	–	–	–	–	–	–	–
24	24.099	Benzaldehyde	100–52-7	C_7H_6O	–	–	7.65 ± 0.04	–	–	–	16.26 ± 0.18	–	–	–	–	–	–	–	–
25	24.647	2,3-Butanediol	24347–58-8	$C_4H_{10}O_2$	–	–	–	9.81 ± 0.33	10.83 ± 0.82	–	–	11.32 ± 0.15	–	–	–	–	7.03 ± 0.06	–	–

(*continued on next page*)

Table 1 (*continued*)

No.	RT (min)	Compound	CAS	Formula	Relative content of volatile compounds in JF (ng/g)					Relative content of volatile compounds in JFL (ng/g)					Relative content of volatile compounds in JFC (ng/g)				
					0 h	12 h	24 h	36 h	48 h	0 h	12 h	24 h	36 h	48 h	0 h	12 h	24 h	36 h	48 h
26	24.663	2-Methyl-2-propanethiol	75–66-1	$C_4H_{10}S$	–	–	–	–	–	–	–	–	27.54 ± 1.44	–	–	–	–	–	–
27	24.663	(S)-(+)-1,3-Butanediol	24621–61-2	$C_4H_{10}O_2$	–	–	28.23 ± 0.69	–	–	–	–	–	–	–	–	–	–	–	–
28	25.646	Lycoxanthin	19891–74-8	$C_{40}H_{56}O$	7.04 ± 0.20	–	–	–	–	–	4.67 ± 0.28	–	–	–	–	–	7.34 ± 0.35	–	–
29	26.06	*α-cis*-Bergamotene	18252–46-5	$C_{15}H_{24}$	9.85 ± 0.13	–	–	–	–	–	–	–	–	–	–	–	–	–	–
30	26.715	Butanoic acid	107–92-6	$C_4H_8O_2$	15.54 ± 0.69	11.48 ± 0.29	9.12 ± 0.14	15.40 ± 0.27	13.50 ± 0.30	13.67 ± 0.82	22.87 ± 0.34	26.70 ± 0.35	32.06 ± 0.18	22.33 ± 0.27	28.19 ± 0.46	15.38 ± 0.33	42.03 ± 0.17	15.19 ± 0.22	9.05 ± 0.09
31	27.267	Ethyl caprate	110–38-3	$C_{12}H_{24}O_2$	–	–	–	–	–	–	–	–	–	–	–	–	6.87 ± 0.35	–	–
32	29.173	3-(Ethylthio) propanol	18721–61-4	$C_5H_{12}OS$	–	–	–	–	–	–	–	–	15.75 ± 0.69	–	–	–	–	–	–
33	29.179	Methyldithio-1-propene	23838–19-9	$C_4H_8S_2$	71.00 ± 0.20	–	73.59 ± 0.21	–	10.53 ± 0.15	–	77.10 ± 0.81	–	–	–	34.35 ± 0.86	19.51 ± 0.22	37.60 ± 0.78.	–	–
34	29.27	Phorboldidecanoate	24928–17-4	$C_{40}H_{64}O_8$	–	–	–	–	–	–	–	–	–	–	–	–	6.83 ± 0.33	–	–
35	31.188	3-Hydroxy-3-methyl-4-phenyl-2-pyrrolidinone	104194–16-3	$C_{11}H_{13}NO_2$	7.48 ± 0.20	–	–	–	–	–	–	–	–	–	–	–	–	–	–
36	31.316	Phenethyl acetate	103–45-7	$C_{10}H_{12}O_2$	–	–	–	–	–	–	–	–	–	–	–	–	47.45 ± 0.37	–	–
37	32.009	Hexanoic acid	142–62-1	$C_6H_{12}O_2$	33.89 ± 0.05	8.20 ± 0.09	28.21 ± 0.11	–	–	–	35.44 ± 0.18	–	–	–	–	15.44 ± 0.69	17.00 ± 0.20	–	–
38	33.303	2-Phenylethanol	60–12-8	$C_8H_{10}O$	–	–	–	–	–	–	–	–	–	–	7.27 ± 0.40	13.46 ± 0.19	95.40 ± 0.93	21.71 ± 0.45	18.27 ± 0.53
39	35.822	Octanoic acid	124–07-2	$C_8H_{16}O_2$	74.66 ± 0.05	–	55.29 ± 0.36	15.04 ± 0.22	14.17 ± 0.92	–	55.55 ± 0.35	14.66 ± 0.18	18.08 ± 0.35	20.12 ± 0.94	28.00 ± 0.47	–	32.96 ± 0.21	–	19.26 ± 0.05
40	38.414	Decanoic Acid	334–48-5	$C_{10}H_{20}O_2$	–	–	20.46 ± 0.16	–	7.42 ± 0.29	–	9.86 ± 0.39	–	11.63 ± 0.25	–	–	8.53 ± 0.35	12.57 ± 0.19	–	10.66 ± 0.69
41	38.415	Ethylpalmitate	628–97-7	$C_{18}H_{36}O_2$	46.52 ± 0.92	–	–	–	–	–	–	–	–	–	–	–	–	–	–

Data were expressed as mean ± SEM (n = 3); JF, spontaneous fermentation on jackfruit flake; JFL, jackfruit flake fermented with lactic acid bacteria; JFC, co-fermented with lactic acid bacteria and yeast on jackfruit flake.

presence of yeast. Unfortunately, with respect to the acid compounds, hexanoic, octanoic, and decanoic acids were detected in all three groups. These compounds contribute to rancid notes. Consequently, additional studies are needed in the future to ensure that fermented samples have a more pleasing aroma composition.

Metabolomics analysis of the metabolites change before and after fermentation

In this work, the changes in the chemical components of unfermented jackfruit flake (JF), spontaneous fermentation of jackfruit flake for 48 h (JFW), fermented jackfruit flake with LAB for 48 h (JFL), and fermented jackfruit flake with LAB and yeast for 48 h (JFC) were assessed with UHPLC-MS/MS based untargeted metabolomics. The untargeted metabolomic data analysis is based on a companion R package (MetaboAnalystR) (Chong & Xia, 2018), such as principal component analysis (PCA) and orthogonal partial least squares-discriminant analysis (OPLS-DA), for identifying differential metabolites for further analysis.

As shown in the Fig. 4A, B, the unsupervised PCA plots indicated that JFC and the other groups were confined to two distinctive widely separated clusters in both the negative and the positive modes, which

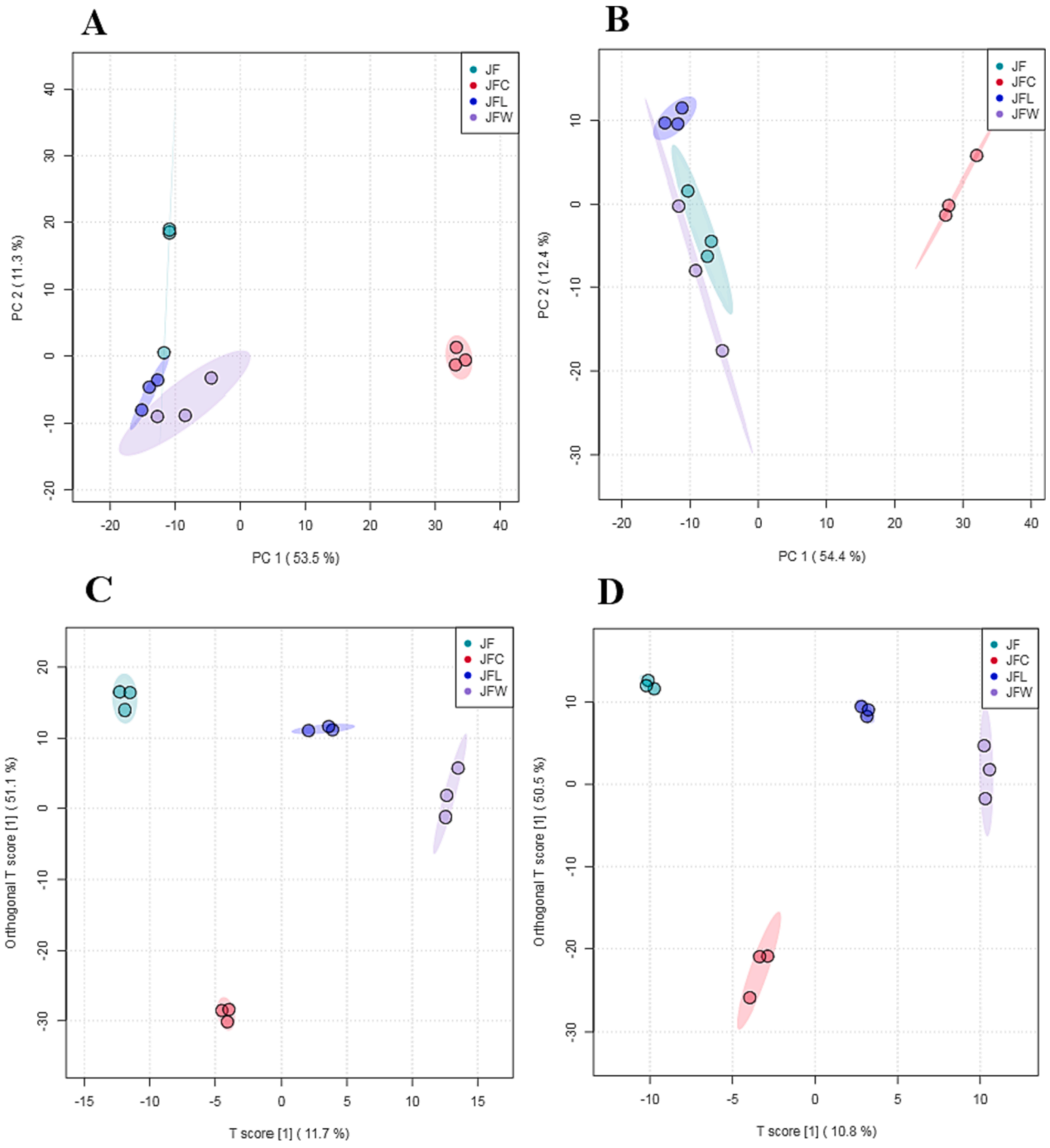

Fig. 4. Score plot of principle component analysis (PCA) of serum metabolites (positive ion (A) and negative ion (B)) and orthogonal partial least-squares discriminant analysis (OPLS-DA) of metabolites (positive ion (C) and negative ion (D)). JF, spontaneous fermentation on jackfruit flake; JFL, jackfruit flake fermented with lactic acid bacteria; JFC, co-fermented with lactic acid bacteria and yeast on jackfruit flake.

Table 2
R2Y and Q2 of the OPLS-DA model.[a]

	Positive mode		Negative mode	
	R2Y	Q2	R2Y	Q2
JF_JFC_JFL_JFW	0.993	0.717	0.998	0.712

[a] JF, jackfruit flake without fermentation; JFW, spontaneous fermentation of jackfruit flake for 48 h. JFL, jackfruit flake fermented with lactic acid bacteria for 48 h; JFC, co-fermented with lactic acid bacteria and yeast on jackfruit flake for 48 h.

suggested that the co-fermentation with LAB and yeast induced significant changes in the profiles of metabolites at the end of fermentation. OPLS-DA, a supervised method of improved classification performance, was further applied to examine the differences in the metabolites among the four groups (Fig. 4C, D). Different from the unsupervised PCA plots, the OPLS-DA score plots showed clear separation of the four groups in four clusters, indicating that the metabolites produced by three fermentation methods are obviously different. To avoid the potential pitfalls of overfitting associated with supervised models, the OPLS-DA model was validated using permutation tests, and the results are presented in Figure S1 and Table 2. The high R2Y (negative mode, 0.998; positive mode, 0.993) and Q2 values (>0.7) thus supported the reliability and predictability of the established OPLS-DA model herein. In addition, VIP (variable importance factor) was used to identify the most prominent variables and VIP greater > 1 ($p < 0.05$) were considered to exert a significant effect on the discrimination of different samples. Here, total 290 metabolites were identified in the four groups (VIP > 1, FDR < 0.05), including 155 effective peaks for the positive mode and 135 effective peaks for the negative mode. So far, untargeted metabolomics data combined OPLS-DA score plots have successfully applied to provide guidance for geographical discrimination of fruits (Li, Liang, Xu, Yang, & Wang, 2021), dairy products from different animal species (Yang et al., 2016),and disease control strategies (Wang et al., 2022), etc.

As shown in Fig. S2A, in the positive ion model, *N*-isovaleroylglycine, DL-stachydrine, D-carnitine, choline and L-norleucine are the top five compounds in relative abundance among the four experimental groups. As to the negative ion model (Fig. S2B), D-(-)-quinic acid, succinic acid, citric acid were the top three compounds in relative abundance in JF group. However, the relative abundance of the top three compounds in JFC group were D-(-)-quinic acid, D-(+)-malic acid, and citric acid.

The volcano plot could clearly depict the differential metabolites in different groups based on fold-change (FC) values and *P*-values. Compared with the JF group, 65 metabolites were significantly ($p < 0.05$) upregulated, and 108 metabolites were significantly downregulated in the JFW group (Table S1). Moreover, JFL exhibited a significant ($p < 0.05$) increase in 113 and a significant ($p < 0.05$) decrease in 95 of the metabolites relative to the JF group (Table S2). The JFC group had 374 significantly ($p < 0.05$) increased and 365 significantly ($p < 0.05$) decreased metabolites compared with the JF group (Table S3). 3-Hydroxyphenylacetic acid (3-HPAA), the major metabolite of quercetin glycosides by microbiota. As shown in Table S3, co-fermentation with LAB and yeast to the jackfruit flake led to significantly upregulated levels of 3-HPAA acid compared to JF group. A recent work by Liu et al. (2022) found that 3-HPAA has a protective potential in hepatocyte models, which may provide new possibilities for the prevention of alcohol-related chronic diseases. Besides,3-HPAA was also believed to be a promising multi-target antimicrobial agent by studying the mechanism of action between 3-HPPA and Pseudomonas aeruginosa with shotgun proteomics (Ozdemir & Soyer, 2020). Thus, it can be inferred that the up-regulation of 3-HPAA due to co-fermentation with LAB and yeast mediates the health-promoting effects of jackfruit flake to some extent.

Based on these potential markers, pathway enrichment and pathway topology analyzes were then carried out to identify key metabolic pathway(s) that were influenced by the different fermentation methods (Figures S3-S5). 26 metabolic pathways (impact value > 0, $P < 0.05$) were found to be enriched in the JFW group relative to the JF group. 31 potential metabolic pathways were screened between the JFL and JF groups. Interestingly, 39 metabolic pathways were significantly altered in the JFC group compared to the JF group. Compared with "JFW *vs.* JF", pathway enrichment and pathway topology analyzes of the current work also showed that the inoculated fermentation (JFL, JFC) significantly modulated pathways associated with phenylpropanoid biosynthesis (ko00940). As to "JFC *vs*. JF", KEGG analysis discovered that six differentially accumulated metabolites (cinnamaldehyde, sinapyl alcohol, chlorogenic acid, *trans*-cinnamic acid, syringing, coniferin) were annotated in the phenylpropanoid biosynthesis pathway. In addition, L-phenylalanine, chlorogenic acid, and sinapyl alcohol are differentially accumulated compounds within the JFL group. To the best of our knowledge, polyphenol and flavonoid are generated via the shikimate pathway and the phenylpropanoid pathway. Wang et al. (2023) found combination of ultrasound and γ-aminobutyric acid enhanced the polyphenol content of mung bean sprouts, and these phenolics are closely related to phenylpropanoid biosynthesis. Recently, Wang et al. (2023) developed a compound wine made from *Lycium barbarum* and *Polygonatum cyrtonema* by different fermentation methods, including *S. cerevisiae* RW only, *D. hansenii* AS2.45 alone, and synergistic fermentation of *D. hansenii* AS2.45 and *S. cerevisiae* RW. Non-targeted metabolomics analysis indicated that the phenylpropanoid biosynthesis pathway was present in all three comparison groups and suggested that it was the metabolic pathway that was critical in affecting samples prepared from different yeast combinations. Thus, in this work, fermented mixed cultures of LAB and yeast were able to modulate the phenylpropanoid biosynthesis pathway to increase the amount of polyphenol and flavonoid, which subsequently enhanced the nutritional value of jackfruit flake.

Conclusion

In this work, we perform a comparative dynamic study of the conversion of jackfruit flake into value-added products by three fermentation methods. The results showed a decrease in pH and total and reducing sugar content, as well as an increase in TA for longer fermentation times in all three groups. The content of total polyphenol and flavonoid, and the α-amylase and pancreatic lipase inhibitory activity increased in JFL and JFC at the end of fermentation. The values of astringency, bitterness, aftertaste-A, and saltiness in the JFC were significantly changed compared to the JF at 48 h. A total of 41 volatile compounds were identified using a HS-SPME-GC–MS. Acetoin is a characteristic flavor in JFL and JFC.3-methyl-1-butanol and 2-phenylethanol exist only in the JFC. Samples fermented synergistically with LAB and yeast are richer in honey, rose, and fruity flavors. Non-targeted metabolomics indicates that different fermentation pathways affect the accumulation of metabolites in jackfruit flake. 290 metabolites were identified in four experimental groups based on the OPLS-DA method. Metabolite profiling and pathway enrichment analysis revealed that 50 metabolic pathways were found before and after three fermentation methods (JF *vs*. JFW *vs*. JFL *vs*. JFC). Our study thus provides, for the first time, strong evidence that jackfruit flake bio-waste is a promising fermentation substrate for obtaining value-added products through fermentation with LAB combined yeast.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CRediT authorship contribution statement

Hao Suo: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing – original draft. **Shan Xiao:** Supervision, Writing – review & editing. **Bo Wang:** Data curation, Investigation, Methodology. **Yan-Xue Cai:** Data curation, Investigation, Methodology. **Ji-Hui Wang:** Resources, Supervision, Writing – review & editing.

Declaration of competing 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.

Data availability

Data will be made available on request.

Acknowledgment

We would like to express our gratitude to Dongguan Prefabricated Food Innovation Development and Quality Control Key Laboratory for providing us with equipment and technical support.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.fochx.2024.101164.

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