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RESEARCH

# Comparative Study of Conventional and Emerging Extraction Methods for Papaya Seed Oil: Process Optimization and Quality Evaluation

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## Abstract

Papaya seed oil (*Carica papaya*) is gaining interest for its potential applications as a functional food ingredient. Papaya seeds, usually discarded as agro-industrial waste, represent a valuable source of oil rich in unsaturated fatty acids. This study evaluated several extraction methods, including Soxhlet extraction, maceration, microwave-assisted extraction (MAE), hydraulic pressing, and ultrasound-assisted extraction (UAE), using pure ethanol and pure isopropanol as green solvents. Soxhlet extraction with hexane for 24 h at 121 °C achieved the highest yield (30.91 ± 0.49%) and was used as the reference. Among the greener techniques, UAE performed at 400 W for 30 min with isopropanol achieved the best compromise between yield (22.50 ± 0.27%) and oil quality, showing the lowest acidity index (9.00 ± 2.16 mg KOH/g). Therefore, UAE was selected for further optimization by varying ultrasound power (0–400 W), extraction time (5–30 min), and solvent composition (isopropanol, 50:50 ethanol–isopropanol mixture, and ethanol). The optimal extraction conditions were 200 W for 30 min using a 1:1 ethanol-isopropanol solvent mixture, which resulted in an extraction yield of 26.34%, corresponding to an oil recovery of approximately 85% relative to the Soxhlet reference. The mixed solvent enhanced extraction efficiency by improving mass transfer through the combined effects of solvent polarity and ultrasonic cavitation, confirming that ultrasound-assisted extraction with green solvent mixtures is an effective method for papaya seed oil recovery.

**Keywords** Green extraction · Solvent efficiency · Mixed solvent · Oil quality characteristics

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## Introduction

Papaya (*Carica papaya L.)* is a tropical fruit native to Mexico and Central America, now widely cultivated in tropical and subtropical regions for its nutritional, medicinal, and industrial value. Global production reached approximately 13.8 million tons in 2025, with India, the Dominican Republic, and Mexico ranking as the top producers (MFK, 2025). Processing generates 20–25% waste, mainly seeds and peels (Vinha et al., 2024), which are often discarded despite their richness in bioactive compounds useful for food, pharmaceutical, and cosmetic applications. Papaya seeds, in particular, represent a promising source of protein, dietary fiber, and oil rich in monounsaturated fatty acids and functional bioactives (Samaram et al., 2013; Gonçalves Rodrigues et al., 2019, Mesquita et al., 2022). Nonetheless, the extraction method and processing conditions play a crucial role in determining the yield, quality, and antioxidant capacity of the resulting oil.

Conventional techniques such as maceration, soxhlet extraction, and cold pressing are widely used for extracting oils and bioactive compounds but have limitations, including long extraction times, high solvent use, and possible degradation of heat-sensitive compounds (Khalid et al., 2024). In addition, the use of toxic organic solvents raises safety and environmental concerns, particularly for food and cosmetic applications. Consequently, emerging techniques like ultrasound-assisted extraction (UAE) and microwave-assisted extraction (MAE) have gained attention as faster, more energy-efficient, and potentially greener alternatives (Chemat et al., 2017; Tiwari, 2015).

Previous research on papaya seed and other oil extractions has shown that conventional solvent extraction using hexane yields high oil outputs, with oil yields ranging from 28.5% to 40.0%, compared to ethanol and ethyl acetate, which yield 8% and 14%, respectively (Goriainov et al., 2023; Keneni et al., 2021; Oladipo & Betiku, 2019; Robles-Apodaca et al., 2024). Mechanical extraction methods, such as hydraulic pressing, have achieved 12.49% oil from Cambodian soybeans (Bunthan et al., 2023), highlighting the generally lower efficiency of non-solvent-based approaches. Additionally, ultrasound-assisted solvent extraction using hexane has shown improved efficiency, with oil yields ranging from 23.23% to 32.27% depending on the extraction conditions (Li et al., 2015; Samaram et al., 2015; Senrayan & Venkatachalam, 2019; Zhang et al., 2019).

Furthermore, green mixed solvent have gained attention as alternatives for oil extraction. Souza et al., (2020) reported that an ethanol-isopropanol mixture (1:1, v/v) achieved a 41.13% almond oil yield under prolonged extraction time (180 min) and elevated temperature (75 °C), surpassing the yields obtained with individual solvents specifically hexane. Similarly, greener extraction of rice bran oil under milder conditions (solid–liquid ratio 5.5:1, cyclohexane/isopropanol, 45 °C, 12 min) achieved 85.8% oil recovery, showing similar extraction efficiency to traditional solvents while better preserving physicochemical properties, fatty acid composition, and bioactive compounds (Wang et al., 2022). In addition, Thanou et al., (2022) replaced chloroform/methanol (2:1) with a hexane/isopropanol (3:2) mixture using UAE for almond oil extraction, achieving 50 g of oil per 100 g of almonds. However, several of these solvents, including hexane and chloroform, are classified as carcinogenic and pose serious health risks, including liver and kidney damage, as well as long-term neurological and reproductive toxicity (Carré et al., 2024; Cravotto et al., 2022). In contrast, ethanol and isopropanol provide safer, renewable alternatives to hexane and chloroform, yet their use in ultrasound-assisted extraction of papaya seed oil remains underexplored.

This study aims to investigate oil extraction using various techniques, including Soxhlet, hydraulic pressing, microwave-assisted, and ultrasound-assisted extraction, with single solvents (hexane, ethanol, and isopropanol), to perform a comparative screening and identify the most effective method. Ultrasound-assisted extraction (UAE) was selected based on and further optimized using single and mixed solvent system of ethanol and isopropanol, varying ultrasound intensity and extraction duration to determine optimal conditions. explore the synergistic effects of solvent mixtures under ultrasonic conditions.

## Materials and methods

### Materials

Papaya seeds Carica Papaya (Caricaceae) were obtained from La Reunion, France. The seeds were ground into powder using a Molino machine (M6_M61_50), with different sieve sizes (4 mm and 2 mm pore dimensions) to achieve varying particle sizes. All chemicals and reagents were used in analytical grade for this study.

### Methods

#### Comparative Screening of Extraction Methods

The experimental design aimed to compare different extraction methods and solvent systems to optimize the yield and quality of papaya seed oil. In the first stage, maceration and ultrasound-assisted extraction (UAE), together with microwave-assisted extraction, hydraulic micro-press, and Soxhlet extraction, were evaluated using pure solvents (100% ethanol and 100% isopropanol). Soxhlet extraction with hexane served as a conventional reference.

**Maceration** The maceration extraction method was conducted in two sets of triplicates, one with ethanol and the other with isopropanol. Ground papaya seeds (32 g) were mixed with pre-heated solvent at 50 °C (1:10 w/v). The suspension was subjected to continuous magnetic stirring for 30 min at 65 °C. Afterward, the suspension was filtered using a Whatman 202 filter paper (90 mm diameter), and the solvent was evaporated using a rotary evaporator to recover the extracted oil.

**Ultrasound-Assisted Extraction** Ultrasound-assisted extraction was performed using a 400 W ultrasonic processor (Hielscher GmbH, Stuttgart, Germany) operating at a frequency of 24 kHz. Extractions were carried out using two different solvents: pure isopropanol, pure ethanol. Prior to each treatment, the selected solvent was heated to 50 °C using a magnetic stirrer plate. A 32 g sample of raw material with a particle size smaller than 2 mm was mixed with the solvent at a constant solvent-to-sample ratio of 1:10 (w/v). Ultrasound was applied for 30 min. The ultrasonic probe (H14, Hielscher GmbH, Germany) was immersed directly in the mixture, and no external cooling or refrigeration system was used during treatment. After ultrasound application, the mixtures were allowed to cool, filtered using a Büchner funnel with Whatman 202 filter paper (90 mm diameter), and the solvents were evaporated using a rotary evaporator. The extracted oil was weighed for further analysis.

**Microwave-Assisted Extraction** A total of 16 g of ground papaya seeds (< 4 mm) were placed in a three-neck flask with ethanol or isopropanol (1:10 w/v). Triplicate extractions were performed for each solvent at 300 W for 30 min, as extending the extraction beyond 30 min may lead to degradation of thermolabile compounds (Khalfi et al., 2024). Following extraction, the liquid extracts were separated from papaya seeds by vacuum filtration on a Büchner funnel. The solvents were then evaporated at 50 °C using a rotary evaporator. After cooling, its mass was measured and recorded for further calculations.

**Hydraulic Micro-Press** 50 g of papaya seeds were soaked in 100 mL of ethanol for one hour. The seeds were then drained and placed in a pressing bag. Once in the pressing chamber, an initial manual pressure was applied, followed by hydraulic pressure reaching a maximum of 500 bars (Pressure was manually increased to 500 bar and maintained during pressing to ensure gradual oil release). The change in seeds mass was recorded. Three replicates were conducted using whole seeds and ground seeds (< 4 mm). The obtained oil was then separated from the solvent using a rotary evaporator at 50 °C.

**Soxhlet Extraction** Two grams of ground papaya seeds were placed in a cellulose extraction cartridge, fitted with cotton wool, and inserted into a Soxhlet apparatus. The apparatus was connected to a round-bottom flask with 400 mL of n-hexane and the extraction was conducted for 24 h at 121 °C. The resulting extract was then subjected to rotary evaporation at 50 °C and 150 rpm to remove the solvent. The extracted oil was placed in a drying oven at 50 °C for 1 h. After cooling, the mass of the oil was measured for further calculations. The experiment was performed in triplicate.

### Experimental Design for UAE Optimization

Based on preliminary results, ultrasound-assisted extraction (UAE) was selected for further optimization due to its higher extraction efficiency and improved oil quality compared with other techniques. Both maceration and ultrasound treatments were applied using three solvent systems: pure isopropanol, pure ethanol, and a mixed solvent consisting of 50:50 (v/v) ethanol–isopropanol.

Optimization experiments first assessed maceration with a 50:50 (v/v) ethanol-isopropanol solvent mixture at various temperatures (30 °C, 50 °C, 65 °C, and 80 °C) for 30 min to evaluate the effect of temperature on oil yield. The temperature of 65 °C was used for subsequent particle size tests and as a reference for comparison with ultrasound-assisted extraction. Further optimization of UAE was then carried out using the same 50:50 solvent system with seed particle sizes under different preheating conditions.

The final optimization phase compared maceration at 65 °C with ultrasound-assisted extraction performed at 200 W and 400 W, using 100% ethanol, 100% isopropanol, and their 50:50 mixture. Three treatment durations (5, 17.5, and 30 min) were tested to determine the most efficient extraction conditions (Table 1). The time range was selected based on literature (Junaid et al., 2023; Thilakarathna et al., 2023) and considering the absence of a cooling system, since prolonged sonication increases energy input and solvent temperature, which can affect ultrasound power transmission and lead to potential quality degradation. Therefore, 30 min was set as the upper limit and based on Section 2.2.1.2, 5 min as the lower limit, and 17.5 min as the central level.

### Fatty Acid Profile of Extracted Oil

5 µL of oil was collected using a positive displacement pipette and dissolved in chloroform to give a total volume of 1 mL. Using a methodology similar to Morad et al. (Chadni et al., 2023), samples were derivatized with TMSH as follows: 40 µL of oil dissolved in chloroform was mixed with 200 µL of TMSH at 0.25 mol/L in methanol, 320 µL of chloroform and 40 µL of unmethylated C13:0 at 12 mg/L. The C13:0 acted as an internal standard, enabling the extraction yield to be corrected. Samples were mixed and left at room temperature for 1 h.

After derivatization, fatty acids were analyzed by GC–MS/MS triple quadrupole (Shimadzu). Gas chromatography separation was performed on an HP-88 (Agilent)

**Table 1** Experimental design of ultrasound treatments

| Ultrasound Power (W) | Treatment time (min) | Solvent (%)* | Initial temperature (°C) | Final temperature (°C) |
|---|---|---|---|---|
| 0 | 5 | 0 | 65 | 65 |
| 0 | 17.5 | 0 | 65 | 65 |
| 0 | 30 | 0 | 65 | 65 |
| 0 | 5 | 50 | 65 | 65 |
| 0 | 17.5 | 50 | 65 | 65 |
| 0 | 30 | 50 | 65 | 65 |
| 0 | 5 | 100 | 65 | 65 |
| 0 | 17.5 | 100 | 65 | 65 |
| 0 | 30 | 100 | 65 | 65 |
| 200 | 5 | 0 | 50 | 45.2 |
| 200 | 17.5 | 0 | 50 | 74.6 |
| 200 | 30 | 0 | 50 | 76.2 |
| 200 | 5 | 50 | 50 | 56.4 |
| 200 | 17.5 | 50 | 50 | 73.2 |
| 200 | 30 | 50 | 50 | 79.2 |
| 200 | 5 | 100 | 50 | 52.1 |
| 200 | 17.5 | 100 | 50 | 72.7 |
| 200 | 30 | 100 | 50 | 71.1 |
| 400 | 5 | 0 | 50 | 58.2 |
| 400 | 17.5 | 0 | 50 | 80.8 |
| 400 | 30 | 0 | 50 | 80.2 |
| 400 | 5 | 50 | 50 | 63.8 |
| 400 | 17.5 | 50 | 50 | 75.8 |
| 400 | 30 | 50 | 50 | 79 |
| 400 | 5 | 100 | 50 | 65.3 |
| 400 | 17.5 | 100 | 50 | 77.4 |
| 400 | 30 | 100 | 50 | 79.3 |

*Solvent (%) indicates the proportion of ethanol used in the solvent system: 100% corresponds to pure ethanol, 0% to pure isopropanol, and 50% to a 1:1 ethanol–isopropanol mixture

100 m × 0.25 mm × 0.20 µm with Helium carrier gas at 2 ml/min. 1 µL of sample is injected with a split of 25. A temperature ramp is then applied as described by Chadni et al., (2023) starting at 50 °C and finishing at 230 °C in 34.5 min. Detection was carried out using a triple quadrupole mass spectrometer with an electron impact source. 2 acquisitions were made for each sample, one for identification in Scan mode and another in MRM mode for quantification. The transitions used in MRM mode are the same as those used by Pozzobon et al., (2020). A calibration range of 2 to 200 mg/L was used, prepared from Supelco 37 component FAME mix, CRM47885 from Sigma-Aldrich.

### Acidity Index

The acidity index is defined as the amount of potassium hydroxide (KOH) in milligrams required to neutralize the acids in one gram of oil. The test was done using the AOCS Ca 5a-40 method. 0.5 g of oil was mixed with 10 mL of 95% ethanol, followed by the addition of 2 to 3 drops of 1% phenolphthalein solution as a color indicator (Metouekel et al., 2024). The mixture was titrated with 0.1 N potassium hydroxide (KOH) solution until a faint pink color appears and persists for a few seconds, indicating the endpoint. The volume of KOH solution used during the titration was recorded.

The acid value ($I_a$) was calculated using the following equation:

$$Ia = \frac{C \times V \times 56.1}{m}$$

where $C$ is the concentration of KOH (mol/L), $V$ is the volume of KOH used to reach the endpoint (mL), $m$ is the mass of the oil sample (g), 56.1 is the molar mass of potassium hydroxide (g/mol).

The acid value is expressed as milligrams of KOH per gram of oil.

### Determination of Oil and Recovery Yield

The oil yield and oil recovery were calculated by comparing the amount of oil extracted to the initial amount of sample used, and by comparing the extracted oil to that obtained by Soxhlet extraction. The yield and recovery were determined using the following formulas:

$$Oilyield(\%) = {}^{amountofoilextracted}\Big/_{amountofsampleused}$$

$$Oilrecovery(\%) = {}^{oilyieldextracted(\%)}\Big/_{oilyieldsoxhlet(\%)}$$

## Statistical Analysis

Statistical analysis was carried out using SPSS software (Version 29.0.1.0, SPSS Inc., Chicago, USA). A one-way ANOVA was used to evaluate significant differences ($p < 0.05$) among the samples subjected to different applied treatments, and Tukey's HSD post hoc test was performed to determine pairwise differences between treatments. In addition, a three-way ANOVA was conducted to evaluate the main and interaction effects of ultrasound power, extraction time, and solvent composition on extraction yield and oil recovery. Response Surface Methodology (RSM) was applied to the experimental data using MATLAB software (Version R2025a, MathWorks Inc., Natick, MA, USA) to model and visualize the combined effects of process variables. A quadratic (poly22) regression model was used to describe the relationship between ultrasound power, treatment time, and extraction yield.

## Results and Discussion

### Effect of Different Extraction Techniques using Single Solvent on Oil Yield

The extraction yield of papaya seed oil varied significantly among the applied treatments, with mechanical pressing yielding the lowest values, while solvent-based extractions exhibited superior efficiency (Fig. 1), as expected.

Cold pressing of whole grains resulted in a yield of 2.95% (±0.68), which improved to 7.35% (±0.52) when the seeds were ground to 4 mm, highlighting the impact of particle size on oil recovery. According to Bunthan et al., (2023), applying a pressure of 50 MPa for 60 min at 60 °C to powdered Cambodian soybean seeds resulted in a maximum oil yield of 12.49%, confirming that particle size reduction plays a crucial role in enhancing oil recovery during mechanical pressing. Similarly, Zhang et al. (2018), reported that screw press extraction achieved only 13.9–15.2% of the total oil content, further highlighting the limitations of mechanical extraction methods compared with solvent-based techniques.

The maceration results highlight the influence of solvent polarity and extraction conditions on oil recovery from papaya seeds. At 65 °C, maceration with ethanol and isopropanol yielded approximately 16% and 17%, respectively, whereas Soxhlet extraction with n-hexane produced a higher yield (≈ 30.6%) due to continuous solvent renewal and the greater affinity of non-polar hexane for neutral lipids. This value is slightly lower than the 33.2% reported by Feltes et al., (2024) for Carica papaya seeds from the Formosa group in Brazil, likely reflecting differences in variety, geographical origin, which influence seed lipid content (Feltes et al., 2024). The lower yields obtained with polar solvents reflect their limited solubility for non-polar triglycerides and the slower mass transfer typical of passive diffusion during maceration. Comparable findings were reported by (Gosu et al., 2024), who observed that ethanol extraction of crude rotenone oil from *Millettia ferruginea* yielded around 20%, lower than the 25% obtained with chloroform and far below the yield achieved with Soxhlet extraction. This consistency across different plant matrices emphasizes that solvent polarity governs lipid recovery, with non-polar solvents enhancing extraction efficiency, while polar solvents such as ethanol favor the recovery of polar bioactive compounds and offer safer alternatives despite lower yields.

In contrast, Microwave-assisted extraction (MAE) with ethanol and isopropanol yielded 17.88% (±2.38) and 23.46% (± 1.38), respectively, with MAE-IPA demonstrating a higher extraction efficiency, likely due to its greater affinity for lipophilic compounds and microwave-induced cell disruption. Similar trends were recently reported for *Moringa oleifera* seeds, where MAE with ethanol achieved up to 42% oil yield under optimized conditions (solid–liquid ratio = 1:34, power = 175 W, extraction time = 1 h) (Souza et al., 2024). The lower yields observed may result from differences in seed composition, solvent ratio, and shorter irradiation time, which limit solvent–solute equilibrium and highlight the trade-off between extraction efficiency and compound integrity in MAE. Ultrasound-assisted extraction (UAE) with ethanol and isopropanol resulted in oil yields of 19.38% (±0.66) and 22.5% (±0.27), respectively, confirming the effectiveness of sonication in enhancing oil release. Comparable UAE yields have been reported for other oilseeds, Piasecka et al., (2023) optimized cranberry seed oil extraction with hexane, obtaining ~ 22% oil at 400 W for 11 min (Piasecka et al., 2023). The higher yield with less time was mainly due to the non-polar nature of hexane compared to the

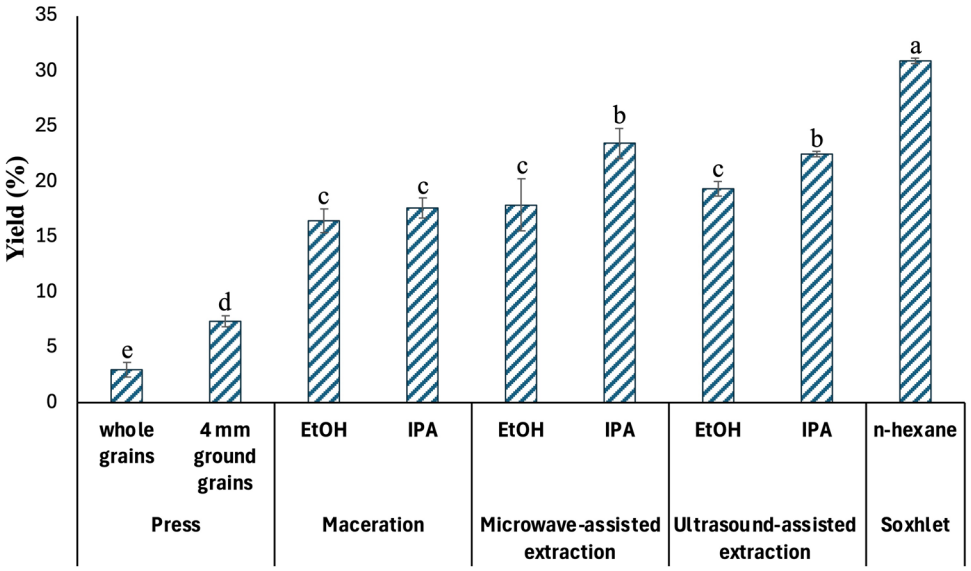



**Fig. 1** Comparison of extraction yields and efficiencies for different treatments: press (whole and ground grains), maceration, ultrasound and microwave (ethanol and isopropanol), and Soxhlet (hexane). Data are expressed as means ± standard deviation. Lowercase letters (**a**, **b**, **c**, **d**, **e**) indicate significant differences among the different extraction treatments ($p < 0.05$)

obtained results within this study, while ultrasound further enhanced oil release by disrupting the seed matrix. Moreover, Gaikwad et al., (2025) reported that canola oil extraction using hexane alone yielded 22.39%, whereas a hexane–isopropanol mixture increased extraction efficiency to 30.66% under optimized conditions (9.12% v/w solvent-to-solid ratio, 69.5 min ultrasonic treatment at 55 °C, 800 W). Comparable improvements were reported for chia and *Moringa peregrina* oils through optimization of solvent composition and liquid–solid ratio. The higher papaya seed oil yield obtained with isopropanol compared to ethanol in this study supports these observations, indicating that combining alcohols (ethanol-isopropanol) could further enhance extraction efficiency while maintaining the use of environmentally friendly solvents. The higher papaya seed oil yield obtained with isopropanol compared to ethanol supports these observations, suggesting that combining alcohols (ethanol-isopropanol) could further improve extraction efficiency while maintaining the use of environmentally friendly solvents.

It is important to note that, although lipid yields varied significantly between the extraction methods, the fatty acid composition of the recovered lipids remained comparable across all samples, as summarized in Table 2.

The extraction methods (pressing, MA, MAE, UAE, and soxhlet extraction) showed minimal variation in the fatty acid profiles of papaya seeds (Table 2), with no significant differences ($p > 0.05$). MUFA content, particularly oleic acid (C18:1), remained relatively stable across all methods, ranging from 68.65% to 71.36%, with slight differences observed in PUFA and linoleic acid (C18:2). The MA-EtOH method yielded the highest PUFA and α-linolenic acid contents. Overall, the extraction technique had a minor impact on the fatty acid composition, suggesting that these methods are similarly effective for extracting fatty acids from papaya seeds. These values are in agreement with the work of Goriainov et al., (2023), who reported oleic acid levels of 68.7–74.9% and low PUFA content in papaya seed oils extracted by Soxhlet from fruits originating from six different countries, confirming the robustness of this oleic-rich, low-PUFA profile(Goriainov et al., 2023). Similarly, Senrayan and Venkatachalam (2019), found that continuous ultrasound assisted extraction of papaya seed oil exhibited a similar fatty acid profile to other methods, with oleic acid (C18:1) being the predominant fatty acid at 75.89%. The oil contained 19.92% SFA, 76.10% MUFA, and 3.96% PUFA, and no significant differences in the fatty acid composition were observed compared to other extraction techniques (Senrayan & Venkatachalam, 2019). These consistent findings indicate that different extraction methods have a minor impact on the overall fatty acid composition of papaya seed oil.

## Acid Index

The results obtained for the acidity index of papaya seed oil, according to the different extraction methods, are presented in Table 3. Each extraction method showed a significant impact on the quality of the oil obtained, as measured by the acidity index. The Soxhlet extraction yielded the highest acidity index (90.12 mg KOH/g oil), likely due to prolonged heat exposure during the 24-h extraction and the drying process of the seeds (Fonseca et al., 2023). This extended exposure to heat could degrade the quality of the oil, leading to the release of free fatty acids, and resulting in a higher acidity index. In contrast**,** Nebolisa et al., (2023) and Kumar et al., (2025) reported acid values of 3–4 mg KOH/g for oils extracted by Soxhlet under milder conditions (4–8 h at 60–90 °C) for *Moringa oleifera* and sunflower seed oil, indicating stable oils with minimal hydrolysis and oxidation. The markedly higher value observed in this study can therefore be attributed to the prolonged extraction time and higher temperature applied in the Soxhlet process.

**Table 2** Comparison of fatty acid composition (MUFA, PUFA, and specific fatty acids) across different treatments: press (whole and ground grains), maceration (MA-EtOH and MA-IPA), microwave-assisted extraction (MAE-EtOH and MAE-IPA), ultrasound-assisted extraction (UAE-EtOH and UAE-IPA), and Soxhlet (n-hexane)

| | MUFA | PUFA | Oleic acid (C18:1) | Linoleic acid (C18:2) | α-linolenic acid (C18:3) |
|---|---|---|---|---|---|
| Press (whole grains) | 71.92 ± 0.15 | 5.57 ± 0.18 | 70.81 ± 0.15 | 5.32 ± 0.16 | 0.25 ± 0.03 |
| Press (4 mm ground grains) | 72.15 ± 0.17 | 5.67 ± 0.10 | 71.08 ± 0.17 | 5.32 ± 0.10 | 0.25 ± 0.01 |
| MA-EtOH | 69.99 ± 1.39 | 7.35 ± 1.06 | 68.65 ± 1.48 | 6.98 ± 0.98 | 0.38 ± 0.08 |
| MA-IPA | 72.09 ± 0.43 | 6.57 ± 1.00 | 70.81 ± 0.33 | 6.26 ± 0.94 | 0.31 ± 0.06 |
| MAE-EtOH | 71.81 ± 0.59 | 5.90 ± 0.58 | 70.67 ± 0.70 | 5.63 ± 0.55 | 0.27 ± 0.04 |
| MAE-IPA | 72.09 ± 0.09 | 6.77 ± 1.13 | 70.83 ± 0.29 | 6.43 ± 1.06 | 0.34 ± 0.08 |
| UAE-EtOH | 71.14 ± 1.36 | 6.24 ± 0.86 | 69.93 ± 1.47 | 5.97 ± 0.80 | 0.28 ± 0.06 |
| UAE-IPA | 71.75 ± 0.47 | 5.72 ± 0.61 | 70.55 ± 0.52 | 5.46 ± 0.58 | 0.25 ± 0.04 |
| n-hexane | 72 ± 2.08 | 5.82 ± 0.68 | 71.36 ± 2.05 | 5.57 ± 0.67 | 0.25 ± 0.02 |

Data are expressed as means ± standard deviation

**Table 3** Effect of extraction method and solvent on the acid index (mg KOH/g oil) of extracted oils

| Method | Acid Index (mg KOH/g oil) | Relative Acid index (%) * |
|---|---|---|
| Soxhlet | $90.12 \pm 2.09^{a}$ | 100 |
| Microwave with ethanol | $17.58 \pm 1.71^{e}$ | 19.51 |
| Microwave with isopropanol | $27.11 \pm 2.12^{d}$ | 30.08 |
| Ultrasound with ethanol | $6.86 \pm 2.16^{fg}$ | 7.61 |
| Ultrasound with isopropanol | $9.0 \pm 2.25^{fg}$ | 9.99 |
| Press with whole seeds | $11.0 \pm 1.56^{f}$ | 12.21 |
| Press with ground seeds | $58.72 \pm 2.34^{c}$ | 65.16 |
| Maceration with ethanol (10 min) | $5.0 \pm 1.47^{g}$ | 5.55 |
| Maceration with ethanol (30 min) | $69.5 \pm 3.47^{b}$ | 77.12 |
| Maceration with isopropanol (10 min) | $5.13 \pm 0.56^{g}$ | 5.69 |
| Maceration with isopropanol (30 min) | $28.6 \pm 1.47^{d}$ | 31.74 |

*The relative acidity index was determined using the Soxhlet extraction as the reference**.** Lowercase letters (a, b, c, d, e, f, g) indicate significant differences in acid index among the different extraction treatments ($p < 0.05$)

The microwave-assisted extraction (MAE) with ethanol yielded an acidity index of 17.58 mg KOH/g oil, which was lower than that obtained by the Soxhlet method. In contrast, MAE with isopropanol produced a higher value of 27.11 mg KOH/g oil, indicating that ethanol, due to its higher polarity, allows more efficient extraction and better preservation of oil quality. Ultrasound-assisted extraction (UAE) resulted in the lowest acidity indices among all methods tested, with $6.86 \pm 2.16$ mg KOH/g oil for ethanol and $9.0 \pm 2.25$ mg KOH/g oil for isopropanol. These results confirm that the milder processing conditions and shorter extraction time of UAE help preserve the physicochemical integrity of the oil. Doan et al. (Doan et al., 2020) reported an acidity value of 3.66 mg KOH/g for papaya seed oil extracted using ultrasound-assisted extraction with hexane, confirming that this technique produces oils with a lower acidity index than conventional extraction methods (Doan et al., 2020). Moreover, Santos et al., (2025) demonstrated that ultrasound-assisted extraction (UAE) also reduces both acidity and peroxide levels below regulatory limits in Brazil nut oil, owing to its gentle processing conditions and reduced oxidative degradation compared with conventional solvent extraction.

Regarding the press extraction, whole seeds produced oil with an acidity index of 11 mg KOH/g, while using ground seeds resulted in a much higher index, 58.72 mg KOH/g. This significant difference can be attributed to the effect of grinding the seeds, which may lead to the release of hydrolytic enzymes or enhanced contact with moisture and oxygen, promoting lipid hydrolysis.

The maceration results showed a significant increase in the acidity index over time. With ethanol, the index rose from 5.0 to 69.5 mg KOH/g between 10 and 30 min, while for isopropanol, it increased from 5.13 to 28.6 mg KOH/g. Ethanol resulted in a more aggressive extraction, leading to a sharper rise in acidity.

In summary, among the various methods studied, ultrasound-assisted extraction (UAE) with ethanol was the most effective for obtaining high-quality papaya seed oil, characterized by a low acidity index. Although both ethanol and isopropanol produced oils with low acidity after 10 min of maceration, with no significant differences were observed compared to UAE with ethanol or isopropanol (Table 3). However, the corresponding yields were much lower ($10.31 \pm 1.49$ and $14.18 \pm 0.56$%, respectively). In contrast, UAE with ethanol achieved a similarly low acidity index with a higher yield in a shorter processing time, confirming its superior extraction efficiency and overall performance.

### Effect of Temperature and Particle Size on Oil Yield using EtOH-IPA

The extraction yield increased from 14.28% at 30 °C to 20.88% at 80 °C, confirming that rising temperature enhances solvent diffusivity and mass transfer by reducing viscosity and increasing solute solubility (Fig. 2). A pronounced increase was observed between 30 °C and 50 °C, attributed to improved solvent penetration and partial disruption of the cellular matrix (Krinski et al., 2025), which facilitated lipid release. Beyond 50 °C, the extraction rate increased more gradually, suggesting that solute–solvent equilibrium had been reached and additional heating provided only marginal gains in yield (Bhadange et al., 2024; Doan et al., 2020).

As the extraction temperature increases, oil solubility in the solvent improves due to reduced viscosity and enhanced molecular diffusion, which accelerate mass transfer and promote oil release from the solid matrix. However, beyond the optimal temperature range, extraction efficiency declines, likely as a result of oil gumming or structural changes within the matrix that reduce effective solvent-solid interaction (Mkhize et al., 2023). Under such conditions, hydrolytic and oxidative degradation may occur, leading to the formation of secondary products and preventing further yield improvement.

The selection of a binary solvent system (ethanol and isopropanol) was based on its intermediate polarity, allowing for the extraction of both non-polar lipids and some polar bioactive compounds. Traditionally, hexane is the preferred solvent for lipid extraction due to its strong affinity for non-polar compounds; however, the ethanol-isopropanol mixture achieved comparable extraction yields while potentially enhancing the recovery of phytochemicals and minor lipid fractions. The increased efficiency of this solvent system can be attributed to its ability to disrupt lipid-protein interactions and improve solvent-matrix interactions, thus facilitating lipid solubilization and extraction.

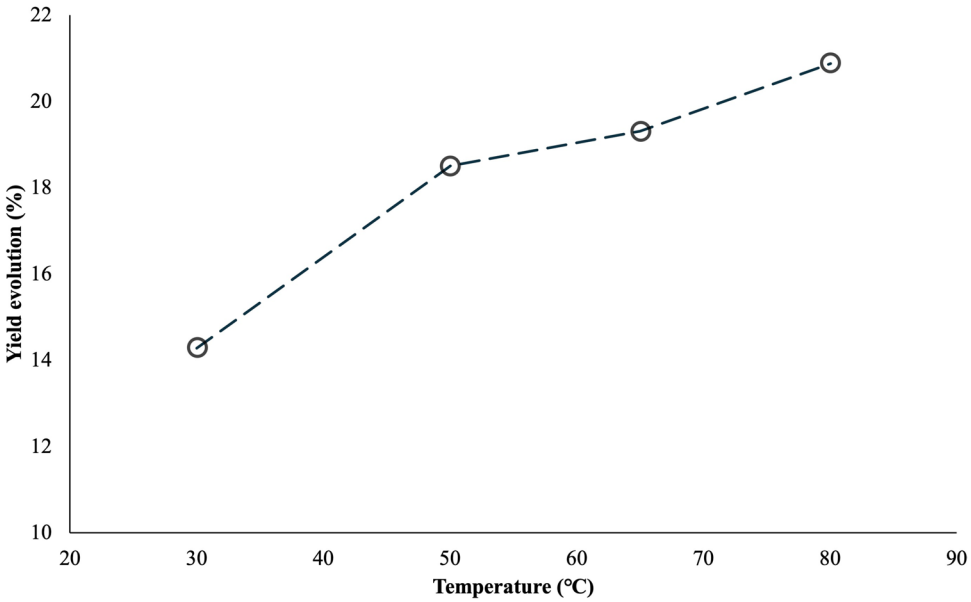



**Fig. 2** Extraction yield (%) under different maceration temperatures (°C), showing the effect of temperature on extraction efficiency

The role of particle size was evaluated by comparing multiple size distributions, revealing a clear correlation between smaller particle sizes and higher extraction yields (Fig. 3). This trend arises because finer particles present a greater surface area for solvent penetration and shorter diffusion paths, thereby enhancing mass transfer and oil release (Nastić et al., 2025). Recent studies confirm that finer particles markedly enhance extraction yield, with Gaikwad et al., (2025) identifying an optimal range of 100–400 µm, and Nastić et al., (2025) demonstrating a sixfold yield reduction when particle size increased to ~ 1000 µm.

A comparison between maceration and ultrasound-assisted extraction (UAE) showed that UAE consistently yielded higher extraction results across all particle sizes. This improved performance is due to the increased solvent penetration and mass transfer facilitated by the ultrasound treatment. The cavitation effect further increases solvent agitation and contact with solid particles, thereby improving extraction efficiency and helping preserve thermolabile compounds (Santos et al., 2025). When performed at 400 W for 30 min, UAE enhanced extraction efficiency even further, particularly in smaller particles. The combination of the ethanol-isopropanol system with ultrasound demonstrated a synergistic effect, improving overall efficiency. This observation is consistent with findings from, who reported that coupling ultrasound with a ternary mixed solvent system (ethyl acetate + water + NADES) increased cottonseed oil recovery from 85.18% to 90.68%, confirming a synergistic effect between ultrasonic cavitation and solvent composition (Kalkan & Maskan, 2025a).

Despite hexane being the conventional solvent due to its strong lipid affinity, the ethanol-isopropanol system

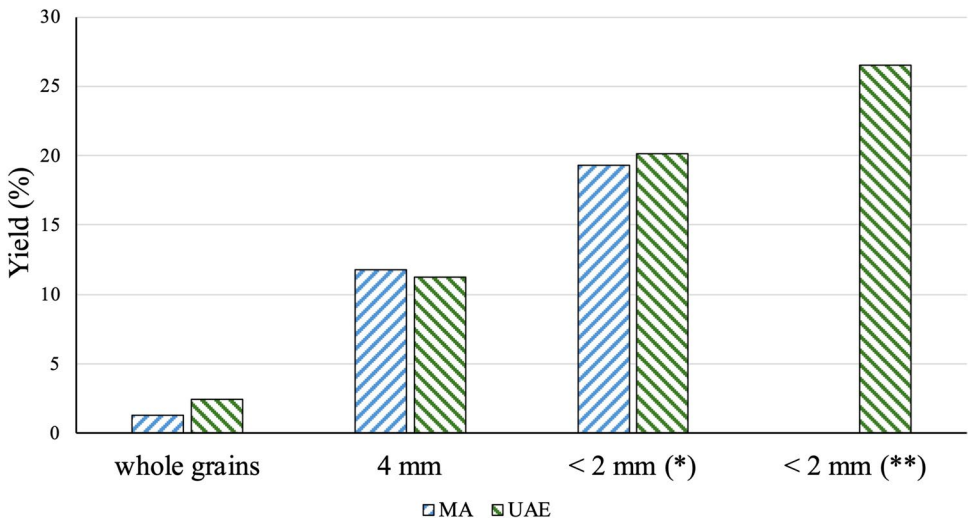



**Fig. 3** Extraction yield (%) for various grinding sizes subjected to maceration (MA) and ultrasound (UAE), evaluating the influence of particle size and pre-heating on extraction efficiency. Legend: (*) = without pre–heating the solvent for UAE treatment; (**) = with pre–heating the solvent for UAE treatment

achieved competitive extraction efficiency while offering environmental advantages. These results highlight that ultrasound-assisted extraction combined with mixed green solvents can deliver yields comparable to petrochemical solvents while enhancing process sustainability.

## Optimization of Ultrasound-Assisted Extraction (UAE) using Mixed Solvent

**Effect of Ultrasound Power, Treatment Time, and Solvent Composition** Three-way ANOVA revealed that ultrasound power (P), treatment time (T), and solvent composition (S) had a highly significant effect on extraction yield and oil recovery ($p < 0.001$), together with all their interactions (Table 4).

The extraction yield was significantly influenced by ultrasound treatment and solvent composition, while thermal treatment alone showed a limited impact (Table 4). Under thermal maceration at 65 °C (Table 4), extraction yields initially increased with time but showed a noticeable decline after 30 min across all solvent systems, with the exception of the 50:50 ethanol:isopropanol mixture. The yield obtained using pure isopropanol (IPA) decreased from 20.78% at 17.5 min to 17.48% at 30 min, and a similar trend was observed with 100% EtOH. This reduction likely results from solvent evaporation during heating, which lowers the solvent-to-solid ratio and limits solute diffusion. In contrast, the 50% ethanol–isopropanol mixture maintained stable yields, likely due to its lower volatility and balanced polarity that preserved solvent-matrix contact. Similarly, Souza et al., (2020) reported that an ethanol-isopropanol mixture (1:1, v/v) achieved a 41.13% almond oil yield under prolonged extraction (180 min at 75 °C), outperforming individual solvents such as hexane, highlighting the advantage of polarity-balanced solvent systems.

In contrast, ultrasound treatment (Table 4), even when resulting in similar final temperatures due to cavitational heating, substantially increased yields. Notably, At 200 W for 30 min with the 50% ethanol-isopropanol mixture, the yield reached 26.57%, while 26.71% was obtained at 400 W. These values were not significantly different ($p > 0.05$, one-way

**Table 4** Effect of ultrasound power, extraction duration, and solvent composition (*Solvent (%) indicates the proportion of ethanol used in the solvent system: 100% corresponds to pure ethanol, 0% to pure isopropanol, and 50% to a 1:1 ethanol–isopropanol mixture) on extraction yield (%) and oil recovery. T*hree*-way ANOVA indicated significant effects ($p < 0.00$*1*) of power (P), treatment time (T), and solvent (S), as well as their interactions (P×T, P×S, T×S, and P×T×S)

| Ultrasound power (W) | Treatment time (min) | Solvent (%)* | Yield (%) | Oil Recovery (%) |
|---|---|---|---|---|
| 0 | 5 | 0 | 20.42 ± 0.13 | 66.05 ± 0.42 |
| 0 | 17.5 | 0 | 20.78 ± 0.22 | 67.24 ± 0.71 |
| 0 | 30 | 0 | 17.48 ± 0.20 | 56.56 ± 0.66 |
| 0 | 5 | 50 | 17.95 ± 0.16 | 58.06 ± 0.50 |
| 0 | 17.5 | 50 | 19.44 ± 0.15 | 62.90 ± 0.47 |
| 0 | 30 | 50 | 19.67 ± 0.24 | 63.64 ± 0.76 |
| 0 | 5 | 100 | 20.46 ± 0.29 | 66.19 ± 0.95 |
| 0 | 17.5 | 100 | 20.34 ± 0.11 | 65.81 ± 0.37 |
| 0 | 30 | 100 | 16.51 ± 0.09 | 53.40 ± 0.30 |
| 200 | 5 | 0 | 23.41 ± 0.11 | 75.73 ± 0.36 |
| 200 | 17.5 | 0 | 22.66 ± 0.25 | 73.31 ± 0.80 |
| 200 | 30 | 0 | 25.51 ± 0.29 | 82.52 ± 0.93 |
| 200 | 5 | 50 | 20.49 ± 0.22 | 66.29 ± 0.71 |
| 200 | 17.5 | 50 | 23.48 ± 0.28 | 75.97 ± 0.91 |
| 200 | 30 | 50 | 26.57 ± 0.29 | 85.97 ± 0.94 |
| 200 | 5 | 100 | 8.42 ± 0.26 | 27.23 ± 0.84 |
| 200 | 17.5 | 100 | 16.61 ± 0.12 | 53.73 ± 0.37 |
| 200 | 30 | 100 | 21.72 ± 0.10 | 70.26 ± 0.34 |
| 400 | 5 | 0 | 22.49 ± 0.37 | 72.75 ± 1.21 |
| 400 | 17.5 | 0 | 23.71 ± 0.26 | 76.72 ± 0.83 |
| 400 | 30 | 0 | 22.64 ± 0.27 | 73.26 ± 0.86 |
| 400 | 5 | 50 | 20.66 ± 0.25 | 66.83 ± 0.80 |
| 400 | 17.5 | 50 | 24.53 ± 0.45 | 79.36 ± 1.45 |
| 400 | 30 | 50 | 26.71 ± 0.18 | 86.42 ± 0.57 |
| 400 | 5 | 100 | 13.52 ± 0.27 | 43.74 ± 0.88 |
| 400 | 17.5 | 100 | 11.66 ± 0.13 | 37.73 ± 0.42 |
| 400 | 30 | 100 | 19.69 ± 0.29 | 63.70 ± 0.93 |

| UAE-Power (P) | Treatment time (T) | Solvent (S) | PxT | PxS | TxS | PxTxS |
|---|---|---|---|---|---|---|
| * | * | * | * | * | * | * |

ANOVA), indicating a plateau in extraction efficiency (Senrayan & Venkatachalam, 2019).

Furthermore, comparing treatments that reached similar final temperatures (≈80 °C), it is evident that ultrasound played a dominant role. Thermal maceration at 80 °C yielded only 20.88% (Fig. 2), whereas ultrasound treatments that reached comparable temperatures due to ultrasonic heating (200 W or 400 W for 30 min) achieved yields above 25%. This indicates that the increase in yield is mainly enhanced by ultrasound rather than by temperature effects.

Oil recovery from papaya seeds using UAE, calculated relative to Soxhlet extraction (30.91%) as the reference, showed substantial variation across treatment conditions. The highest oil recovery was achieved under the condition of 400 W ultrasound power, 30 min, and 50% ethanol-isopropanol, resulting in 85.86% recovery, followed closely by 200 W, 30 min, and 50% EtOH-IPA, yielding 85.25%. These values considerably exceed the 73% maximum recovery previously reported for papaya seed oil using UAE at 700 W ultrasound power (hexane as solvent) and longer extraction times (Samaram et al., 2015), indicating the superior efficiency of the optimized parameters employed in the present study. In comparison, Kalkan and Maskan, (2025c) reported 80.44% oil recovery from cottonseed using ultrasound–homogenization with ethyl acetate as a single green solvent (65.7 min, 30.1 °C, solvent-to-solid ratio 5.6:1), which is lower than the best UAE yield obtained here with the binary ethanol-isopropanol system. In a subsequent study, the same authors increased cottonseed oil recovery to 90.68% by employing a mixed NADES-ethyl acetate-water solvent system (Kalkan & Maskan, 2025a). Taken together with the present results, this pattern supports the advantage of moving from single green solvents to appropriately designed mixed solvent systems under ultrasound to enhance oil extraction efficiency. The enhanced recoveries observed in this study can be attributed to the combined effects of the use of a 50% EtOH-IPA binary solvent system, which proved to be highly effective for oil recovery, offering a significant advantage over traditional hexane-based extraction methods.

**Response Surface Modeling of Ultrasound-Assisted Extraction** The relationship between extraction yield (%) and the independent variables, ultrasound power (x) and treatment time (y), was described using a second-order polynomial model (Eq. 1):

$$f(x,y) = a + bx + cy + dx^2 + exy + fy^2 \quad (1)$$

where $a$ is the intercept, $b$ and $c$ are the linear coefficients (ultrasound power and treatment time), $d$ and $f$ are the quadratic terms, and $e$ represents the interaction between ultrasound power and treamtent time (Table 5).

The response surface and contour plots (Fig. 4) clearly demonstrate how ultrasound-assisted extraction (UAE) intensity and treatment time influenced oil yield under the three solvent systems tested. In the mixed-solvent system, both parameters had significant positive effects on oil recovery, with the yield progressively increasing up to 400 W and 30 min, where the highest values were observed. However, the treatment at 200 W for 30 min resulted in a comparable extraction yield, showing no statistically significant difference ($p > 0.05$) from that obtained at 400 W according to one-way ANOVA. This results are consistent with the high recoveries reported by Kalkan and Maskan, (2025b), who achieved 86.40% oil recovery using ultrasound-assisted homogenization optimized by RSM with hexane, a value comparable to the ≈ 85% obtained in the present study under milder conditions (200 W, 30 min) using a greener 50% ethanol-isopropanol mixed solvent. Moreover, Matei et al., (2023) reported an 87% recovery of blackberry seed oil under optimized ultrasound conditions with hexane, further confirming the effectiveness of ultrasound-assisted extraction, though the use of conventional solvent limits its environmental sustainability.

The fitted quadratic model exhibited excellent adequacy ($R2 = 0.973$, $RMSE = 0.51$, $AIC = -24.87$), with

**Table 5** Regression coefficients, significance levels (p-values), and model performance parameters (R2, RMSE, AIC) of the quadratic (poly22) models (Eq. 1) describing extraction yield (%) as a function of ultrasound power and treatment time under different solvent systems

| | Isopropanol (100%) | | Mixed solvent | | Ethanol (100%) | |
|---|---|---|---|---|---|---|
| Coefficient | Estimate | p-Value | Estimate | p-Value | Estimate | p-Value |
| a | 20.29 | < 0.001 | 16.685 | < 0.001 | 19.691 | < 0.001 |
| b | 0.029 | < 0.001 | 0.025 | < 0.001 | −0.0426 | 0.018 |
| c | 0.018 | 0.249 | 0.205 | 0.003 | −0.1107 | 0.563 |
| d | −0.000065 | < 0.001 | 0.00005 | < 0.001 | 0.000036 | 0.544 |
| e | 0.00031 | 0.062 | 0.000 | < 0.001 | 0.00101 | 0.022 |
| f | −0.0025 | 0.825 | −0.003 | 0.108 | 0.00329 | 0.613 |
| $R^2$ | 0.7815 | | 0.9728 | | 0.5810 | |
| RMSE | 1.1573 | | 0.5052 | | 4.3704 | |
| AIC | 68.9497 | | −24.8685 | | 68.9497 | |
| AIC of Removed non-significant coefficient | 14.1045 | | −21.985 | | 62.9497 | |

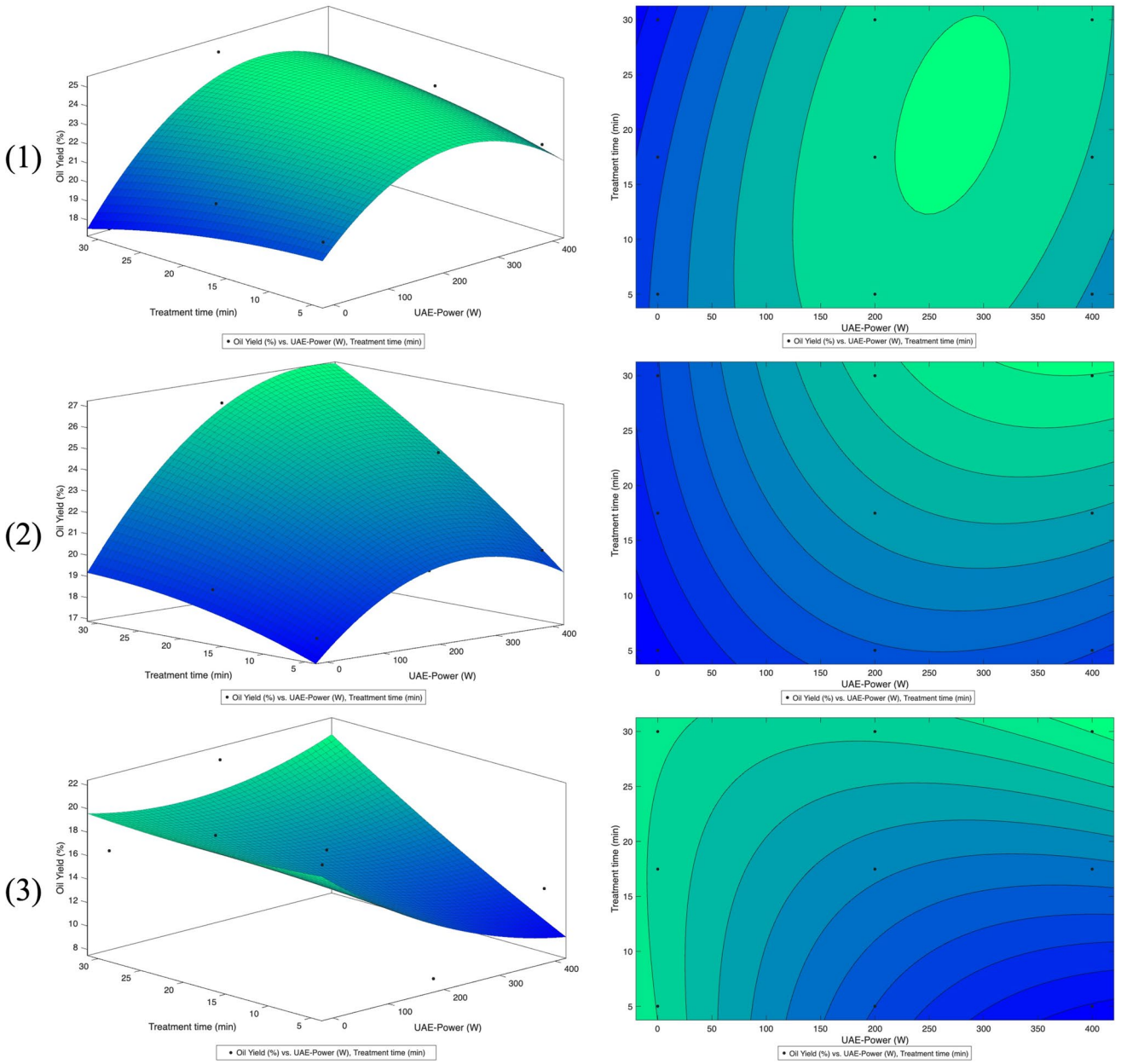



**Fig. 4** Response surface (left) and contour (right) plots illustrating the combined effects of ultrasound power (W) and treatment time (min) on extraction yield (%) under three solvent systems: (1) pure isopropanol, (2) 50% ethanol-isopropanol mixture, and (3) pure ethanol. The fitted quadratic (poly22) models underlying these plots are detailed in Table 5

significant linear effects of intensity ($b = 0.025$, $p < 0.001$) and time ($c = 0.205$, $p = 0.003$), as well as significant quadratic ($d = 0.00005$, $p < 0.001$) and interaction ($e = 0.000$, $p < 0.001$) terms (Table 5). This interaction highlights the synergistic influence of ultrasound intensity and extraction time on oil yield in the mixed solvent. In contrast, the isopropanol and ethanol models showed weaker predictive ability ($R2 = 0.78$ and 0.58) and higher RMSE, indicating limited sensitivity to UAE parameters. The enhanced extraction observed with the mixed solvent is attributed to synergistic polarity effects that intensify cavitation and mass transfer, facilitating greater solute diffusion and oil release than single solvents. Overall, 200 W for 30 min in the mixed-solvent system represents an optimal balance between extraction efficiency and energy consumption.

### Effect of Energy Consumed on Yield (%)

At 200 W, oil yields increased progressively with both extraction time and specific energy input (Fig. 5). For instance,

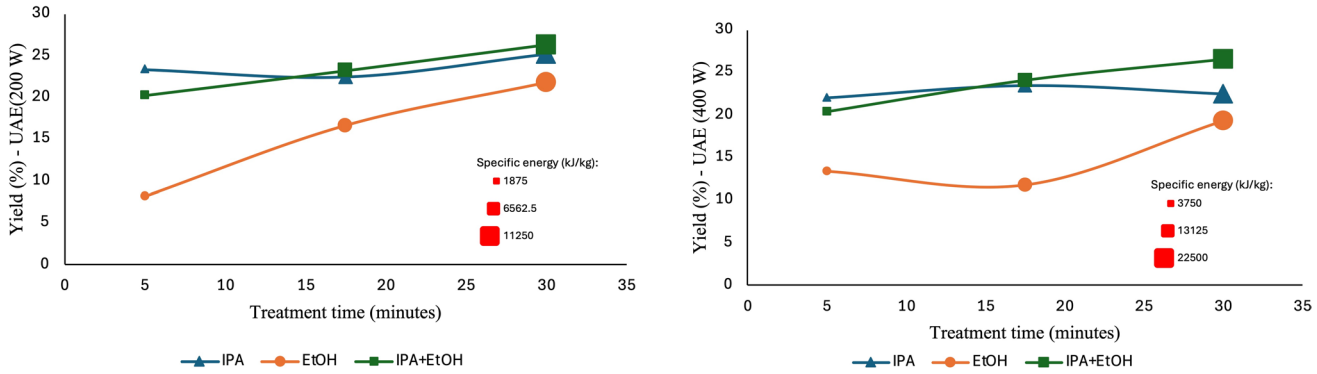



**Fig. 5** Effect of specific energy (kJ/kg) on yield (%) for different ultrasound power levels and solvents extractions

with pure isopropanol (0% EtOH), yield rose from 23.31% at 1875 kJ/kg (5 min) to 25.18% at 11250 kJ/kg (30 min). A comparable pattern was observed using the 50% EtOH-IPA mixture, where yield reached 26.34% at the same energy level. However, when the ultrasound power was increased to 400 W, resulting in a maximum specific energy of 22500 kJ/kg, the additional gains in oil yield were marginal and not significant ($p > 0.05$). For example, under these intensified conditions, the yield only slightly improved to 26.53% with the 50% EtOH-IPA solvent. This behavior strongly indicates a saturation point, beyond which increasing power or energy input does not substantially enhance oil recovery. This plateau effect is likely caused by cavitation shielding, where excessive bubble formation interferes with effective energy transmission (Choudhary et al., 2023; Zhang et al., 2017), and thermal saturation, where rising temperatures reduce cavitation efficiency and may even degrade the target compounds. Moreover, Bodea et al., (2025) reported that ultrasound-assisted extraction can achieve high extraction efficiencies under milder conditions and substantially lower energy consumption than conventional extraction methods, further supporting the advantage of operating at reduced power levels. Therefore, operating at 200 W appears more energy-efficient, as it achieves comparable extraction yields to 400 W with significantly lower specific energy consumption, offering a cost-effective extraction approach.

## Conclusion

This study demonstrated that ultrasound-assisted extraction (UAE) using a 1:1 ethanol-isopropanol mixture is an effective method for recovering papaya seed oil. Under optimized conditions (200 W, 30 min), the process achieved about 85% oil recovery relative to Soxhlet extraction, confirming the efficiency of the mixed green solvent system. The synergistic interaction between solvent polarity and ultrasonic cavitation enhanced extraction performance while enabling the use of food-grade, low-toxicity solvents instead of hexane.

From an industrial perspective, UAE offers shorter extraction time, reduced solvent use, and lower energy demand, supporting its potential for scale-up through continuous or multi-probe systems. However, to confirm industrial feasibility, future studies should evaluate solvent recovery efficiency, energy cost, and performance consistency at larger scales.

Although this work was limited to a single papaya seed variety and the oil composition was assessed only for single-solvent extractions, these findings highlight the promise of the mixed green solvent system. Further research should include detailed compositional and stability evaluations under optimized UAE conditions to validate the broader applicability of this green extraction approach.

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**Authors Contribution** Neamtallah Assaf: Methodology, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing. Amira Metouakel: Investigation, Data curation, Writing – review & editing. Lynn Rhayem: Investigation, Writing – review & editing. Cedric Guerin: Supervision, Validation, Writing – review & editing. Malak Tabib: Investigation, Writing – review & editing. Shuli Liu: Investigation. Massimiliano Rinaldi: Supervision, Writing – review & editing. Emma Chiavaro: Supervision. Gwenn Atheaux: Funding support. Nabil Grimi: Project administration, Conceptualization, Supervision, Validation, Writing – review & editing.

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**Data Availability** The data will be made available upon reasonable request.

## Declarations

**Competing Interest** The authors declare no competing interests.

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