Teknomekanik, Vol. 9, No. 3, 2026, pp. 302-329
e-ISSN: 2621-8720 p-ISSN: 2621-9980

Systematic solvent screening and selection for papaya seeds oil (PSO) extraction

Misbahudin Alhanif[1,2], Andri Cahyo Kumoro[1,2*], Dyah Hesti Wardhani[1,2]

[1] Doctorate Program of Chemical Engineering, Faculty of Engineering, Universitas Diponegoro, **Indonesia**
[2] Institute of Food and Remedies Biomaterial, Department of Chemical Engineering Faculty of Engineering, Universitas Diponegoro, **Indonesia**

*Corresponding Author: andrewkomoro@che.undip.ac.id
Received: 23 January 2026; *Revised:* 10 June 2026; *Accepted:* 20 June 2026

Cite this https://doi.org/10.24036/teknomekanik.v9i3.53672

Abstract: Papaya seed oil (PSO) is a promising sustainable edible oil, owing to its high oleic acid content. PSO extraction can be carried out by first determining the appropriate solvent, method, and operating conditions. Solvent selection significantly influences extraction efficiency, energy demand, and operating cost. However, selecting a solvent via quantitative experiments across various solvents is expensive and time-consuming. Therefore, this study proposes a systematic framework to screen 50 solvents using key criteria: Hansen solubility parameters (HSPs), physical properties, and safety, health, and environment (SHE) aspects. Five selected solvents, including ethyl acetate, acetone, n-hexane, ethanol, and water, were combined in binary and ternary mixtures for experimental testing. The main findings showed that PSO extraction using the Soxhlet method for 6 hours with a binary mixture of ethyl acetate–n-hexane (77.20 and 22.80 vol%) produced the highest yield of 19.28 ± 0.21 wt%, followed by a ternary mixture of n-hexane–acetone–ethanol (64.58, 8.13, and 27.28 vol%) with a yield of 19.15 ± 0.22 wt%. Despite its slightly lower yield, the ternary mixture of n-hexane–acetone–ethanol has physical properties that may improve mass transfer and reduce energy demand during extraction and separation. A preliminary assessment based on current market price indicates that the ternary solvent mixture is cheaper (997.5 USD/MT) than the binary solvent of ethyl acetate–n-hexane (1247.3 USD/MT). Therefore, while identifying the ideal solvent for PSO extraction depends on specific factors, this study offers a systematic approach to solvent selection that streamlines screening and reduces the number of solvents requiring experimental testing.

Keywords: extraction; papaya seeds oil; solvent mixture; solvent screening

1. Introduction

Papaya *(Carica papaya L.)* is a fruit that is widely cultivated in equatorial regions [1], with Indonesia among its main producers. Processing papaya for consumption generates significant waste, especially seeds, which account for 15–20% of the fruit mass [2], [3]. Given that papaya seed oil (PSO) constitutes 27–34% of seed weight [4] and is rich in oleic acid and nutraceuticals, it offers promising opportunities for high-quality food and industrial applications [5]. However, the potential of these seeds remains largely untapped, and the development of PSO as a viable product is hampered by the lack of a robust and environmentally friendly extraction method. Current processing often relies on empirical extraction methods that use a single solvent or a mixture of empirically selected solvents, or consider only one aspect. Therefore, it is crucial to establish a PSO extraction framework that balances yield performance with safety and environmental impact.

Extraction performance is governed by key parameters, such as solvent type, extraction method, and the implemented operating conditions [6]. PSO can be extracted using conventional methods, such as Soxhlet extraction, or non-conventional methods, such as ultrasound or microwave [7]. Among conventional methods, Soxhlet extraction is often used as the standard for extracting analytes from solid samples. This preference is due to its simplicity, cost-effectiveness, ease of use, and its ability to maintain high temperatures and perform simultaneous extraction without additional filtration [6], [8]. Nevertheless, despite these advantages, the Soxhlet method has several disadvantages, including long extraction times, large solvent consumption, high energy requirements, and thermal degradation of heat-sensitive compounds [9], [10].

On the other hand, to achieve an efficient PSO extraction process, the solvent must be selected appropriately based on solubility parameters, boiling points, and SHE (safety, health, and environment) considerations. Based on the principle of "like dissolves like", Hansen Solubility Parameters (HSPs) are used to match the polarity of the solvent to the solute to improve extraction performance [6], [11]. Technically, the selection of solvents based on HSPs refers to the composition data and thermophysical properties of PSO, such as molecular weight and normal boiling point, supported by comprehensive literature on the characteristics of the constituent fatty acids [4], [12], [13], [14], [15], [16]. In addition to HSPs' suitability, the solvent's boiling point must be set low enough to facilitate extraction (especially Soxhlet) and separation, thereby potentially reducing overall energy consumption. However, solvents with very low boiling points should also be avoided, as their volatility can cause significant solvent loss during extraction [17]. Furthermore, in potential solvent extraction for food, pharmaceutical, or cosmetic applications, reducing the use of petroleum-derived solvents and selecting safer alternatives can help reduce health and environmental impacts.

In solvent selection, the CHEM21 guide classifies solvents based on SHE criteria into four categories: recommended, problematic, hazardous, and highly hazardous [18]. While these categories serve as important guidelines for solvent selection, the classification of hazardous and highly hazardous solvents often varies across regulatory agencies and industries [19], [20]. To date, research on solvent selection for PSO extraction remains limited, particularly regarding HSPs, boiling points, and SHE. Most studies still use a single solvent, such as n-hexane, petroleum ether, or ethanol [21], [22], [23], [24]. Previous studies reported that n-hexane yielded slightly superior extraction efficiencies to petroleum ether [22], and both were superior to more polar solvents such as ethanol [25]. Although its use is permitted, especially in food applications under the European Union Directive 2009/32/EC [26], n-hexane is recognized as a toxic solvent and has long been associated with occupational diseases. Consequently, it is classified as STOT RE 2 under the REACH regulation, indicating that it is suspected of causing organ damage following prolonged or repeated exposure [27]. In addition, n-hexane is relatively expensive compared to other solvents such as petroleum ether and ethanol [28], [29]. Therefore, the quantity of this solvent should be reduced by using binary or ternary mixtures with other solvents, which can also improve its extraction performance for PSO [30], [31].

Overall, the main objective of this study was to establish a systematic solvent-screening protocol for PSO extraction based on three criteria: HSPs, boiling-point, and SHE. The selected solvents were also prepared in binary and ternary mixtures to obtain several solvent systems (single, binary, and ternary) for experimental assessment via PSO extraction using the Soxhlet method. This study serves as a critical preliminary screening phase, utilizing a fundamental approach to identify appropriate solvent systems as a foundation for subsequent detailed physicochemical characterization and statistical optimization. Although individual criteria of this screening framework, such as HSPs analysis, boiling point screening, and solvent ranking based on SHE, have been widely described, their systematic integration for PSO extraction has not been previously reported. To our knowledge, this study represents the first comprehensive approach to

systematically screen a wide range of single, binary, and ternary solvents for PSO. By shifting from traditional empirical selection to a structured framework, this study provides a methodology expected to be applicable to other vegetable oil extraction processes.

2. Material and methods

2.1 Material

Papaya seeds were obtained from California papaya fruits collected in Semarang, Indonesia. Fresh black seeds were hand-collected from fully ripe fruits and stored in a cool place until use. For grinding, dried papaya seeds were processed using a grain grinder and passed through a 40-mesh sieve. Analytical-grade ethanol, n-hexane, acetone, and ethyl acetate were obtained from PT. Smart Lab Indonesia for solvent extraction.

2.2 Methods

2.2.1 Preparation and drying of papaya seeds

Fifteen fresh and ripe California papaya *(Carica papaya L.)* fruits were halved, and the seeds were collected and carefully cleaned from the pulp. The seeds (100 g) were dried at 55 °C in a natural convection oven until constant weight was achieved [32]. After drying, the papaya seeds were ground using a grain grinder and sieved through a 40-mesh sieve. The resulting dried papaya seed powder was then used to extract PSO with various solvents using the Soxhlet method (Figure 1).

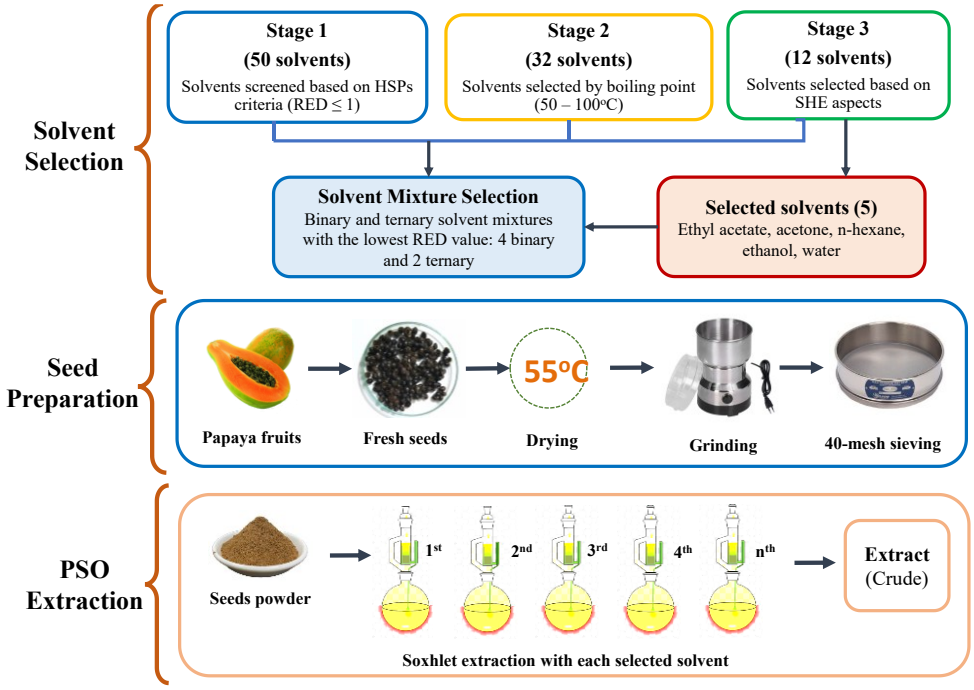

Figure 1. Flowchart of the entire process in this research

2.2.2 Solvent selection based on HSPs criteria

Solvent selection was based on several assessment criteria, including solubility parameters, solvent physical properties (boiling point), and SHE criteria (Figure 1). A total of 50 solvents, derived from the hydrocarbon, alcohol, ketone, ether, ester, amine, polar aprotic, and haloalkane groups, and used in the mixing and dissolution of coconut oil [33] and a solvent review [18], were prepared in a data set equipped with HSPs values of each solvent, based on literature data sources [34]. Then, the HSP values of the solvent were used to evaluate its solubility towards PSO by calculating the relative distance *(D)* and relative energy difference *(RED)* using Eqs. (1) and (2) [34].

$$D = \sqrt{4\left(\delta_d^{PSO} - \delta_d^{Solvent}\right)^2 + \left(\delta_p^{PSO} - \delta_p^{Solvent}\right)^2 + \left(\delta_{hb}^{PSO} - \delta_{hb}^{Solvent}\right)^2} \quad (1)$$

where D represents the relative distance of the solubility difference between PSO and the solvent. The parameters δ_d^{PSO}, δ_p^{PSO}, and δ_{hb}^{PSO} represent the contributions of dispersion, polar, and hydrogen-bonding HSPs to PSO, respectively, while $\delta_d^{Solvent}$, $\delta_p^{Solvent}$, and $\delta_{hb}^{Solvent}$ represent the contributions of dispersion, polar, and hydrogen-bonding HSPs to the solvent, respectively.

$$RED = \frac{D}{R_0} \quad (2)$$

where *RED* represents the relative energy differences between PSO and solvent. R_0 is the radius of the solubility sphere of oils [33].

The ranking of solvents and solvent mixtures can be determined using the RED value. A low RED value indicates close solubility properties between PSO and the solvent [33]. If RED = 0, the solvent and PSO have the same solubility. If RED ≤ 1, the solvent is within the PSO range (a good solvent). Conversely, if RED > 1, the solvent is outside the PSO range (a poor solvent). Of the 50 solvents that have been evaluated, the solvent with a RED value ≤ 1 was selected. From this criterion, 18 solvents were eliminated due to the predetermined rejection limit. A total of 32 selected solvents were used for further screening based on physical properties, including boiling points.

2.2.3 Solvent selection based on boiling point criteria

The remaining 32 solvents were assessed according to the solvent boiling-point selection criteria. The boiling point limits considered were based on a combination of the CHEM21 and GlaxoSmithKline (GSK) guidelines, with some adjustments [18], [35]. The selected range was restricted to solvents with low-to-medium boiling points (50–100 °C). Beyond considering energy consumption during extraction and solvent recovery, using solvents with high boiling points can degrade or even damage the bioactive compounds (vitamin C, phenols, flavonoids) present in PSO and other agricultural products [36], [37], [38]. Based on these criteria, 20 solvents were eliminated, leaving 12 solvents to be re-selected according to safety, health, and environmental (SHE) criteria.

2.2.4 Solvent selection based on SHE criteria

Generally, SHE criteria are considered in solvent selection due to their impact on food, pharmaceutical, and cosmetic applications. In this study, to simplify the selection process, these three criteria were integrated into a unified scoring system. Each criterion was assigned a score from 1 to 10, with 10 indicating the highest level of hazard. Furthermore, a color-coding system was implemented: green for scores 1-3, yellow for 4-6, and red for 7-10. The final composite scores derived from these three SHE criteria facilitate an initial classification into three main categories: recommended, problematic, and hazardous (Table 1) [18]. No distinction was made between hazardous and extremely hazardous solvents. However, any solvent with a score of 10 is considered extremely hazardous. Although the basic scoring guidelines presented in Table 2 range from 1 to 9, a maximum score of 10 can be achieved through specific hazard adjustments. Specifically, additional points are added to the safety score for low autoignition temperature (AIT < 200 °C), high resistivity (>10^8 Ω.m), or peroxide formation (EUH019), and to the health score for high volatility (BP <85 °C) carcinogens. In addition, a direct score of 10 is assigned to ozone-depleting substances (H420) [18].

Table 1. Ranking by default of solvent [18]

SHE scores	Categories
One score ≥ 8	Hazardous
Two "red" scores	Hazardous
One score = 7	Problematic
Two "yellow" scores	Problematic
Not all of the criteria above	Recommended

Based on the previously established criteria, the 12 remaining solvents were reselected based on the SHE scoring system, as presented in Table 2 [18]. Solvents categorized as "recommended" were prioritized as suitable candidates. Furthermore, to examine the extraction phenomenon across diverse solvent properties, representatives from different functional groups were selected. For example, if there are acetic acid and citric acid in the "recommended" category, then only one (based on the lowest boiling point) of the two solvents will be selected because both solvents have the same functional group (carboxyl group). This step was taken with the understanding that solvents with relatively similar functional groups will have identical solubility properties.

Table 2. SHE assessment criteria for solvent selection [18]

Parameters	Scoring								
	1	2	3	4	5	6	7	8	9
Safety criteria									
Flash Point (°C)	>60		24 - 60	23 – 0	-1 to -20		< -20		
Globally Harmonized System (GHS)			H226		H225, H224				
Health criteria									
Carcinogen						H341 H351 H361			H340 H350 H360
Single target organ toxicity		H304 H371 H373		H334		H370 H372			
Acute toxicity		H302 H312 H332 H336 EUH070				H301 H311 H331			H300 H310 H330
Irritation		H315 H317 H319 H335 EUH066		H318			H314		
Environment criteria									
Boiling Point (°C)			70 –139		50–69, 140–200		<50, >200		
GHS					H412 H413		H400 H410 H411		

Based on these criteria, ethyl acetate and acetone were identified as the most promising candidates. Additionally, n-hexane, ethanol, and water were included in the experimental design as control solvents, allowing observation of the interactions among polar, semipolar, and nonpolar solvent mixtures and providing information on the effect of polarity interactions on PSO yield. The inclusion of n-hexane is based on its use as a dominant solvent in oil extraction due to its efficiency, low cost, and ability to maintain oil quality [39], making it a suitable benchmark. Similarly, ethanol and water were included to span a broad range of polarities, enabling a systematic evaluation of the effect of solvent polarity on PSO yield. Furthermore, industrial feasibility factors, such as cost-effectiveness and solvent availability, were considered to ensure that the experimental findings were practical and economically relevant.

2.2.5 Design of binary and ternary mixture interactions of five selected solvents against HSPs

Experimental design is a statistical approach used to analyze relationships between independent and response variables using linear, nonlinear, quadratic, and other empirical models. By employing methodologies such as factorial design [40], response surface methodology [41], [42], and mixture design [43], [44], the effects of one or more factors and process parameters on system responses can be efficiently and systematically investigated. Since the binary and ternary mixture compositions of the five selected solvents cannot be applied in their entirety due to time and cost reasons, determining the appropriate mixture composition in this study must be done. All non-negative compositions of the solvents involved must have a total fraction of one, as expressed in Eq. (3) [45].

$$x_1 + x_2 + x_3 + \cdots + x_n = 100\% \tag{3}$$

with

$$0 \leq x_i \leq 100\%$$

where x_i represents the volume composition of solvents 1 and 2 for binary mixtures, and solvents 1, 2, and 3 for ternary mixtures.

The simplex-lattice and I-optimal designs were applied in this study because the response variable (RED) is a continuous function of the component proportions, so a mixture design that is able to systematically arrange sample points (simplex lattice) or minimize the variance of predictions in the formulation space (I-optimal) becomes logical to use. The simplex lattice and I-optimal design approaches have also been widely applied in extraction studies involving solvent mixing [46], [47]. The simplex lattice and I-optimal mixture designs were programmed in Design-Expert software (version 13.0). Two to three independent variables, solvent 1, solvent 2, and solvent 3, and one response, RED, were included in the mixture design.

The experimental setup consisted of 8 runs for binary mixtures: 3 minimum model points, 3 replicates, and 2 lack-of-fit measurements. Meanwhile, the ternary mixture consisted of 18 runs: 10 minimum model points, 3 replicates, and 5 lack-of-fit measurements. Optimization was performed to find the optimum point with the highest desired level. The desired optimum point is the solvent mixture with the lowest RED.

2.2.6 Soxhlet-based PSO extraction

Conventional Soxhlet-based extraction [48] was performed with minor modifications. A total of 10 g of ground, sifted dried papaya seeds was placed in a cellulose thimble, and 300 mL of solvent was used for extraction. A total of 11 selected solvents, both single, binary, and ternary, were used for

PSO extraction, as presented in Figure 1. The condenser unit received a constant supply of cooling water. The extraction was conducted under total reflux at the solvent–oil mixture's boiling point for 6 hours. Samples were collected hourly for concentration analysis using a calibration curve derived from mixtures of the respective solvents and commercial PSO. The calibration curve demonstrated high linearity ($R^2 > 0.980$). Finally, the PSO yield can be calculated by Eq. (4):

$$Yield(\%) = \frac{C_{PSO}\ x\ V\ x\ \rho_{PSO}}{m_{seeds}} x100\% \quad (4)$$

Where C_{PSO} is the concentration of PSO in the extract (mL/L), V is the extracting volume (L), ρ_{PSO} is the density of PSO (g/mL), and m_{seeds} is the mass of seeds used for extraction (g). All measurements were performed in triplicate. Results are expressed as mean ± standard deviation (error bar). One-way analysis of variance (ANOVA) was performed in MS Excel 2016 and Minitab 18 to assess significant differences among samples at the 95% confidence level ($p < 0.05$). Where significant differences were found, a Tukey's post-hoc test was applied to perform pairwise comparisons between solvent systems. The measurement uncertainty was accounted for by considering the precision of the analytical balance (±0.001 g), volumetric glassware (±0.05 mL), and the regression statistics of the calibration curve.

3. Results and discussion

3.1 Selected solvent for PSO extraction based on HSPs

The initial criterion for selecting an appropriate solvent for PSO extraction is the evaluation of HSPs. The HSPs values for PSO at 298.15 K were estimated using a group contribution model (GCM) [4]. Based on this model, the HSPs values of PSO consist of the parameters δ_d, δ_p and δ_{HB}, which are 16.48, 3.18, and 5.97 $MPa^{1/2}$, respectively [4]. These three parameters serve as a basic reference for evaluating the solubility affinity of various solvents to PSO. To determine the solvents with the highest affinity, physical interaction was evaluated using the Relative Energy Difference (RED) metric, as defined in Eq. (2) [34]. The RED values of 50 candidate solvents are presented in Table 3. This table also provides complete information on the three solvent HSPs obtained from various literature [33], [34], as well as the interaction distance (D) values obtained by applying Eq. (1).

Furthermore, the solubility interactions between PSO and solvents can be represented in the three-dimensional HSPs space, with PSO as the coordinate center marked with a star symbol. This representation shows the relative position of PSO to various solvents in the form of a Hansen solubility sphere, as shown in Figure 2. The figure shows the Hansen solubility sphere for PSO, plotted with three-dimensional axes, for 50 organic and inorganic solvents. The three-dimensional (3D) space coverage of PSO is limited by the surface of the Hansen solubility sphere, which is indicated by the blue area and represents solvents with the criterion RED ≤ 1. Visually, solvents with RED values < 1 are within the Hansen solubility sphere region, indicating a high affinity for PSO. The RED value = 1 (R_0 = 9.8) corresponds to the boundary condition for the transition region, while RED values > 1 indicate low affinity and decrease with increasing RED [34], [49]. Thus, solvents with RED values ≤ 1 have the potential to interact effectively with PSO and are considered suitable for PSO extraction.

Based on the RED criteria, n-butyl acetate, chloroform, ethyl acetate, and anisole showed the closest HSP distances to PSO with RED values of 0.152, 0.271, 0.286, and 0.295, respectively. In addition to these four solvents, there are 28 other solvents that meet the RED ≤ 1 requirement, and all of them are within the Hansen solubility sphere. Thus, 32 solvents are predicted to exhibit favorable solubility for PSO and are worthy of consideration for the next solvent selection stage. The distribution of chemical groups of these solvents shows that solvents with RED values ≤ 1

consist of hydrocarbons (31.25%), alcohols and ethers (15.63%), haloalkanes (12.50%), esters and ketones (9.38%), and amines (6.25%). These findings indicate that the diversity of solvent chemical structures can still result in HSPs being compatible with PSO, as long as the δ_d, δ_p and δ_{HB} components are in a similar solubility range [4], [33].

Table 3. Solvent-PSO interactions based on HSPs expressed as *"D"* and *"RED"* [33], [34]

No	Solvents	Unit of $MPa^{1/2}$			Solvent-PSO interactions based on HSPs	
		δ_d	δ_p	δ_{HB}	*D*	RED
1	n-heptane	15.30	0.00	0.00	7.16	0.731
2	Cyclohexane	16.80	0.00	0.20	6.62	0.675
3	Benzene	18.40	0.00	2.00	6.37	0.650
4	o-xylene	17.60	1.00	3.10	4.24	0.433
5	Toluene	18.00	1.40	2.00	5.31	0.542
6	Ethylbenzene	17.80	0.60	1.40	5.87	0.599
7	n-hexane	14.90	0.00	0.00	7.47	0.762
8	n-pentane	7.10	0.00	0.00	19.94	2.035
9	Methanol	15.10	12.30	22.30	18.91	1.929
10	Ethanol	15.80	8.80	19.40	14.62	1.492
11	Isopropyl alcohol	15.80	6.10	16.40	10.92	1.114
12	n-octanol	17.00	3.30	11.90	6.02	0.614
13	n-hexanol	15.90	5.80	12.50	7.13	0.728
14	Iso-butanol	15.10	5.70	15.90	10.61	1.083
15	n-butanol	16.00	5.70	15.80	10.19	1.040
16	Ethylene glycol	17.00	11.00	26.00	21.53	2.197
17	Acetone	15.50	10.40	7.00	7.55	0.771
18	Cyclohexanone	17.80	6.30	5.10	4.18	0.426
19	Methyl isobutyl ketone	7.50	3.00	2.00	18.39	1.877
20	Ethyl acetate	15.80	5.30	7.20	2.80	0.286
21	n-Butyl acetate	15.80	3.70	6.30	1.49	0.152
22	Diethyl malonate	16.10	7.70	8.30	5.14	0.525
23	m-Cresol	18.00	5.10	12.90	7.81	0.797
24	Pyridine	19.00	8.80	5.90	7.55	0.770
25	Dimethylformamide	17.40	13.70	11.30	11.94	1.218
26	Acetonitrile	15.30	18.00	6.10	15.01	1.531
27	Aniline	19.40	5.10	10.20	7.46	0.761
28	Ethanolamine	17.00	15.50	21.20	19.62	2.002
29	Nitrobenzene	15.80	8.60	5.10	5.66	0.577
30	Diethyl ether	14.50	2.90	5.10	4.06	0.415
31	1,4-Dioxane	19.00	1.80	7.40	5.42	0.553
32	Dimethyl sulfoxide	18.40	16.40	10.20	14.40	1.470
33	1,2-Dichloroethane	16.50	7.80	3.00	5.49	0.560
34	Diethylene glycol	16.60	12.00	20.70	17.17	1.752
35	Tri-ethylene glycol	16.00	12.50	18.60	15.73	1.605
36	Anisole	17.80	4.10	6.70	2.89	0.295
37	Glycerol	17.40	12.10	29.30	25.04	2.556
38	Tetrahydrofuran	16.80	5.70	8.00	3.30	0.337
39	Chlorobenzene	9.29	2.10	0.98	15.26	1.557
40	Benzyl alcohol	18.40	6.30	13.70	9.18	0.937
41	Formic acid	14.60	10.00	14.00	11.19	1.141
42	tert-Butyl methyl ether	14.80	4.30	5.00	3.67	0.375
43	Acetic acid	14.50	8.00	13.50	9.78	0.998
44	n-amyl alcohol	15.90	5.90	13.90	8.46	0.864
45	Carbon tetrachloride	17.80	0.00	0.60	6.78	0.691
46	Dichloromethane	18.20	6.30	6.10	4.65	0.474
47	Benzonitrile	17.40	9.00	3.30	6.66	0.680
48	4-Methyl pentanone	15.30	6.10	4.10	4.19	0.428
49	Petroleum ether	15.00	0.00	0.00	7.38	0.753
50	Chloroform	17.80	3.10	5.70	2.65	0.271

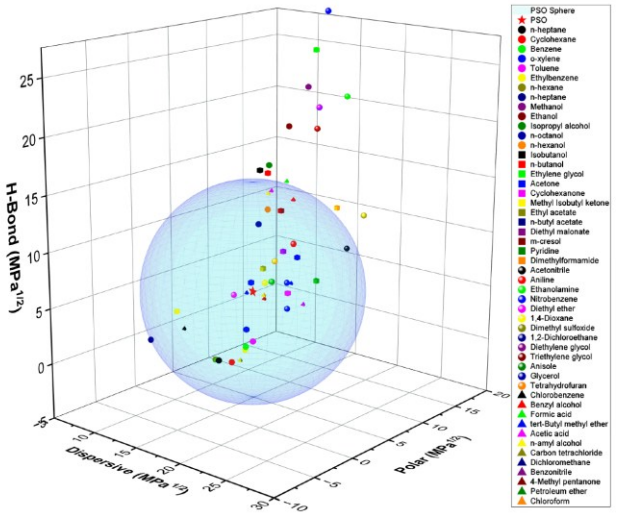

Figure 2. 3D plots of δ_d, δ_p and δ_{HB} of the PSO-solvent Hansen solubility sphere

Previous studies typically extracted oil or lipid components from vegetable and animal matrices using hydrocarbon solvents, especially n-hexane [39], [50]. N-hexane is a volatile, inexpensive (USD 1090/MT), and readily available compound derived from petrochemical fractions. Despite these advantages, it is recognized as toxic and non-renewable, and has significant environmental impacts. Therefore, it is not considered "*generally recognized as safe*" (GRAS) [51]. Based on HSPs, n-hexane is well suited for extracting vegetable oils, as indicated by RED values < 1 for several oils, including used frying oil (0.824), coconut oil (0.855), and palm oil (0.996) [33]. For PSO, n-hexane is also suitable, as indicated by a RED value of 0.762, showing close physical properties to PSO.

However, solvents in the hydrocarbon group generally have lower HSP compatibility towards PSO compared to solvents from the ester group (e.g., n-butyl acetate and ethyl acetate), ethers (anisole and THF), and ketones (cyclohexanone and 4-methylpentanone). PSO, composed of long-chain fatty acids such as oleic, palmitic, and stearic acids, mainly interacts through δ_d forces. However, PSO also exhibits δ_{HB} interactions through the -OH and C=O functional groups, making it partially non-polar [52]. Consequently, solvents with more balanced contributions of δ_p and δ_{HB} forces tend to have higher physical affinity towards PSO than non-polar hydrocarbon solvents. In line with it, p-cymene, D-limonene, isopropanol, butanol, and α-pinene, which include terpenes and alcohols, provide higher rapeseed oil extraction yields than n-hexane due to their more balanced polarity and contribution of δ_p and δ_{HB} [53]. However, solvents from the terpene group, some alcohols, and hydrocarbons also need to be further evaluated because their boiling points are generally high, which can increase energy requirements during the recovery process [54].

In this study, the R_0 value of 9.8 $MPa^{1/2}$ used in the RED calculation was derived from coconut oil data [33]. This selection was based on the close proximity of HSPs between PSO and coconut oil [4]. In addition, the relatively high R_0 broadens the potential solvent candidates for PSO extraction. Although this value is a reasonable theoretical assumption and an approximation, further analysis shows that it does not significantly alter the final solvent categorization. Nevertheless, experimental determination of R_0 for PSO via systematic solubility testing is recommended in future studies to refine predictions from solvent screening.

3.2 Selected solvent for PSO extraction based on boiling point

In addition to HSPs' suitability, boiling point is also an important criterion in solvent selection. Specifically, a sufficiently low boiling point is needed to facilitate extraction (especially Soxhlet)

and separation, thereby potentially reducing overall energy consumption. While a low boiling point is advantageous, solvents with very low boiling points should be avoided, as their volatility can lead to significant solvent loss during extraction. Thus, proper consideration of boiling points will facilitate the recovery of PSO and solvents, making them potentially applicable on a larger scale [17]. Based on the CHEM21 guidelines, suitable solvents have a boiling point range of 50 – 200 °C and a recommendation score of 3 or 5 (Table 2). The guidelines give poor ratings to solvents with boiling points < 50 °C (because they are highly volatile and have the potential to produce high VOCs), and to solvents with boiling points > 200 °C (because of the high evaporation and recovery energy requirements) [18]. Meanwhile, GlaxoSmithKline (GSK) sets a stricter limit: solvents with boiling points < 40 °C or > 120 °C are not recommended for selection [35].

In this study, the solvent selection was determined by considering a combination of CHEM21 and GSK guidelines and was further narrowed to a boiling point range of 50-100 °C (marked with blue circles in Figure 3). Thus, solvents with boiling points < 50 °C or > 100 °C (red square symbols) were not considered for the PSO extraction process. This limitation successfully filtered out 12 of the 32 solvents that met the RED ≤ 1 criteria (from the previous stage) for use in the next selection stage. The selected solvents included hydrocarbons (petroleum ether, n-hexane, benzene, cyclohexane, and n-heptane), haloalkanes (chloroform, carbon tetrachloride, and 1,2-dichloroethane), ethers (tertiary-butyl methyl ether and THF), esters (ethyl acetate), and ketones (acetone).

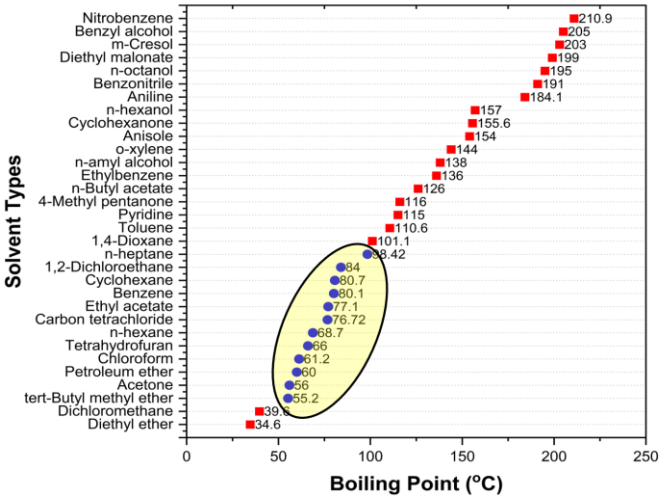

Figure 3. 2D visualization of selected solvents based on low - moderate boiling points

Furthermore, restrictions on the use of high-boiling solvents are not only related to energy requirements for extraction and recovery but also directly affect life cycle analysis (LCA). High-boiling solvents generally require greater evaporation energy during both extraction and recovery processes, thereby increasing the energy demand (ED) throughout their life cycle [55]. In addition, the use of high-temperature solvents can damage heat-sensitive components in extracts, such as total phenolics and antioxidant capacity [56].

On the other hand, solvents with relatively high boiling points offer advantages in repeated heating-based extraction methods such as Soxhlet extraction. A higher boiling point allows the process to proceed at a stable, elevated temperature, thereby increasing solubility, accelerating solvent diffusion, and expanding the pores in the solid matrix. Increasing solvent boiling points (and thus extraction temperatures) correlated with significantly improved oil extraction efficiency [57]. Furthermore, low-volatility solvents are beneficial because they maintain a consistent condensation rate and minimize solvent loss during repeated evaporation-condensation cycles.

Therefore, solvent selection based on boiling point requires a balance between process efficiency and sustainability. A too-low boiling point leads to high volatility and solvent loss, ultimately impacting the environment. Meanwhile, a too-high boiling point increases energy requirements and the risk of thermal degradation during extraction and separation. Following CHEM21 and GSK limits, and setting a solvent boiling point range of 50-100 °C is a logical, safe, efficient, and suitable choice for PSO extraction, while further selecting solvents that meet the HSP criteria.

3.3 Selected solvent for PSO extraction based on SHE

The third criterion for solvent selection, based on the CHEM21 guidelines, is the consideration of SHE criteria [18]. As shown in Table 2, these three criteria are scored from 1 to 9, with higher scores indicating a higher level of hazard. To account for additional risks, the safety score is increased by one point if a solvent exhibits a low auto-ignition temperature (AIT < 200 °C), a tendency to accumulate electrostatic charge (resistivity > 10^8 $\Omega.m$), or a propensity to form explosive peroxides (EUH019 in Classification, Labelling, and Packaging). The combined SHE scores are subsequently used to establish an initial solvent ranking into three categories, recommended, problematic, and hazardous, as explained in Table 1.

From a safety perspective, the assessment parameters refer to flammability hazard based on flash point (FP) and are classified using the H2xx code [58]. Of the twelve solvents selected based on boiling-point criteria (Table 4), carbon tetrachloride and chloroform are the safest solvents because they are included in the non-flammable category (score 1, recommended) [59], [60]. The highest score (7, hazardous) is given to n-hexane, tert-butyl methyl ether, and petroleum ether because they have FP < -20 °C with the code H225 (highly flammable liquid and vapor, GHS category 2) [61], [62] or H224 (Extremely flammable liquid and vapor, GHS category 1) [63]. Meanwhile, the other seven solvents are given a score of 5 (problematic) with the GHS code H225 [64], [65], [66], [67], [68], [69], [70], as summarized in Table 4.

Table 4. List of Solvent Selection Based on SHE Aspects

Solvent	BP (°C)	FP (°C)	Worst			Safety score	Health score	Env. score	Rank by CHEM21 criteria
			H2xx[1]	H3xx[2]	H4xx[3]				
n-heptane	98.42	-4.0	H225	H336	H410	5	3	7	Problematic
Cyclohexane	80.70	-17.0	H225	H336	H410	5	3	7	Problematic
Benzene	80.10	-11.0	H225	H350	H412	5	10	5	Hazardous
n-hexane	68.70	-22.0	H225	H361f	H411	7	7	7	Hazardous
Acetone	56.00	-18.0	H225	H336	None	5	3	1	Recommended
Ethyl acetate	77.10	-4.0	H225	H319	None	5	3	1	Recommended
1,2-Dichloroethane	84.00	13.0	H225	H350	None	5	10	1	Hazardous
Tetrahydrofuran	66.00	-14.0	H225	H351	None	5	7	1	Problematic
tert-Butyl methyl ether	55.20	-28.0	H225	H315	None	7	3	1	Problematic
Carbon tetrachloride	76.72	na	None	H351	H420	1	7	10	Hazardous
Petroleum ether	60.00	-40.0	H224	H336	H411	7	3	7	Hazardous
Chloroform	61.20	na	None	H351	None	1	7	1	Problematic

[1]Safety aspect, [2]Health aspect, [3]Env. aspect

In terms of health, the assessment is based on the hazard statement in the GHS/CLP system, which is coded H3xx and relates to effects of exposure via inhalation or direct contact (Table 4). Benzene and 1,2-dichloroethane are assigned the highest score (10, hazardous) because both are carcinogenic (H350) and have boiling points < 85 °C [66], [69]. In addition, n-hexane (H361) [61], THF, carbon

tetrachloride, and chloroform (H351) [59], [60], [70] each received a score of 7 (hazardous). The code H361f indicates potential fertility impairment [61], while H351 indicates suspected carcinogenic properties [70]. Meanwhile, other solvents are given a score of 3 (recommended) because they are only associated with low to moderate hazards, such as H336 (may cause drowsiness and dizziness) [64], H319 (causes serious eye irritation) [68], or H315 (causes skin irritation) [62].

The environmental aspect assessment focused on criteria related to environmental issues, such as ozone layer depletion and impacts on aquatic life, and was categorized using the H4xx code, as shown in Table 4. The assessment results showed that carbon tetrachloride has the most hazardous impact (score 10) because it damages the ozone layer (H420) [59]. n-heptane, cyclohexane, n-hexane, and petroleum ether received a score of 7 (hazardous) because they are classified as toxic (H411) or very toxic to aquatic organisms with long-term effects (H410) [61], [63], [64], [65]. Benzene had a lower impact (score 5, problematic) because it is dangerous to aquatic life and has long-term effects (H412) [66]. Meanwhile, other solvents do not have a GHS/CLP code indicating environmental hazards (score 1, recommended).

CHEM21 has provided ranking guidelines that cover all three aspects of SHE, as presented in Table 1. Based on the assessment of these three aspects, the overall conclusion is that two solvents are recommended: ethyl acetate (ester group) and acetone (ketone group). Meanwhile, the "problematic" and "hazardous" categories each include five solvents (Table 4). The two selected solvents will then be mixed in various volume ratios to obtain the most suitable HSPs characteristics for PSO.

3.4 Single, binary, and ternary solvents based on mixing rules for PSO extraction

In the previous section, two recommended solvents were selected based on HSPs, boiling points, and SHE criteria: ethyl acetate and acetone. The RED values of ethyl acetate and acetone against PSO were 0.297 and 0.776, respectively. When visualized in the Hansen solubility sphere, both solvents are within the solubility range of PSO. However, the solvent used for PSO extraction is expected to recover more than just fatty acids. It is also expected to extract nutraceutical components from papaya seeds, including phenolic compounds (e.g., gallic acid), carotenoids (α- and β-carotene), and vitamin C (ascorbic acid).

Yara-varon *et al.* [54] reported that α-carotene and β-carotene have HSPs that are closer to n-hexane (RED = 1.31 and 1.34) than ethyl acetate (RED = 2.10 and 1.95). Pagano *et al.* [71] also found that phenolic compounds such as caffeic acid (δ_d, δ_p and δ_{HB} = 20.70, 8.30, and 19.0) have better solubility affinity with a mixture of ethyl lactate - water (75:25) (D = 10.90) than pure ethyl lactate (D = 13.40). Another phenolic compound, often represented as gallic acid, also shows a higher affinity for HSPs in an ethanol-water (50:50) mixture (D = 7.7) than in pure ethanol (D = 9.9) or pure water (D = 8.0) at the solvent's boiling temperature [72]. The highest solubility of gallic acid was achieved in an acetic acid-water mixture (40:60), not in pure acetic acid or water [73]. Furthermore, vitamin C in the form of ascorbic acid (δ_d, δ_p and δ_{HB} = 18.10, 12.00, and 27.80) shows a greater affinity of HSPs to alcohol groups, such as glycerol (D = 2.10), ethylene glycol (D = 3.00), methanol (D = 8.10) and ethanol (D = 10.10) compared to acetone (D = 21.50), ethyl acetate (D = 22.10) and n-hexane (D = 30.90) [74]. Ascorbic acid is also quite close to water HSPs (D = 15.90), which indicates that ascorbic acid tends to interact strongly with semi-polar to polar solvents compared to non-polar solvents.

Recently, the effect of various solvents on the quality of seed oils was evaluated by considering several parameters, and then compared with n-hexane using a scoring system [75]. Ethanol and methanol received the highest scores (5) because they showed the least negative effects on all oil quality parameters. Isopropanol received a lower score (4) due to an increase in peroxide value and

no effect on sterol content. Acetone and dichloromethane were also classified with a score of 4. Acetone was reported to reduce polyunsaturated fatty acid content, whereas dichloromethane increased oil acidity. On the other hand, 2-methyloxolane and ethyl acetate received the lowest scores (2). 2-Methyloxolane negatively affects the oil's oxidative stability and can promote the formation of hydroperoxides, although this solvent offers advantages for extracting phenolic compounds and tocopherols. Meanwhile, ethyl acetate improves the extraction of phenolic compounds but does not significantly improve other oil quality parameters.

These findings indicate that extracting oils from seeds, including PSO, and their nutraceutical compounds requires solvents with a wide range of polarities. From an economic perspective, ethyl acetate and acetone are relatively more expensive than n-hexane, ethanol, and water. Table 5 shows that the prices of ethyl acetate and acetone reached 1281 and 1250 USD/MT, respectively, while n-hexane, ethanol, and water (DI) had lower prices, namely 1090, 741, and 60 USD/MT [28], [76]. Based on these considerations, water, ethanol, and n-hexane can be used as either sole or complementary solvents in the PSO extraction process.

Table 5. List of five selected solvents based on CHEM21 criteria, representing polar, semi-polar, and non-polar solvents, along with their respective market prices

Code	Family	Solvent	HSPs ($MPa^{1/2}$)				RED	Price (USD/MT) [28]
			δ_d	δ_p	δ_{HB}	δ_T		
A	Esters	Ethyl acetate	15.80	5.30	7.20	18.15	0.297	1281
B	Hydrocarbons	n-hexane	14.90	0.00	0.00	14.90	0.743	1090
C	Ketones	Acetone	15.50	10.40	7.00	19.94	0.776	1250
D	Alcohols	Ethanol	15.80	8.80	19.40	26.52	1.512	741
E	Water	Water	15.50	16.00	42.30	47.81	3.957	60 [76]

Based on the previous discussion, five solvents were selected as potential candidates, considering solubility (polarity), boiling point, SHE criteria, selectivity towards nutraceutical compounds, and market price (Table 5). Each solvent has its advantages and limitations, as explained in the previous section. The five solvents were then combined into binary and ternary mixtures by calculating the parameters δ_d, δ_p, and δ_{HB} using solubility mixing rules based on volume fractions [16], [30]. To obtain the optimal formulation, the RED value of the solvent mixture against PSO was used as the evaluation parameter.

Figure 4 (a-j) presents the results of the optimization of RED values from various binary solvent mixtures. In Figure 4 (a), the ethyl acetate-n-hexane mixture shows the best condition at a composition of 78.33:21.67 vol%. The parameters δ_d, δ_p and δ_{HB} of the mixture are 15.61, 4.15, and 5.64 $MPa^{1/2}$, respectively, with a RED value of 0.208. The addition of n-hexane at 21.67 vol% provides a positive contribution by decreasing the polarity of the mixture. This is reflected in the reduced δ_p and δ_{HB} values, resulting in a better affinity of HSPs with PSO compared to ethyl acetate or n-hexane alone, as indicated by a smaller RED value. However, the presence of n-hexane slightly decreases the δ_d value, which increases the deviation from the δ_d value of PSO.

Figure 4 (b-d) shows the interaction of a mixture of ethyl acetate with acetone, ethanol, and water on PSO at various compositions (vol%). The three solvents did not have a positive impact on the change in the HSPs values of ethyl acetate because ethyl acetate itself is quite polar, with δ_p and δ_{HB} values of 5.30 and 7.20 $MPa^{1/2}$, respectively, due to the presence of a carbonyl group (C=O), which is part of the ester functional group (-COO-) [34]. Therefore, mixing it with a more polar solvent actually increases the δ_p and δ_{HB} values of the mixture, thereby distancing it from the δ_p and δ_{HB} values of PSO, and does not confer any advantage in terms of HSPs' suitability.

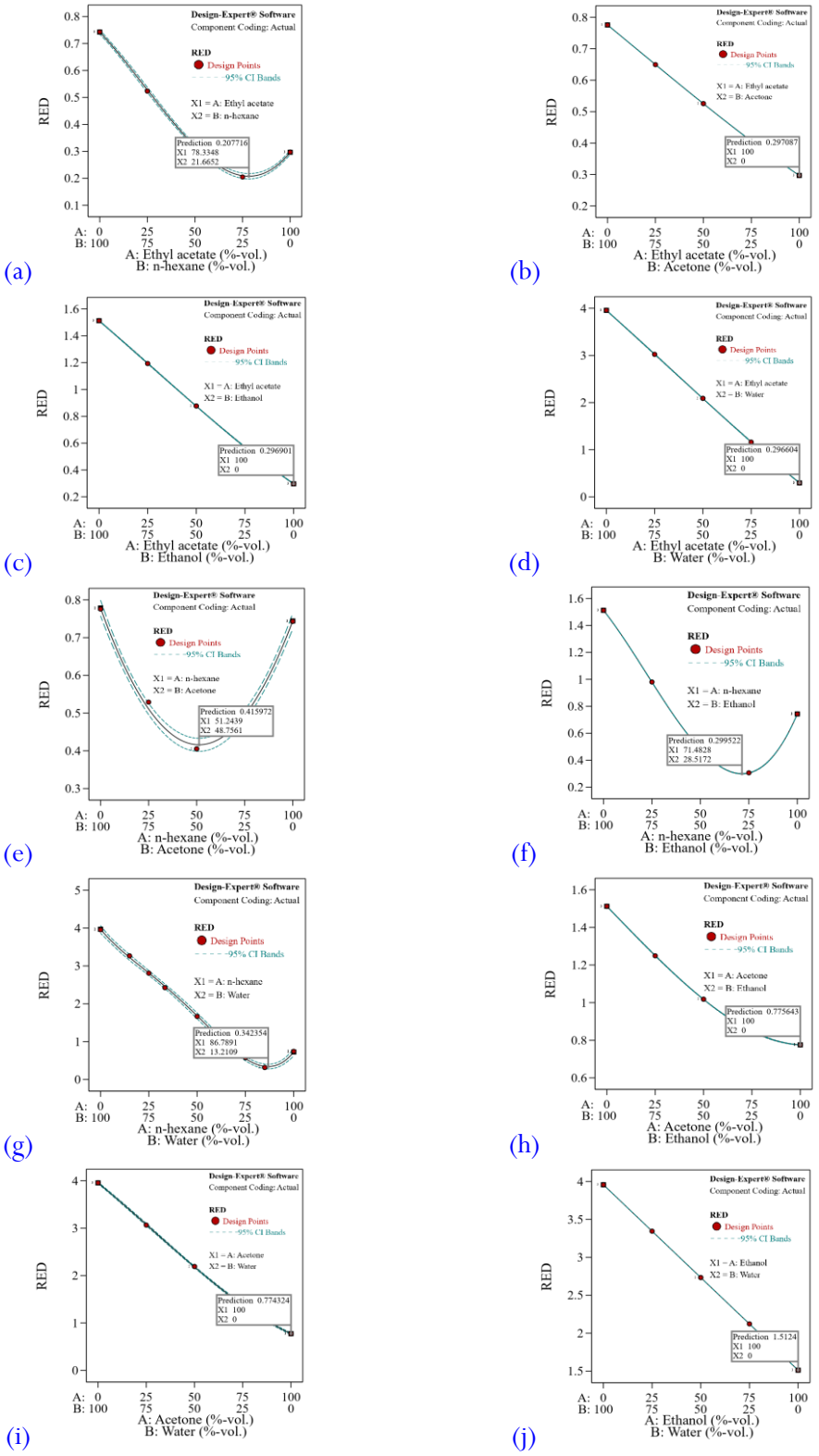

Figure 4. Binary mixture interaction of five selected solvents, (a) ethyl acetate – n-hexane, (b) ethyl acetate – acetone, (c) ethyl acetate – ethanol, (d) ethyl acetate – water, (e) n-hexane – acetone, (f) n-hexane – ethanol, (g) n-hexane – water, (h) acetone – ethanol, (i) acetone – water, and (j) ethanol – water

Furthermore, Figure 4 (e-g) shows the interactions of HSPs in a mixture of n-hexane, acetone, ethanol, and water towards PSO at various compositions (vol%). The three solvents contributed positively to the increase in the HSP values of n-hexane. The best conditions were obtained at a composition of acetone 48.76 vol%, ethanol 28.52 vol%, and water 13.21 vol%, which

respectively produced HSPs values of n-hexane - acetone mixture (δ_d, δ_p, δ_{HB}) = 15.19, 5.07, 3.41 $MPa^{1/2}$, n-hexane - ethanol = 15.15, 2.48, 5.46 $MPa^{1/2}$, and n-hexane - water = 14.98, 2.11, 5.59 $MPa^{1/2}$. The three mixtures showed greater HSPs affinity to PSO, with RED values of 0.416, 0.300, and 0.342, respectively. This phenomenon occurs because n-hexane, which naturally only contributes to the δ_d parameter and has a low polarity, requires the presence of a more polar solvent to increase the δ_p and δ_{HB} parameters. In addition, the higher the polarity of the complementary solvent, the smaller the volume fraction required to produce changes in HSPs that approach the characteristics of PSO (polarity order: acetone < ethanol < water). Ethanol is overall more polar than acetone because it can act as a hydrogen-bond donor and acceptor through its -OH group, resulting in stronger intermolecular interactions [77]. In addition, ethanol also has a higher δ_{HB} and dielectric constant than acetone [78], so its total polarity is greater even though the δ_p value is lower (Table 5).

Furthermore, Figure 4 (h-i) shows the interaction of HSPs from acetone-ethanol and acetone-water mixtures with PSO based on the RED value. The addition of ethanol or water at various concentrations (vol%) did not improve the suitability of HSPs, and in some cases, increased the RED value. This is due to the higher δ_p and δ_{HB} values of acetone than those of PSO, or to its greater polarity. Thus, its mixture with ethanol or water actually increases polarity by increasing δ_{HB}. Meanwhile, the contribution of δ_d from ethanol is not enough to balance the increase in polarity. As a result, acetone alone still provides the best HSPs suitability for PSO compared to its mixture with ethanol or water. A similar phenomenon is observed in the ethanol-water mixture (Figure 4 (j)), where adding water at various concentrations (vol%) does not improve the suitability of HSPs for PSO, as indicated by an increase in the RED value. Thus, the ethanol-water mixture does not provide better interaction than ethanol alone and is not recommended for PSO extraction. Overall, several binary mixtures showed good compatibility of HSPs to PSO, namely ethyl acetate–n-hexane (78.33:21.67 vol%, RED = 0.208), n–hexane–acetone (51.24:48.76 vol%, RED = 0.416), n-hexane – ethanol (71.48:28.52 vol%, RED = 0.300), and n-hexane – water (86.78:13.21 vol%, RED = 0.342). These four mixtures can be considered as potential solvent candidates that complement the five single solvents in Table 5.

In the ternary solvent mixtures, the ten formulations analyzed showed different interaction patterns towards PSO (Figure 5 (a-j)). For the mixture of ethyl acetate-n-hexane with acetone, ethanol, and water, the lowest RED values produced were in the range 0.196 - 0.206. These values were found at n-hexane compositions of 22.39 - 25.31 vol%, as shown in Figure 5 (a-c). This indicates that adding a third solvent does not improve the suitability of HSPs for PSO. Conversely, the addition of acetone, ethanol, or water with higher polarity actually increases the δ_p and δ_{HB} values of the mixture. As a result, the HSPs of the mixture move farther from the PSO HSPs, and the RED value increases, as evidenced by the shift in the color contour from green to red. Since these three mixtures, as well as the binary mixture of ethyl acetate - n-hexane in Figure 4 (a), produced almost identical optimal compositions, one representative formulation was chosen: ethyl acetate - n-hexane 77.20:22.80 vol% (RED = 0.206).

Furthermore, the ethyl acetate–acetone–ethanol, ethyl acetate–acetone–water, and ethyl acetate–ethanol–water mixtures also showed no interactions, thereby increasing the suitability of HSPs for PSO. These three mixtures actually produced higher RED values than single ethyl acetate (RED = 0.297). This pattern is evident in the change in contours, moving from blue to green, yellow, and red as the composition moves away from single ethyl acetate (Figure 5 (d-f)). This finding is consistent with the results of the binary mixtures in Figure 4 (b-d), which indicate that ethyl acetate is already quite polar due to the presence of the carbonyl group (C=O) [34]. Therefore, mixing ethyl acetate with a more polar solvent, in both binary and ternary systems, increases the δ_p and δ_{HB} of the mixture, moving it away from PSO HSPs and providing no advantage in terms of HSP suitability.

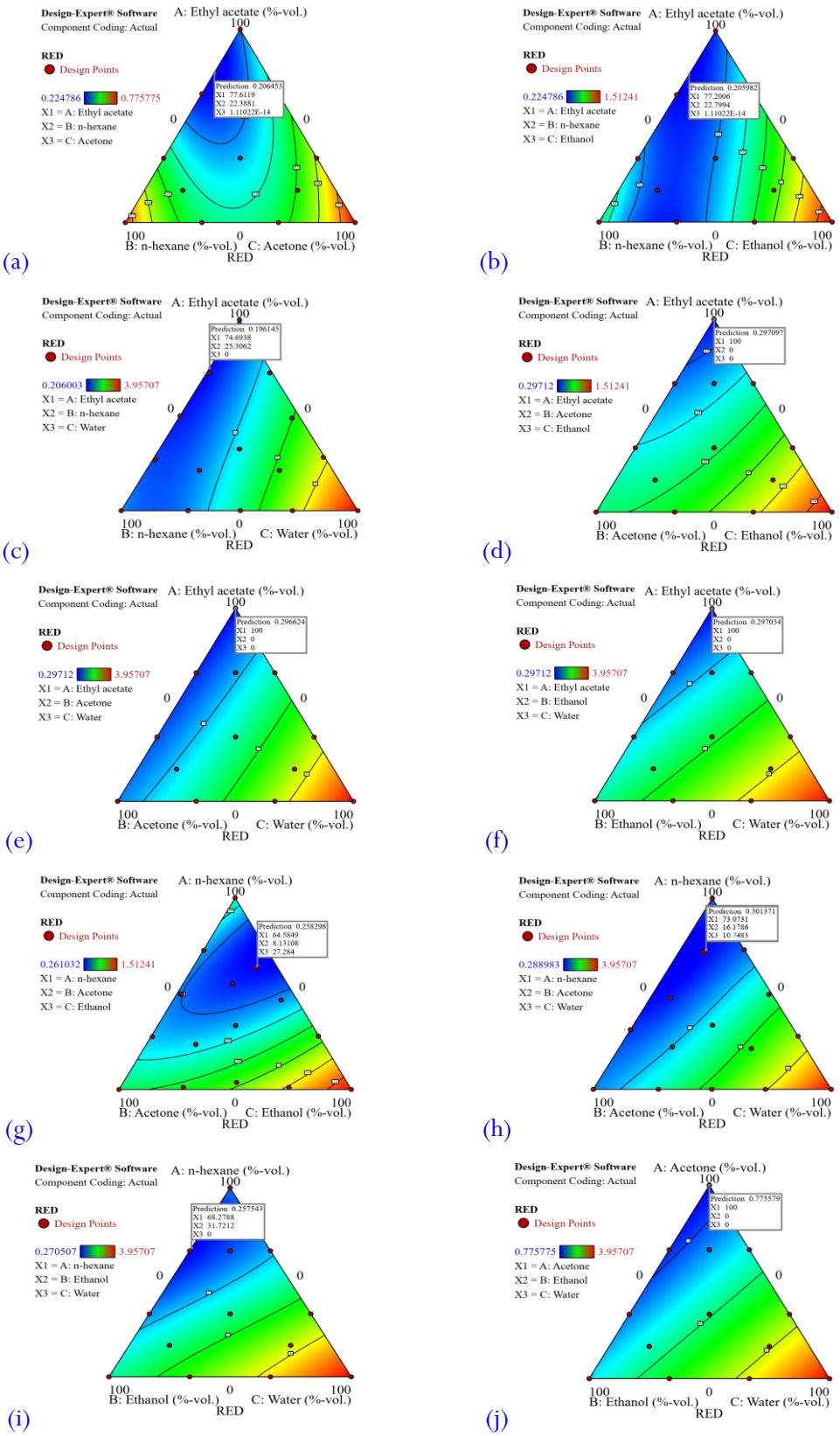

Figure 5. Ternary mixture of five selected solvents, (a) ethyl acetate – n-hexane – acetone, (b) ethyl acetate – n-hexane – ethanol, (c) ethyl acetate – n-hexane – water, (d) ethyl acetate – acetone – ethanol, (e) ethyl acetate – acetone – water, (f) ethyl acetate – ethanol – water, (g) n-hexane – acetone – ethanol, (h) n-hexane – acetone – water, (i) n-hexane – ethanol – water, and (j) acetone – ethanol – water

The n-hexane–acetone–ethanol mixture showed positive results, increasing the values of δ_d, δ_p and δ_{HB}. The addition of acetone and ethanol to n-hexane increased these three parameters, yielding an optimal composition of 64.58:8.13:27.28 vol% with δ_d, δ_p and δ_{HB} values of 15.19, 3.25, and 5.86 $MPa^{1/2}$, respectively, and a RED value of 0.258 (Figure 5 (g)). The increase can be attributed to the complementary effects of acetone and ethanol. Acetone predominantly increased δ_{HB} toward the corresponding value of PSO, whereas ethanol primarily enhanced δ_d and δ_p, bringing the solvent mixture closer to the HSP profile of PSO. In mixtures with a more polar solvent, namely water, the volume fraction of water required to achieve the minimum RED value was less than that of ethanol. It is reflected in the higher proportions of n-hexane and acetone in the mixture with water than with ethanol. Figure 5 (h) shows that the mixture of n-hexane–acetone–water produces the lowest RED value of 0.301 at the composition of 73.07:16.18:10.75 vol%.

Figure 5 (i) shows the interaction of the n-hexane–ethanol–water mixture with PSO. This mixture produces the lowest RED value (0.258) at a composition of 68.28:31.72:0.00 vol%, similar to the results for the binary n-hexane–ethanol mixture (Figure 4(f)), but with a slightly lower RED value. The presence of water as a third solvent does not contribute positively due to its highly polar nature, which increases the deviation of the mixture's HSPs from the PSO HSPs. A similar phenomenon is also observed in the acetone–ethanol–water mixture, where the addition of polar solvents (ethanol and water) does not improve the acetone HSPs. Thus, single acetone still provides the best match (lower RED) compared to its mixtures with ethanol or water, as shown in Figure 4(h).

Of all the ternary solvent mixtures, there are two mixtures that show the lowest RED values, namely n-hexane–acetone–ethanol (64.58:8.13:27.28 vol%) and n-hexane–acetone–water (73.07:16.18:10.75 vol%), each with RED values of 0.258 and 0.301 (Figure 5 (g–h)). In addition, some ternary mixtures also produce lower RED values than predicted in their binary mixtures. For example, the mixtures of ethyl acetate–n-hexane (77.20:22.80 vol%) and n-hexane–ethanol (68.28:31.72 vol%) gave RED values of 0.206 and 0.258, better than the results for the respective binary mixtures (RED = 0.208 and 0.300), as shown in Figures 4(a) and 4(f). These findings indicate that in some cases, the presence of a third solvent can produce small changes in the HSPs of the mixture, thus increasing its affinity for PSO. Furthermore, its presence as an independent variable in the experiment also influences the optimization results, leading to shifts in RED values that are not always predictable from the behavior of the binary mixture. Finally, all the binary and ternary solvent mixtures resulted in six mixed solvents, 4 binaries and 2 ternaries, completing the list of single solvents. Complete data regarding the best solvent mixtures are summarized in Table 6. All selected solvents were used for the PSO extraction process using the Soxhlet method.

Table 6. The list of all solvent mixtures with the lowest RED for Soxhlet-based PSO extraction

No	Mixture	Solvent Code	Solvent quantities (vol%)			RED	Price (USD/MT) [28]
			1	2	3		
1	Single	A	100.00	-	-	0.297	1281
2		B	100.00	-	-	0.743	1090
3		C	100.00	-	-	0.776	1250
4		D	100.00	-	-	1.512	741
5		E	100.00	-	-	3.957	60 [76]
6	Binary	AB	77.20	22.80	-	0.206	1247.3
7		BC	51.24	48.76	-	0.416	1175.2
8		BD	68.28	31.72	-	0.258	964.8
9		BE	86.79	13.21	-	0.342	896.2
10	Ternary	BCD	64.58	8.13	27.28	0.258	997.5
11		BCE	73.07	16.18	10.75	0.301	963.5

Note: for mixed solvent prices were estimated based on mass fraction (A = ethyl acetate, B = n-hexane, C = acetone, D = ethanol, and E = water)

3.5 Performance evaluation of PSO extraction

The solvents selected for extracting oil from papaya seeds were selected based on their ability to dissolve the target components (PSO and its nutraceutical compounds) through their proximity to the HSPs values of PSO, ease of extraction process, and solvent separation from the final product through boiling points that affect energy requirements, SHE aspects, market prices, and solvent mixture interactions. The results of PSO extraction using the Soxhlet method with various solvent variations, both single, binary, and ternary, for 360 minutes, are presented in a graph of the relationship between time (t) and yield as shown in Figure 6. The results showed that increasing the extraction time increased PSO yield until it approached its equilibrium value. This condition occurs because prolonged contact between the solvent and the seeds allows the solvent to penetrate the seed matrix, thereby increasing its ability to dissolve and carry PSO out of the seeds [79]. This finding is in line with the report by Senrayan and Venkatachalam [80], which showed that PSO yield increased with increasing extraction time at initial extraction time (< 6 hours).

Figure 6 also shows that almost all extraction curves exhibit a rapid initial phase (0 – 240 min), followed by a slow or plateau phase (240 – 360 min). This pattern illustrates that mass transfer is very intensive in the initial stage, then becomes limited by oil diffusion from within the seed particles in subsequent stages. In the initial phase (washing stage), oil is released primarily from free oil on the surface or from easily broken cells, resulting in a high extraction rate. Next, the process enters the diffusion stage, in which the solvent penetrates the cell walls and carries oil out of the seed matrix via diffusion [81]. In addition, according to Fick's law, the oil concentration gradient between the seed matrix and the solvent remains large at the initial stage of extraction, resulting in a high diffusion rate. However, this gradient decreases with time, so the diffusion rate and increase in yield become slower towards the end of the process [82].

Further observations showed that at extraction times of 300 – 360 minutes, the change in PSO yield was very small (maximum 0.008%/minute). This occurs because the diffusion rate begins to decrease and approaches a near-constant value. Therefore, increasing the extraction time beyond 300–360 minutes is no longer efficient, and 300 minutes is the optimal condition. Furthermore, the energy supply during the last 60 minutes is also ineffective. On the other hand, this 60-minute time span can be used to prepare for the next batch extraction.

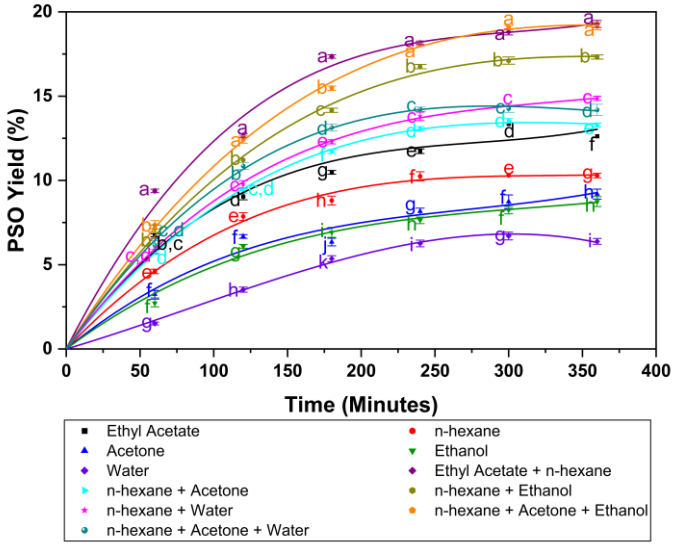

Figure 6. Effect of solvent type on oil yield in papaya seed samples during the 360-minutes Soxhlet extraction process (values within the same extraction time are considered significantly different if indicated by different letters)

Furthermore, PSO extraction with various solvents, both single and mixed, produced widely varying yields. A mixture of solvents containing n-hexane and other organic solvents (ethyl acetate, acetone, or ethanol) gave a higher PSO yield (14 – 19 wt%) compared to pure n-hexane (10.29±0.13 wt%), polar solvents such as water (6.38±0.18 wt%) and ethanol (8.74±0.29 wt%). The highest yield was obtained in PSO extraction using a mixture of ethyl acetate – n-hexane (19.28±0.21 wt%) and n-hexane – acetone – ethanol (19.15±0.22 wt%). This indicates that using solvent mixtures offers advantages during the extraction process, primarily because PSO is more soluble in these mixtures. When using a single solvent, semipolar solvents such as ethyl acetate and nonpolar solvents such as n-hexane gave higher yields than the more polar solvents, such as acetone, ethanol, and water (Figure 6). Therefore, semi- and nonpolar solvents are often used for PSO extraction and are known to produce high yields [22], [24], [83].

Similarly, the highest yield of sweet orange peel oil with n-hexane (6.15%) compared to ethanol (4.89%) and distilled water (1.67%), due to its polarity, which is compatible with sweet orange peel oil [84]. On the other hand, soybean oil extraction using ethyl acetate as a solvent produced higher yields compared to n-hexane [85]. This is due to the semipolar nature of ethyl acetate, which allows it to extract components soluble in both oil and water, resulting in a higher yield than with n-hexane. A supporting report revealed that a higher soybean oil yield with ethyl acetate (25.33±0.44%) than with n-hexane (24.28±1.58%) [86]. Soybean oil is known to have HSPs characteristics of δ_d, δ_p and δ_{HB} of 15.33, 3.77, and 6.87 $MPa^{1/2}$, respectively, which are similar to PSO (δ_d, δ_p and δ_{HB}= 16.48, 3.18, and 5.97 $MPa^{1/2}$).

Furthermore, PSO, which is generally composed of oleic, palmitic, and linoleic acids that are nonpolar, tends to prefer nonpolar solvents. However, the use of a mixture of nonpolar and slightly polar solvents can increase penetration into the solid matrix and mobilize more PSO, resulting in a higher yield compared to the use of a single solvent, as shown in Figure 6. PSO is composed of long-chain fatty acids that have one carboxylic group (-COOH) at the end of the molecule. Although the majority of its structure is a nonpolar hydrocarbon chain, the -COOH group is polar due to the presence of highly electronegative oxygen atoms (C=O and O-H), resulting in a dipole moment at the end of the molecule (δ_p contribution). This group can also act as a hydrogen bond donor and acceptor (donor through H in -OH and acceptor through carbonyl oxygen C=O) (δ_{HB} contribution) [34]. Therefore, although the overall molecule is nonpolar, its ends still contribute δ_p (polar) and δ_{HB} (hydrogen bond) to the HSPs value. In addition, for unsaturated fatty acids such as oleic and linoleic acids, the δ_d, δ_p and δ_{HB} values also increase with the increase in the number of double bonds. Similar results were found by Peña-Gil *et al.* [87], who estimated the HSPs of vegetable oils and showed that the presence of δ_p and δ_{HB} contributions increases the interaction of the oil with slightly polar solvents, such as ethyl acetate, acetone, and ethanol, in their mixtures with n-hexane.

Theoretically, the use of these mixed solvents is expected to provide operational benefits by modifying the viscosity, surface tension, and boiling point of the solvent system. For instance, adding n-hexane (0.33 cP, 18 mN/m) to ethyl acetate (0.43 cP, 24 mN/m) may reduce viscosity and surface tension. This may enhance PSO mass transfer into the solvent and increase yield compared with using ethyl acetate alone [88]. Adding ethyl acetate as a cosolvent with ethanol not only increases soybean oil yield but also reduces energy consumption by lowering the mixture's boiling point [89]. Similarly, the use of acetone as a cosolvent in a ternary system is thought to facilitate interactions between n-hexane and ethanol [90], [91], while ethanol helps modulate the mixture's boiling point. While these physical properties suggest potential advantages for mass transfer and solvent volatility, they are preliminary predictions based on the physical properties of the solvent.

Overall, although the binary mixture of ethyl acetate-n-hexane and the ternary mixture of n-hexane-acetone-ethanol yielded the highest PSO yields, the ternary mixture was proposed as a more advantageous solvent. This is based on its favorable physical properties, particularly its lower surface tension and boiling point (21.01 mN/m, 56 °C) compared to the binary mixture (22.99 mN/m, 71 °C), calculated under mixed conditions, which may improve mass transfer and decrease energy consumption during extraction and separation. Regarding economic considerations, a preliminary assessment based on current market prices indicates that the ternary solvent mixture is cheaper (997.5 USD/MT) than the binary solvent ethyl acetate–n-hexane (1247.3 USD/MT). However, these technical and economic advantages are still theoretical. Comprehensive techno-economic analysis, energy balance, and life cycle assessment (LCA) are recommended in future studies to accurately quantify their impacts on the PSO extraction and separation process.

Although n-hexane remains present in the selected ternary mixture, its concentration decreases significantly (from 100% to 64.58%) with the addition of acetone and ethanol. This blending approach serves as a risk mitigation strategy by reducing the partial pressure of n-hexane vapor, thereby reducing the risk of exposure during extraction. Specifically, the higher electrical conductivity of ethanol and acetone may reduce the risk of ignition from static discharge compared to pure n-hexane [92]. Furthermore, partial replacement of n-hexane with a more polar solvent results in a mixture with a potentially better toxicological profile and lower VOC emissions [92]. While this ternary mixture offers a safer profile, it is important to emphasize that this is a partial improvement, not a complete elimination of the potential hazard.

Regarding the quality of the extracted PSO, the selection of solvent systems is expected to influence the fatty acid profile and the concentration of bioactive components [93]. Based on the HSPs, the use of ternary mixtures (n-hexane-acetone-ethanol) provides a more balanced polarity, facilitating the co-extraction of polar components, such as phospholipids and phenolic compounds, which generally act as natural antioxidants for increasing the oxidative stability of the oil [94], [95]. Although the study successfully determined the optimal solvent combinations, a complete characterization of the oil (i.e., fatty acid profile and physicochemical properties) is needed to validate the quality of the final product. This research represents an initial screening phase to identify the solvent that produces the best yield before more intensive characterization studies.

On the other hand, although the Soxhlet method serves as a standard for determining the maximum extractable oil yield and as part of the framework for solvent screening, it is recognized that extraction efficiency can be further improved by employing more intensive extraction methods. Comparative studies have shown that modern methods, such as Ultrasonic Assisted Extraction (UAE) or Supercritical Fluid Extraction (SFE), often achieve higher extraction rates in shorter times compared to Soxhlet extraction [96], [97]. Although the uses of modern methods and detailed comparative experimental data on PSO extraction are beyond the scope of this solvent screening study, ongoing investigations into UAE for PSO are being conducted to examine the relationship between solvent-solute thermodynamic compatibility (as determined by HSP and RED values) and the resulting yield. Future comparisons are expected to provide a comprehensive evaluation of the best operating methods and conditions, extraction kinetics, and energy efficiency, which are crucial for the development of PSO extraction processes.

Furthermore, while the present work demonstrates the great potential of mixed solvent systems, it should be noted that the extraction process was evaluated using a conventional one-factor-at-a-time (OFAT) approach. While this allows a basic assessment of solvent affinity based on HSPs and physical properties, it does not account for interactions among extraction parameters, such as temperature, extraction time, and solids-to-solvent ratio. Therefore, further optimization using a DoE approach such as Response Surface Methodology (RSM) is recommended for future studies. The application of DoE will result in more stringent statistical evaluations, improved identification

of synergistic interactions between independent and dependent variables, and the evolution of robust mathematical models to predict and maximize PSO extraction yields.

4. Conclusion

This study investigated a systematic solvent screening for PSO extraction, narrowing 50 potential solvents to 5 based on HSPs, physical properties (boiling point), and SHE criteria. Furthermore, binary and ternary interactions among these five solvents yielded six potential solvent mixtures, which were evaluated for PSO solubility, physical properties, and cost. Experimental results showed that the solvent mixtures performed better than the pure solvents, with the highest yields obtained in the mixtures of ethyl acetate-n-hexane (77.20:22.80 vol%) and n-hexane-acetone-ethanol (64.58:8.13:27.28 vol%), yielding 19.28 ± 0.21 wt% and 19.15 ± 0.22 wt%, respectively. Among the tested solvent mixtures, the n-hexane-acetone-ethanol mixture was proposed as the most promising candidate for further implementation. This selection was supported by its high solubility and favorable theoretical properties regarding surface tension, boiling point, and cost. Overall, this systematic approach efficiently identified the best solvent mixture for PSO extraction. The multi-criteria solvent screening approach significantly reduces the number of experimental trials while providing valuable methodological guidance for future research on vegetable oil extraction. Despite these findings, further research should focus on the comprehensive characterization of PSO extracts, such as fatty acid and nutraceutical profiles, to validate PSO quality. Furthermore, a transition from an OFAT-based research approach to a DoE is recommended to investigate interactions among extraction variables. Finally, process intensification, such as the use of UAE and SFE, will be crucial for future comparisons of yield, extraction kinetics, and energy efficiency.

Author's declaration

Author contribution

Misbahudin Alhanif: Conceptualization, Methodology, Software, Investigation, Writing - Original Draft. **Andri Cahyo Kumoro**: Conceptualization, Methodology, Supervision, Writing - Review & Editing. **Dyah Hesti Wardhani**: Data Curation, Supervision, Writing - Review & Editing.

Funding statement

This study was fully funded by the Directorate General of Higher Education, Ministry of Education, Culture, Research and Technology, Republic of Indonesia through the *Program Magister Menuju Doktor Sarjana Unggul (PMDSU)* scholarship awarded to Misbahudin Alhanif, which supported his M.Eng. and Ph.D. studies and the research reported in this manuscript.

Data availability

Data can be requested from the corresponding author.

Acknowledgements

The authors thank Universitas Diponegoro for providing facilities during this research.

Competing interest

The authors declare no financial or non-financial conflicts of interest related to the subject matter of this manuscript.

Ethical clearance

Not applicable

AI statement

Grammarly was used to enhance the grammatical structure, but was not used to generate, interpret, analyze, or modify the study's data, results, or scientific conclusions. The revised manuscript subsequently underwent a comprehensive proofreading by a professional English-language expert. The authors have carefully reviewed and verified all revisions, retained full control over the final text, and take full responsibility for the accuracy, integrity, and scientific content of the manuscript.

Publisher's and Journal's note

Universitas Negeri Padang as the publisher, and Editor of Teknomekanik state that there is no conflict of interest towards this article publication.

References

[1] Y. Zhou *et al.*, "Screening and characterization of phenolic compounds by LC-ESI-QTOF-MS/MS and their antioxidant potentials in papaya fruit and their by-products activities," *Food Bioscience*, vol. 52, pp. 1–16, 2023, https://doi.org/10.1016/j.fbio.2023.102480

[2] S. Samaram, H. Mirhosseini, C. P. Tan, and H. M. Ghazali, "Ultrasound-assisted extraction and solvent extraction of papaya seed oil: Crystallization and thermal behavior, saturation degree, color and oxidative stability," *Industrial Crops and Products*, vol. 52, pp. 702–708, 2014, https://doi.org/10.1016/j.indcrop.2013.11.047

[3] M. Anwar, M. G. Rasul, and N. Ashwath, "Production optimization and quality assessment of papaya (Carica papaya) biodiesel with response surface methodology," *Energy Conversion and Management*, vol. 156, pp. 103–112, 2018, https://doi.org/10.1016/j.enconman.2017.11.004

[4] M. Alhanif, A. C. Kumoro, and D. H. Wardhani, "Prediction of the thermophysical properties of papaya seed oil influencing solvent selection based on the new group contribution model," *Sains Malaysiana*, vol. 52, no. 1, pp. 107–127, 2023, https://doi.org/10.17576/jsm-2023-5201-09

[5] S. M. Abdel-Hameed, N. A. R. Abd Allah, M. M. Hamed, and O. I. A. Soltan, "Papaya fruit by-products as novel food ingredients in cupcakes," *Annals of Agricultural Sciences*, vol. 68, no. 1, pp. 60–74, 2023, https://doi.org/10.1016/j.aoas.2023.05.003

[6] Q. W. Zhang, L. G. Lin, and W. C. Ye, "Techniques for extraction and isolation of natural products: A comprehensive review," *Chinese Medicine (United Kingdom)*, vol. 13, no. 20, pp. 1–26, 2018, https://doi.org/10.1186/s13020-018-0177-x

[7] S. S. Tan, "Papaya (Carica papaya L.) seed oil," in *Fruit Oils: Chemistry and Functionality*, 1st ed., M. Ramadan, Ed., Springer Cham, 2019, pp. 615–626. https://doi.org/10.1007/978-3-030-12473-1_31

[8] M. D. L. de Castro and F. Priego-Capote, "Soxhlet extraction: Past and present panacea," *Journal of Chromatography A*, vol. 1217, no. 16, pp. 2383–2389, Apr. 2010, https://doi.org/10.1016/j.chroma.2009.11.027

[9] X. H. Nguyen, D. N. Vu, Q. M. Bui, Q. T. Nguyen, and A. T. Nguyen, "Comparative efficiency of soxhlet and accelerated solvent extraction (ASE) methods for dioxin/furan analysis in ash samples: A green chemistry perspective," *Green Analytical Chemistry*, vol. 12, pp. 1–8, 2025, https://doi.org/10.1016/j.greeac.2025.100227

[10] G. R. B. Webster, "Soxhlet and ultrasonic extraction of organics in solids," in *In Encyclopedia of Analytical Chemistry*, R. A. Meyers and M. P. Miller, Eds., John Wiley & Sons, Ltd., 2006. https://doi.org/10.1002/9780470027318.a0864

[11] E. Stefanis and C. Panayiotou, "Prediction of hansen solubility parameters with a new group-contribution method," *International Journal of Thermophysics*, vol. 29, pp. 568–585, 2008, https://doi.org/10.1007/s10765-008-0415-z

[12] C. L. Yaws, *Chemical properties handbook: Physical, thermodynamic, environmental, transport, safety, and health related properties for organic and inorganic chemicals*, 1st ed. New York: McGraw-Hill Education, 1999.

[13] NIST, "NIST chemistry webbook," National Institute of Standards and Technology. Accessed: Sep. 17, 2025. [Online]. Available: https://webbook.nist.gov/

[14] RSC, "Search and share chemistry," Royal Society of Chemistry. Accessed: Sep. 17, 2025. [Online]. Available: https://www.chemspider.com/

[15] CAS, "SciFinder," Chemical Abstracts Service. Accessed: Sep. 17, 2025. [Online]. Available: https://scifinder.cas.org

[16] A. C. Kumoro, *Technology for extracting bioactive compounds from medicinal plants*. Yogyakarta: Plantaxia, 2015.

[17] F. J. M. Novaes, F. A. Lima, V. Calado, P. J. Marriott, F. R. D. A. Neto, and C. Moraes, "Isolating valuable coffee diterpenes by using an inexpensive procedure," *Industrial Crops & Products*, vol. 152, no. November 2019, pp. 1–9, 2020, https://doi.org/10.1016/j.indcrop.2020.112494

[18] D. Prat *et al.*, "CHEM21 selection guide of classical- and less classical-solvents," *Green Chemistry*, vol. 18, no. 1, pp. 288–296, 2016, https://doi.org/10.1039/C5GC01008J

[19] D. Prat *et al.*, "Sanofi's solvent selection guide: A step toward more sustainable processes," *Organic Process Research & Development*, vol. 17, no. 12, pp. 1517–1525, Dec. 2013, https://doi.org/10.1021/op4002565

[20] T. Laird, "Green chemistry is good process chemistry," *Organic Process Research & Development*, vol. 16, no. 1, pp. 1–2, 2012, https://doi.org/10.1021/op200366y

[21] S. Samaram, H. Mirhosseini, C. P. Tan, and H. M. Ghazali, "Ultrasound-assisted extraction (UAE) and solvent extraction of papaya seed oil: Yield, fatty acid composition and triacylglycerol profile," *Molecules*, vol. 18, no. 10, pp. 12474–12487, 2013, https://doi.org/10.3390/molecules181012474

[22] N. Sultana *et al.*, "Modeling and optimization of non-edible papaya seed waste oil synthesis using data mining approaches," *South African Journal of Chemical Engineering*, vol. 33, pp. 151–159, 2020, https://doi.org/10.1016/j.sajce.2020.07.009

[23] S. C. Iweka, F. C. Ozioko, E. D. Edafiadhe, and T. F. Adepoju, "Bio-oil production from ripe pawpaw seeds and its optimal output: Box-behnken design and machine learning approach," *Scientific African*, vol. 21, pp. 1–12, 2023, https://doi.org/10.1016/j.sciaf.2023.e01826

[24] M. T. N. Doan, M. C. Huynh, A. N. V. Pham, N. D. Q. Chau, and P. T. K. Le, "Extracting seed oil and phenolic compounds from papaya seeds by ultrasound-assisted extraction method and their properties," *Chemical Engineering Transactions*, vol. 78, pp. 493–498, 2020, https://doi.org/10.3303/CET2078083

[25] N. Assaf *et al.*, "Comparative study of conventional and emerging extraction methods for papaya seed oil: Process optimization and quality evaluation," *Food and Bioprocess Technology*, vol. 19, no. 60, pp. 1–15, 2026, https://doi.org/10.1007/s11947-025-04083-2

[26] The European Parliament and of the Council, *Directive 2009/32/EC of the European Parliament and of the Council of 23 April 2009 on the approximation of the laws of the Member States*

on extraction solvents used in the production of foodstuffs and food ingredients (Recast), no. L 141. 2009, pp. 3–11. [Online]. Available: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32009L0032

[27] ECHA, "Registry of CLH intentions until outcome," European Chemical Agency. Accessed: Jan. 19, 2026. [Online]. Available: https://echa.europa.eu/fr/registry-of-clh-intentions-until-outcome/-/dislist/details/0b0236e18166df77

[28] ChemAnalyst, "Pricing overview," ChemAnalyst. Accessed: Jan. 19, 2026. [Online]. Available: https://www.chemanalyst.com/Pricing/Pricingoverview

[29] T. F. Scientific, "Petroleum ether 30-40°C, certified AR for analysis, n-hexane <0.1%, Fisher Chemical," Thermo Fisher Scientific. Accessed: Jan. 19, 2026. [Online]. Available: https://www.fishersci.co.uk/shop/products/petroleum-ether-30-40-c-certified-ar-analysis-n-hexane-0-1-fisher-chemical/10171670

[30] A. Zuorro, "Enhanced lycopene extraction from tomato peels by optimized mixed-polarity solvent mixtures," *Molecules*, vol. 25, no. 9, pp. 1–14, 2020, https://doi.org/10.3390/molecules25092038

[31] P. K. Soares, R. E. Bruns, and I. S. Scarminio, "Statistical mixture design investigation of fractionated and total extracts from Erythrina speciosa Andrews leaves," *Journal of Separation Science*, vol. 32, pp. 644–652, Feb. 2009, https://doi.org/10.1002/jssc.200800534

[32] M. Alhanif, A. C. Kumoro, and D. H. Wardhani, "Mass transfer, energy utilization, physical and nutritional properties evaluations during drying of papaya (Carica papaya L.) seeds at low to moderate temperatures," *Arabian Journal for Science and Engineering*, vol. 47, no. May, pp. 6245–6267, May 2022, https://doi.org/10.1007/s13369-021-06226-x

[33] M. M. Batista, R. Guirardello, and M. A. Krähenbühl, "Determination of the Hansen solubility parameters of vegetable oils, biodiesel, diesel, and biodiesel–diesel blends," *Journal of the American Oil Chemists' Society*, vol. 92, no. January, pp. 95–109, 2015, https://doi.org/10.1007/s11746-014-2575-2

[34] C. M. Hansen, *Hansen solubility parameters: A user's handbook*, 2nd ed. Boca Raton: CRC Press, 2007. https://doi.org/10.1201/9781420006834

[35] R. K. Henderson *et al.*, "Expanding GSK's solvent selection guide – embedding sustainability into solvent selection starting at medicinal chemistry†," *Green Chemistry*, vol. 13, no. 4, pp. 854–862, 2011, https://doi.org/10.1039/C0GC00918K

[36] L. E. Kurozawa, I. Terng, M. D. Hubinger, and K. J. Park, "Ascorbic acid degradation of papaya during drying: Effect of process conditions and glass transition phenomenon," *Journal of Food Engineering*, vol. 123, pp. 157–164, 2014, https://doi.org/10.1016/j.jfoodeng.2013.08.039

[37] J. Y. Yap, C. L. Hii, S. P. Ong, K. H. Lim, F. Abas, and K. Y. Pin, "Effects of drying on total polyphenols content and antioxidant properties of Carica papaya leaves.," *Journal of the Science of Food and Agriculture*, vol. 100, pp. 2932–2937, Feb. 2020, https://doi.org/10.1002/jsfa.10320

[38] P. J. Szychowski *et al.*, "Kinetics, biocompounds, antioxidant activity, and sensory attributes of quinces as affected by drying method," *Food Chemistry*, vol. 255, pp. 157–164, Jul. 2018, https://doi.org/10.1016/j.foodchem.2018.02.075

[39] P. Carré, S. Berthold, T. Piofczyk, S. Bothe, and S. Hadjiali, "Solvent solutions: Comparing extraction methods for edible oils and proteins in a changing regulatory landscape. General introduction," *OCL - Oilseeds & fats Crops and Lipids*, vol. 32, no. 3, pp. 1–4, 2025, https://doi.org/10.1051/ocl/2024034

[40] M.-G. Guízar-Amezcua *et al.*, "Evaluation of pectin extractions and their application in the alkaline Maillard reaction," *Scientific Reports*, vol. 12, pp. 1–12, 2022, https://doi.org/10.1038/s41598-022-22002-9

[41] S. Suherman *et al.*, "Response surface optimization of time and pressure for freeze-drying mango slices," *Food Research*, vol. 7, no. 1, pp. 182–195, 2023, https://doi.org/10.26656/fr.2017.7(1).816

[42] N. Namini *et al.*, "Optimization of Nigella sativa extraction in olive oil and development of a nondestructive method for thymoquinone quantification: A comprehensive approach by multivariate statistical methods," *Journal of Food Measurement and Characterization*, vol. 20, pp. 4153–4168, 2026, https://doi.org/10.1007/s11694-025-03567-1

[43] A. F. Carneiro, C. N. Carneiro, L. de N. Pires, L. S. G. Teixeira, S. M. Azcarate, and F. de S. Dias, "D-optimal mixture design for the optimization of extraction induced by emulsion breaking for multielemental determination in edible vegetable oils by microwave-induced plasma optical emission spectrometry," *Talanta*, vol. 219, pp. 1–8, 2020, https://doi.org/10.1016/j.talanta.2020.121218

[44] Y. Li, Y. Zhang, M. Wang, L. Jiang, and X. Sui, "Simplex-centroid mixture design applied to the aqueous enzymatic extraction of fatty acid-balanced oil from mixed seeds," *Journal of the American Oil Chemists' Society*, vol. 90, no. 3, pp. 349–357, Mar. 2013, https://doi.org/10.1007/s11746-012-2180-1

[45] F. Dalanta, T. D. Kusworo, N. Aryanti, and N. H. Othman, "Optimization of AC/TiO2/CeO2 composite formulation for petroleum refinery wastewater treatment via simultaneous adsorption-photocatalytic process using D-optimal mixture experimental design," *Journal of Environmental Chemical Engineering*, vol. 9, no. 6, pp. 1–16, 2021, https://doi.org/10.1016/j.jece.2021.106517

[46] C. Benkirane *et al.*, "Bioactive compounds from hemp (Cannabis sativa L.) seeds: Optimization of phenolic antioxidant extraction using simplex lattice mixture design and HPLC-DAD/ESI-MS2 analysis," *RSC Advances*, vol. 12, no. 39, pp. 25764–25777, 2022, https://doi.org/10.1039/d2ra04081f

[47] H. Moussa, F. Dahmoune, M. malik Mahdjoub, N. Kadri, and H. Remini, "Definitive screening design and I-optimal design for optimization of ultrasound-assisted extraction of phenolic content and antioxidant capacity from Salvia officinalis L. leaves," *Sustainable Chemistry and Pharmacy*, vol. 29, pp. 1–15, 2022, https://doi.org/10.1016/j.scp.2022.100820

[48] R. C. N. Thilakarathna, L. F. Siow, T.-K. Tang, E.-S. Chan, and Y.-Y. Lee, "Physicochemical and antioxidative properties of ultrasound-assisted extraction of mahua (Madhuca longifolia) seed oil in comparison with conventional Soxhlet and mechanical extractions," *Ultrasonics Sonochemistry*, vol. 92, pp. 1–10, 2023, https://doi.org/10.1016/j.ultsonch.2022.106280

[49] M. M. Cascant, C. Breil, S. Garrigues, M. D. la Guardia, A. S. Fabiano-Tixier, and F. Chemat, "A green analytical chemistry approach for lipid extraction : Computation methods in the selection of green solvents as alternative to hexane," *Analytical and Bioanalytical Chemistry*, vol. 409, pp. 3527–3539, 2017, https://doi.org/10.1007/s00216-017-0323-9

[50] D. B. Nde and A. C. Foncha, "Optimization methods for the extraction of vegetable oils: A review," *Processes*, vol. 8, no. 2, pp. 1–21, 2020, https://doi.org/10.3390/pr8020209

[51] F. J. M. Novaes, D. C. de Faria, F. Z. Ferraz, and F. R. de A. Neto, "Hansen solubility parameters applied to the extraction of phytochemicals," *Plants*, vol. 12, no. 16, pp. 1–18, 2023, https://doi.org/10.3390/plants12163008

[52] D. F. Tirado, M. J. Tenorio, A. Cabañas, and L. Calvo, "Prediction of the best cosolvents to solubilise fatty acids in supercritical CO2 using the Hansen solubility theory," *Chemical Engineering Science*, vol. 190, pp. 14–20, 2018, https://doi.org/10.1016/j.ces.2018.06.017

[53] Y. Li *et al.*, "Evaluation of alternative solvents for improvement of oil extraction from rapeseeds," *Comptes Rendus Chimie*, vol. 17, no. 3, pp. 242–251, 2014, https://doi.org/10.1016/j.crci.2013.09.002

[54] E. Yara-Varón, A. S. Fabiano-Tixier, M. Balcells, R. Canela-Garayoa, A. Bily, and F. Chemat, "Is it possible to substitute hexane with green solvents for extraction of carotenoids? A theoretical versus experimental solubility study," *RSC Advances*, vol. 6, no. 33, pp. 27750–27759, 2016, https://doi.org/10.1039/c6ra03016e

[55] S. Zapata-Boada, M. Gonzalez-Miquel, M. Jobson, and R. M. Cuéllar-Franca, "Life cycle environmental evaluation of alternative solvents used in lipid extraction—The case of algae biodiesel," *ACS Sustainable Chemistry and Engineering*, vol. 11, no. 32, pp. 11934–11946, 2023, https://doi.org/10.1021/acssuschemeng.3c01995

[56] F. E. Eddaoudi, H. El Moudden, C. El Guezzan, M. Saber, H. Harhar, and M. Tabyaoui, "Effect of extraction process on quality of oil from Asphodelus tenuifolius seeds," *OCL - Oilseeds & fats Crops and Lipids*, vol. 30, no. 20, pp. 1–10, 2023, https://doi.org/10.1051/ocl/2023020

[57] I. Efthymiopoulos *et al.*, "Influence of solvent selection and extraction temperature on yield and composition of lipids extracted from spent coffee grounds," *Industrial Crops and Products*, vol. 119, pp. 49–56, 2018, https://doi.org/10.1016/j.indcrop.2018.04.008

[58] SDS, "Free safety data sheet (SDS)," SDS Manager. Accessed: Sep. 18, 2025. [Online]. Available: https://sdsmanager.com/us/search/

[59] Sigma-Aldrich, "Safety data sheet of carbon tetrachloride," 2024. Online]. Available: https://www.sigmaaldrich.com/ID/en/sds/ALDRICH/571016?userType=undefined

[60] Sigma-Aldrich, "Safety data sheet of chloroform," 2026. [Online]. Available: https://www.sigmaaldrich.com/ID/en/sds/sigald/650498?userType=undefined

[61] Sigma-Aldrich, "Safety data sheet of n-hexane," 2026. [Online]. Available: https://www.sigmaaldrich.com/ID/en/sds/sial/296090?userType=undefined

[62] Sigma-Aldrich, "Safety data sheet of tert-Butyl methyl ether," 2025. [Online]. Available: https://www.sigmaaldrich.com/ID/en/sds/sigald/443808?userType=undefined

[63] Chem-lab, "Safety data sheet of petroleum ether 40-60 a.r.," 2023. [Online]. Available: https://nextsds.com/sds/en/281331501271165/petroleum-ether-40-60-a-r

[64] H. Carless, "Safety data sheet of n-Heptane ASTM," 2024. [Online]. Available: https://nextsds.com/sds/en/281331501271002/n-heptane-astm

[65] Sigma-Aldrich, "Safety data sheet of cyclohexane," 2025. [Online]. Available: https://www.sigmaaldrich.com/ID/en/sds/sigald/179191?userType=undefined

[66] Sigma-Aldrich, "Safety data sheet of benzene," 2025. [Online]. Available: https://www.sigmaaldrich.com/ID/en/sds/sigald/319953?userType=undefined

[67] Sigma-Aldrich, "Safety data sheet of acetone," 2026. [Online]. Available: https://www.sigmaaldrich.com/ID/id/sds/sigald/32201?userType=undefined

[68] Sigma-Aldrich, "Safety data sheet of ethyl acetate," 2026. [Online]. Available: https://www.sigmaaldrich.com/ID/en/sds/sial/270989?userType=undefined

[69] Sigma-Aldrich, "Safety data sheet of 1,2-dichloroethane," 2025. [Online]. Available: https://www.sigmaaldrich.com/ID/en/sds/sigald/319929?userType=undefined

[70] Sigma-Aldrich, "Safety data sheet of tetrahydrofuran," 2025. [Online]. Available: https://www.sigmaaldrich.com/ID/en/sds/sial/401757?userType=undefined

[71] I. Pagano *et al.*, "Selective extraction of high–value phenolic compounds from distillation wastewater of basil (Ocimum basilicum L.) by pressurized liquid extraction," *Electrophoresis*, vol. 39, pp. 1–8, 2018, https://doi.org/10.1002/elps.201700442

[72] S. R. Dewi, L. A. Stevens, A. E. Pearson, R. Ferrari, D. J. Irvine, and E. R. Binner, "Investigating the role of solvent type and microwave selective heating on the extraction of phenolic compounds from cacao (Theobroma cacao L.) pod husk," *Food and Bioproducts Processing*, vol. 134, pp. 210–222, 2022, https://doi.org/10.1016/j.fbp.2022.05.011

[73] Y. Park and B. Lee, "Solubility of gallic acid in single and mixed solvents," *Separations*, vol. 11, no. 36, pp. 1–16, 2024, https://doi.org/10.3390/separations11010036

[74] R. J. Lehnert and R. Schilling, "Accuracy of molar solubility prediction from Hansen parameters. An exemplified treatment of the bioantioxidant L-ascorbic acid," *Applied Sciences*, vol. 10, pp. 1–11, 2020, https://doi.org/10.3390/app10124266

[75] P. Carré, T. Piofczyk, and S. Bothe, "Solvent solutions: Comparing extraction methods for edible oils and proteins in a changing regulatory landscape. Part 7: Overall comparison

between solvent solutions," *OCL - Oilseeds & fats Crops and Lipids*, vol. 32, no. 9, pp. 1–17, 2025, https://doi.org/10.1051/ocl/2025013

[76] Indotrading, "Aquadest surabaya air murni aquadest," Indotrading. Accessed: Oct. 08, 2025. [Online]. Available: https://www.indotrading.com/nusaindahmegah/aquadest-surabaya-air-murni-aquadest-p890173.aspx

[77] C. Reichardt and T. Welton, *Solvents and solvent effects in organic chemistry*, 4th ed. Wiley-VCH Verlag GmbH & Co. KGaA, 2010. https://doi.org/10.1002/9783527632220

[78] M. Mohsen-Nia, H. Amiri, and B. Jazi, "Dielectric constants of water, methanol, ethanol, butanol and acetone: Measurement and computational study," *Journal of Solution Chemistry*, vol. 39, no. 5, pp. 701–708, 2010, https://doi.org/10.1007/s10953-010-9538-5

[79] M. H. Hamzah *et al.*, "Extraction of fixed oils from sacha inchi (Plukenetia volubilis) seeds via ohmic heating: Optimization and comparative study," *Food Analytical Methods*, vol. 19, no. 81, pp. 1–24, 2026, https://doi.org/10.1007/s12161-026-02994-0

[80] J. Senrayan and S. Venkatachalam, "Solvent-assisted extraction of oil from papaya (Carica papaya L.) seeds: evaluation of its physiochemical properties and fatty-acid composition," *Separation Science and Technology*, vol. 53, no. 17, pp. 2852–2859, 2018, https://doi.org/10.1080/01496395.2018.1480632

[81] R. K. Saini, P. Prasad, X. Shang, and Y.-S. Keum, "Advances in lipid extraction methods—A review," *International Journal of Molecular Sciences*, vol. 22, no. 24, pp. 1–19, 2021, https://doi.org/10.3390/ijms222413643

[82] H. A. Harouna-Oumarou, H. Fauduet, C. Porte, and Y. S. Ho, "Comparison of kinetic models for the aqueous solid-liquid extraction of Tilia sapwood a continuous stirred tank reactor," *Chemical Engineering Communications*, vol. 194, no. 4, pp. 537–552, 2007, https://doi.org/10.1080/00986440600992511

[83] S. Goriainov *et al.*, "Study of the chemical composition of Carica papaya L. seed oils of various geographic origins," *Horticulturae*, vol. 9, no. 11, pp. 1–14, 2023, https://doi.org/10.3390/horticulturae9111227

[84] A. Syahadat, H. Yaturramadhan, and A. Diningsih, "The effect of solvent type on oil yield on essential oil of sweet orange peel extract (Citrus X Sinensis)," *Journal of Public Health and Pharmacy*, vol. 1, no. 3, pp. 59–62, 2021, https://doi.org/10.56338/jphp.v1i3.3726

[85] D. Shejawale, J. Lavania, N. Muthuganesan, T. Jeyarani, N. K. Rastogi, and R. Subramanian, "Alternate solvent for soybean oil extraction based on extractability and membrane solvent recovery," *Environmental Science and Pollution Research*, vol. 32, no. 52, pp. 29592–29606, 2025, https://doi.org/10.1007/s11356-024-34038-7

[86] H. Gasparetto, A. L. B. Nunes, F. de Castilhos, and N. P. G. Salau, "Soybean oil extraction using ethyl acetate and 1-butanol: From solvent selection to thermodynamic assessment," *Journal of Industrial and Engineering Chemistry*, vol. 113, pp. 450–460, 2022, https://doi.org/10.1016/j.jiec.2022.06.020

[87] A. D. La Peña-Gil, J. F. Toro-Vazquez, and M. A. Rogers, "Simplifying Hansen solubility parameters for complex edible fats and oils," *Food Biophysics*, vol. 11, pp. 283–291, 2016, https://doi.org/10.1007/s11483-016-9440-9

[88] NIH, "PubChem," National Library of Medicine. Accessed: Sep. 17, 2025. [Online]. Available: https://pubchem.ncbi.nlm.nih.gov/

[89] J. L. A. Dagostin, D. Carpiné, P. R. S. dos Santos, and M. L. Corazza, "Liquid-liquid equilibrium and kinetics of ethanolic extraction of soybean oil using ethyl acetate as co-solvent," *Brazilian Journal of Chemical Engineering*, vol. 35, no. 2, pp. 415–427, 2018, https://doi.org/10.1590/0104-6632.20180352s20160175

[90] S. Song and C. Peng, "Viscosities of binary and ternary mixtures of water, alcohol, acetone, and hexane," *Journal of Dispersion Science and Technology*, vol. 29, no. 10, pp. 1367–1372, 2008, https://doi.org/10.1080/01932690802313006

[91] M. J. Zarrinmehr *et al.*, "The effect of solvents polarity and extraction conditions on the microalgal lipids yield, fatty acids profile, and biodiesel properties," *Bioresource Technology*, vol. 344, no. Part B, pp. 1–10, 2022, https://doi.org/10.1016/j.biortech.2021.126303

[92] P. Carré, C. dev Borah, T. Piofczyk, M. Gärtner, S. Bothe, and S. Hadjiali, "Solvent solutions: comparing extraction methods for edible oils and proteins in a changing regulatory landscape. Part 2: Hazards control," *OCL - Oilseeds and Fats, Crops and Lipids*, vol. 31, no. 33, pp. 1–12, 2024, https://doi.org/10.1051/ocl/2024028

[93] R. Tir, P. C. Dutta, and A. Y. Badjah-Hadj-Ahmed, "Effect of the extraction solvent polarity on the sesame seeds oil composition," *European Journal of Lipid Science and Technology*, vol. 114, no. 12, pp. 1427–1438, 2012, https://doi.org/10.1002/ejlt.201200129

[94] M. A. Alcântara *et al.*, "Effect of the solvent composition on the profile of phenolic compounds extracted from chia seeds," *Food Chemistry*, vol. 275, pp. 489–496, 2019, https://doi.org/10.1016/j.foodchem.2018.09.133

[95] H. D. Belayneh, R. L. Wehling, E. B. Cahoon, and O. N. Ciftci, "Effect of extraction method on the oxidative stability of camelina seed oil studied by differential scanning calorimetry," *Journal of Food Science*, vol. 82, no. 3, pp. 632–637, 2017, https://doi.org/10.1111/1750-3841.13652

[96] J. Shao, D. Ding, Z. Zhu, and X. Chen, "Ultrasound-assisted extraction of sumac fruit oil and analysis of its fatty acid composition," *Journal of Food Science*, vol. 89, no. 11, pp. 7653–7663, 2024, https://doi.org/10.1111/1750-3841.17452

[97] A. Mishra *et al.*, "Advancement in microalgal metabolites extraction techniques: Multi-factorial considerations," *Journal of Microbiological Methods*, vol. 238, pp. 1–11, 2025, https://doi.org/10.1016/j.mimet.2025.107280

Nomenclature

Symbols	Descriptions	Units
δ_d	Contributions of dispersion	[$MPa^{1/2}$]
δ_P	Contributions of polar	[$MPa^{1/2}$]
δ_{HB}	Contributions of hydrogen bonding	[$MPa^{1/2}$]
D	Relative distance	-
RED	Relative energy difference	-
x_i	Volume compositions	[%]
C_{PSO}	Concentration of PSO	[mL/L]
V	Volume extract	[L]
ρ	Density of PSO	[g/mL]
m_{seeds}	Mass of seeds	[g]