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Ultrasound-assisted liquid biphasic extraction of fucoidan from *Sargassum sp.*

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ABSTRACT

Sargassum sp. is an essential source of fucoidan. This work aims to extract fucoidan from *Sargassum sp.*. using a liquid biphasic system assisted by ultrasonics. It observes the effects of various process parameters on fucoidan yield, determines the optimum extraction conditions, and develops a model for extraction kinetics. This work confirms that FTIR and HPLC techniques successfully identified fucoidan, with a yield of 14.1% achieved at a *Sargassum*-to-solvent ratio of 0.04 g/mL, an extraction time of 20 minutes, and an ultrasonic power of 70%. The results indicate that extraction time is a significant factor compared to power and the *Sargassum*-to-solvent ratio. The diffusion coefficient (D_e) of 1.425118×10^{-2} m²/s suggests relatively rapid diffusion under the applied extraction conditions. The results highlight the efficacy of the ultrasound-assisted liquid biphasic method for optimising fucoidan extraction from *Sargassum sp.*

1. Introduction

Indonesia is renowned for cultivating a diverse range of algae, with the brown alga *Sargassum sp.* being one of the most economically significant [1,2]. This remarkable alga is a key source of fucoidan [3], a compound primarily composed of fucose, along with other monosaccharides including galactose, glucose, xylose, and mannose [4]. Fucoidan is extracted through specific processes and is utilised in the pharmaceutical, functional food, and cosmetic industries due to its beneficial properties [5].

The selection of the extraction method and solvent type is critical in determining the bioactivity quality of fucoidan [6]. Employing an unsuitable extraction technique frequently results in the structural degradation of fucoidan, consequently reducing its bioactive properties. Thus, the isolation of fucoidan necessitates the adoption of an appropriate extraction method that preserves its inherent structural integrity, particularly with respect to its high fucose content, which is vital for sustaining its biological activity [7,8].

Biphasic systems are gaining recognition for their environmental advantages, offering a sustainable approach that reduces energy consumption and minimises ecological impact in algal processing [9]. These systems facilitate the separation and purification of bioactive compounds in a single operational step, conducted under mild conditions and utilising non-toxic, water-based solvents. Such characteristics render two-phase liquid systems particularly well-suited for preserving the chemical integrity of fucoidan while enhancing extraction efficiency and minimising the degradation of its active components [10,6].

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A range of extraction methodologies has been employed in the isolation of fucoidan, encompassing both conventional techniques and modern advanced technologies. Traditional extraction methods often present significant limitations, including the need for elevated temperatures, prolonged extraction times, and large solvent volumes. These factors collectively contribute to the structural degradation of fucoidan, which is crucial for its bioactivity. In contrast, advanced extraction techniques, such as Microwave-Assisted Extraction (MAE) and Ultrasound-Assisted Extraction (UAE), demonstrate superior efficacy in preserving the chemical integrity of fucoidan while concurrently enhancing extraction yields. These innovative methodologies enable more efficient extraction processes and maintain the stability of bioactive compounds throughout the extraction phase. Furthermore, ultrasound-assisted extraction has been reported to improve extraction efficiency via cavitation, enhancing cell disruption and facilitating solvent penetration into the plant matrix. This mechanism accelerates mass transfer and enables higher yield compared to conventional extraction methods [11]. While typically it may compromise the stability of the fucoidan structure, UAE offers a controlled extraction environment conducted at ambient temperatures. This characteristic is particularly significant for safeguarding the integrity of the fucoidan chemical structure, especially the sulfate groups, which play a pivotal role in its biological activity. Consequently, the UAE is regarded as a more advantageous approach for extracting high-quality fucoidan, thereby optimising its potential biological efficacy [12,13,14].

Scaling up fucoidan extraction processes requires careful consideration of energy consumption, process efficiency, and product quality. Ultrasound-assisted extraction (UAE) has been identified as a promising green and scalable technique due to its lower energy requirements, reduced solvent usage, and shorter processing time compared to conventional methods [15].

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However, challenges remain at pilot and industrial scales, particularly related to techno-economic feasibility, energy demand, and process optimisation [16]. In addition, integrated biorefinery approaches and optimised extraction techniques have been explored to enhance the resource efficiency and economic viability of fucoidan production [17,18].

The study by [19] reports that Ultrasound-Assisted Extraction (UAE) of Sargassum polycystum significantly increased extraction yield and antioxidant activity, indicating that this method is effective in preserving the quality of bioactive compounds. Furthermore, the UAE is considered an environmentally friendly extraction technique, as it requires less solvent and consumes less energy than conventional methods. Ultrasound-assisted extraction (UAE) operates at moderate power (150–350 W) with shorter extraction times (2–59 minutes) and lower temperatures (25–70°C) compared to conventional methods, which typically require prolonged heating at 80–85°C for several hours, resulting in higher energy consumption and potential thermal degradation. UAE has been reported to enhance fucoidan yield by approximately 20–50% relative to conventional extraction, primarily due to acoustic cavitation that disrupts cell structures and improves mass transfer [20,21]. In terms of solvent usage, UAE typically utilizes lower solvent-to-solid ratios, generally in the range of 10:1 to 30:1 (mL/g), compared to conventional extraction which often requires higher ratios of approximately 20:1 to 60:1 (mL/g) to achieve comparable yields. This reduction in solvent volume contributes to lower chemical consumption and reduced downstream processing requirements [22]. Moreover, UAE reduces solvent usage and environmental impact, including lower CO_2 emissions, confirming its classification as a more efficient and sustainable extraction method compared to conventional techniques [6,23]. These findings are consistent with studies by [5] and [24], which reported that UAE enhances extraction efficiency through acoustic cavitation, leading to cell wall disruption and accelerating the release of intracellular bioactive compounds, thereby improving both yield and biological activity. Moreover, these studies also emphasized that UAE operates under relatively mild conditions, which is highly beneficial for maintaining the stability of sensitive compounds such as fucoidan.

In addition, liquid biphasic systems (LBS) have emerged as a promising green extraction approach that enables simultaneous extraction and partial purification of biomolecules in a single step. These systems utilize aqueous two-phase media, offering advantages such as low toxicity, reduced solvent consumption, and improved selectivity, thereby preserving the structural integrity of fucoidan [25,26]. Despite these advantages, studies integrating UAE with LBS for fucoidan extraction are still limited, particularly in terms of understanding the extraction kinetics and diffusion mechanisms involved [18,27].

Previous studies have primarily focused on optimizing extraction yield and evaluating the bioactivity of fucoidan, while relatively limited attention has been given to a comprehensive understanding of extraction kinetics and diffusion mechanisms, particularly in integrated systems such as ultrasound-assisted extraction combined with liquid biphasic systems. Most existing studies emphasize process parameters and yield improvement rather than mechanistic modeling of mass transfer [28]. Although some works have explored extraction kinetics in polysaccharide systems, these remain limited and are rarely extended to fucoidan or hybrid extraction approaches [29]. This lack of mechanistic insight hinders the rational design of efficient and scalable extraction processes for industrial applications. Therefore, this study aims to address these gaps by extracting fucoidan from Sargassum sp. using an ultrasound-assisted liquid biphasic system, systematically evaluating the effects of key process parameters on extraction yield, determining the optimum operating conditions, and developing a kinetic model based on diffusion mechanisms to elucidate mass transfer behavior during the extraction process.

2. Method

2.1 Material and instrument

The primary raw material used in this study was the brown seaweed *Sargassum sp.*, obtained from the southern coastal area of Jember, Indonesia. 2-propanol (ROFA, Indonesia), dipotassium hydrogen phosphate (K_2HPO_4, >99 wt%) (ROFA, Indonesia), Calcium chloride ($CaCl_2$) (Haizhiyuab, China), ethanol 96% (PT. Fuku Sejahtera, Indonesia), commercial fucoidan (PT Soho Indonesia), potassium bromide (KBr) (Merck KgaA, Germany) was used for FT-IR analysis, ammonium formate (Sigma Aldrich), acetonitrile pro HPLC grade (Mallinckrodt), and water pro HPLC grade (Merck, US/Canada). As used in this study included a centrifuge (Oregon LC-04S, Indonesia), an ultrasonic probe (LUHS-A12, United Kingdom) of the maximum power 650 W, a Fourier Transform Infrared (FT-IR) spectrophotometer (Shimadzu IRTracer-100, Japan), and an Agilent 1100 series HPLC system equipped with an Agilent 380 ELSD detector and a Zorbax HILIC Plus column (100 × 4,6 mm; 3,5 µm).

3. Result and Discussion

3.1 The effect of extraction parameters on the yield

The ultrasound-assisted extraction of fucoidan from *Sargassum sp.* powder was performed in various conditions. The process also involves alginate separation, ensuring the purity of the extracted fucoidan and providing reliability in this method. The 17 experiments were run using Box-Behnken Design. Thus, three independent parameters, ultrasonic power levels of 60%, 65%, and 70% of 650 W, extraction durations of 10, 15, and 20 minutes, and a *Sargassum sp.* powder to solvent ratio of 0.03, 0.04, and 0.05 g/mL, were explored. The fucoidan yield was taken as the dependent parameter. The results are provided in Table 1.

The centre point of the central composite design was measured five times (runs 3, 5, 10, 11, and 16). Experimentally, the highest extract yield was approximately 14.1 wt% and was achieved at an extraction time of 20 minutes, a *Sargassum sp.* to solvent ratio of 0.04 g/mL, and an ultrasound power level of 70% corresponding to 455 W. This finding is higher than those reported in Table 3. This work also suggests that ultrasound-assisted extraction (UAE) coupled with a liquid biphasic system (UAE–LBS) using a 2-propanol–aqueous solvent system achieves better performance than that reported in Table 3. The effectiveness of this method can be attributed to the combined action of ultrasonic cavitation and biphasic partitioning. Ultrasound enhances cell wall disruption and mass transfer, facilitating the release of fucoidan from the *Sargassum* matrix. At the same time, the liquid biphasic system promotes selective partitioning of the target fucoidan, thereby improving extraction efficiency and reducing co-extraction of impurities. Therefore, the superior performance of UAE–LBS arises from the synergistic integration of physical intensification and solvent-

based selectivity, making it a more effective approach for fucoidan extraction from *Sargassum sp.*

Table 1. Yield between various condition of Fucoidan extraction from *Sargassum sp.*

Run	A: Extraction Time (Minutes)	B: *Sargassum sp.* powder to solvent ratio (g/ml)	C: Power UAE (%)	Yield (%)
1	10	0.04	70	7.41
2	10	0.05	65	7.10
3	15	0.04	65	8.60
4	10	0.04	60	6.80
5	15	0.04	65	9.20
6	15	0.03	60	8.10
7	20	0.04	60	11.2
8	10	0.03	65	7.00
9	15	0.05	60	8.40
10	15	0.04	65	8.80
11	15	0.04	65	9.00
12	20	0.03	65	12.00
13	15	0.03	70	9.40
14	20	0.04	70	14.14
15	15	0.05	70	9.07
16	15	0.04	65	8.70
17	20	0.05	65	11.49

Table 2. Fucoidan extraction results from *Sargassum sp.* in previous studies

Method	Solvent	Extraction condition	Yield (%)	Reference
Acid extraction	HCL 0,1 N	Extraction time, ratio of material to solvent	2,71	[30]
Acid extraction	HCL 0,1 N	Extraction time, ratio of material to solvent	2,46	[31]
Microwave-assisted extraction	HCL	MAE power, extraction time	9,90	[32]
Microwave-assisted extraction	Water	Temperature, extraction time, ratio of material to solvent	4,50	[33]
Ultrasound-assisted extraction	Water	Temperature, extraction time	3,93	[27]
Ultrasound-assisted extraction			2.77	[34]
Ultrasound-assisted extraction			6.94	[5]
Ultrasound-assisted extraction – Liquid Biphasic System (UAE-LBS)	2-propanol + Aquadest	Extraction time, UAE power, ratio of material to solvent	14,1	This Research

Table 2 states that extraction using the UAE-LBS method gains a higher value than conventional methods, such as acid extraction and single-step extraction. This finding demonstrates the effectiveness of modern extraction methods, particularly the UAE-LBS, in improving the efficiency of bioactive compound extraction. Additionally, it recommends that 2-propanol and a K_2HPO_4 solution are a promising combination for extracting seaweed-active compounds, including those from *Sargassum sp.*, thereby increasing fucoidan yield. K_2HPO_4 was chosen as the optimal salt because of its ability to maintain solution pH stability, increase the solubility of the target compound, facilitate the separation of two liquid phases, and enable a safe, non-toxic process [35].

Meanwhile, based on this work, the fucoidan yield from *Sargassum sp.* as the raw material, as shown in Table 3, was higher than that from other algae. This indicates that *Sargassum sp.* demonstrates significant potential as a rich source of fucoidan. The cell wall structure of *Sargassum sp.* may be more readily broken than that of other algae, allowing solvents to extract bioactive fucoidan compounds more effectively. The results of this study provide additional insight into selecting the optimal raw material for extracting the fucoidan bioactive compound to achieve high yields.

Table 3. Fucoidan extraction from various algae

Raw Material	Extraction Method	Yield (%)	Reference
Undaria pinnatifida	Assisted by a microwave	12.3	[36]
Ecklonia maxima	Assisted by ultrasonic waves and enzymes	7.91	[1]
Sargassum sp.	Assisted by ultrasonic waves	2.77	[34]
Sargassum siliquosum	Assisted by a microwave	6.94	[5]
Fucus vesiculosus	Assisted by ultrasonic waves	6.5	[37]
Padina tetrastromatica	Assisted by subcritical water	13	[38]
Sargassum sp.	Assisted by ultrasonic waves and LBS	14.1	This work

The effectiveness of this method can be attributed to the combined action of ultrasonic cavitation and biphasic partitioning, which enhances mass transfer while simultaneously enabling selective separation of fucoidan. Ultrasonic cavitation disrupts the rigid brown algal cell wall, reduces mass-transfer resistance and accelerates polysaccharide diffusion into the solvent phase [39]. Compared to previous studies in Table 2, the UAE–LBS method produced a markedly higher yield (14.1%) than acid extraction (2.46–2.71%) [30,31], conventional UAE (2.77–6.94%) [34,5], and microwave-assisted extraction (up to 9.90%) [32]. This consistent improvement indicates that the enhanced performance is not solely due to intensified cavitation, but more importantly, due to the incorporation of the liquid biphasic system, which enables in-situ separation and reduces solute loss during downstream processing limitations that are commonly observed in single-step extraction methods [31,40].

However, comparison with Table 3 suggests that high yields can also be achieved using other optimised techniques, such as subcritical water extraction of *Padina tetrastromatica* (13%) [38] and microwave-assisted extraction of *Undaria pinnatifida* (12.3%) [36]. This indicates that extraction

efficiency is influenced not only by the method, but also by intrinsic factors such as algal species, cell wall structure, initial fucoidan content, and the targeted purity level [1,6,41]. Nevertheless, unlike other methods that primarily focus on extraction enhancement, the UAE–LBS approach integrates extraction and separation in a single system. This integration provides a mechanistic advantage by combining cavitation-induced cell disruption with phase partitioning, which improves recovery efficiency and reduces impurity co-extraction [42]. Kinetic studies of conventional and microwave-assisted extraction also show that forcing more severe conditions to maximize yield often leads to fucoidan degradation, loss of fucose and sulfate, and increased co-extraction of laminarin and other impurities [43], underscoring the importance of intensification strategies that preserve structure while improving recovery. Hence, the novelty of this work lies not merely in achieving higher yield, but in demonstrating a dual-function extraction–separation strategy that addresses fundamental limitations of conventional and single-intensification techniques.

3.2 Statistical modelling

A variance analysis was conducted to assess the significance of process variables on yield and to develop a statistical model using the Response Surface Methodology (RSM) with the Box-Behnken Design (BBD). The process variables consist of ultrasonic extraction time (UAE time), ultrasonic power, and the raw material-to-solvent ratio. These variables were analysed simultaneously to determine their individual and combined effects on extraction yield and to generate a predictive model that illustrates how variations in operational conditions influence the extraction process yield. The result of the variance analysis is given in Table 4.

Table 4. Analysis of variance of yield

Source	Sum of Squares	Df	Mean Square	F-value	p-value	
Model	61.21	9	6.80	53.22	< 0.0001	significant
A: Time	52.53	1	52.53	411.09	< 0.0001	
B: *Sargassum sp.*. to solvent ratio	0.0200	1	0.0200	0.1565	0.7042	
C: Power	3.78	1	3.78	29.59	0.0010	
AB	0,0900	1	0.0900	0.7043	0.4291	
AC	1.32	1	1.32	10.35	0.0147	
BC	0.0900	1	0.0900	0.7043	0.4291	
A^2	2.92	1	2.92	22.84	0.0020	
B^2	0.3602	1	0.3602	2.82	0.1370	
C^2	0.1402	1	0.1402	1.10	0.3296	
Residual	0.8945	7	0.1278			
Lack of Fit	0.6625	3	0.2208	3.81	0.1146	not significant
Pure Error	0.2320	4	0.0580			

According to the findings presented in Table 4, extraction time is the predominant factor influencing fucoidan yield. While the power and the *Sargassum sp.* -to-solvent ratio also contribute to the extraction process, their overall effects are comparatively less pronounced than those of extraction time. It is noteworthy that, despite the critical role of extraction time in enhancing yield, prolonged exposure to ultrasonic waves promotes fucoidan degradation, including the cleavage of glycosidic bonds. This degradation subsequently reduces both the molecular weight and biological activity of fucoidan [44]. Furthermore, at excessively high intensities, the application of acoustic energy can inflict molecular damage on fucoidan, thereby adversely affecting the final yield [1].

The dominance of extraction time observed in this study is consistent with previous optimisation studies on fucoidan extraction, where extraction time was identified as the most significant factor influencing yield due to enhanced diffusion and solubilization processes [45]. A longer extraction time allows greater disruption of cell walls and facilitates mass transfer, thereby increasing yield. The dominant effect of extraction time can be further explained through mass transfer theory. Prolonged ultrasonication enhances the effective diffusivity of fucoidan from the algal matrix into the solvent phase. According to Fick's law, the mass transfer rate is governed by the concentration gradient and the diffusion coefficient. Ultrasound-induced cavitation reduces the thickness of the boundary layer surrounding solid particles and enhances micro-mixing in the liquid phase, thereby increasing the effective diffusivity and accelerating solute transport [46], [47]. In addition, extended extraction time facilitates deeper solvent penetration into the intracellular matrix, promoting the release of fucoidan from complex cell wall structures. Similarly, the significant effect of ultrasonic power aligns with previous findings indicating that power has a strong but nonlinear influence on extraction efficiency [48].

Mechanistically, the effect of ultrasonic power is associated with cavitation bubble dynamics. Increasing ultrasonic power intensifies the formation and collapse of cavitation bubbles, generating localized high temperature and pressure, micro-jets, and shockwaves. These phenomena not only disrupt cell walls but also significantly reduce internal mass transfer resistance by improving solvent accessibility to intracellular compounds [49,50]. However, excessive ultrasonic intensity may induce depolymerization of fucoidan through glycosidic bond cleavage under extreme localized conditions, explaining the nonlinear relationship between power and extraction yield observed in this study. This differs slightly from the present study, where power is significant but less dominant, indicating that the relative importance of variables depends on the experimental range used. In contrast, the *Sargassum sp.* to solvent ratio was found to be insignificant in this study, which differs from several studies reporting its strong influence on extraction yield through its effect on concentration gradient and mass transfer driving force [51]. This discrepancy suggests that the selected range (0.03–0.05 g/mL) may limit the observable impact of this variable.

This observation can also be interpreted in terms of ultrasonic energy density. At higher solvent volumes, the applied ultrasonic energy is distributed over a larger medium, thereby reducing the effective energy density (W/mL). This leads to weaker cavitation intensity per unit volume and limits the enhancement of mass transfer despite increased solvent availability [52]. Conversely, at lower solvent volumes, although cavitation intensity is higher, limited solvent availability restricts solute diffusion, indicating a trade-off between energy density and mass transfer capacity.

Furthermore, while interaction effects in this study are relatively weak, other studies have reported significant interactions between extraction variables, particularly between extraction time and power or temperature [53]. This indicates that interaction effects may become more pronounced under broader experimental conditions. This differs slightly from the present study, where power is significant but less dominant, indicating that the relative importance of variables depends on the experimental range used. In contrast, the *Sargassum sp.* to

solvent ratio was found to be insignificant in this study, which differs from several studies reporting its strong influence on extraction yield through its effect on concentration gradient and mass transfer driving force [51]. This discrepancy suggests that the selected range (0.03–0.05 g/mL) may limit the observable impact of this variable. Furthermore, while interaction effects in this study are relatively weak, other studies have reported significant interactions between extraction variables, particularly between extraction time and power or temperature [53]. This indicates that interaction effects may become more pronounced under broader experimental conditions. In addition to cavitation and diffusion effects, solvent partitioning dynamics also influence extraction efficiency. The distribution of fucoidan between the solid matrix and liquid phase is governed by partition equilibrium. Increasing solvent volume initially enhances the mass transfer driving force; however, beyond a certain point, the system approaches equilibrium, resulting in diminishing returns despite increasing extraction intensity [54].

The use of a quadratic model in this study is consistent with previous RSM-based optimization studies [55], where second-order polynomial models effectively describe the nonlinear relationship between process variables and extraction yield [56]. However, it is important to critically emphasize that optimization based solely on yield ma

y not fully represent the overall extraction performance. Previous studies [57] have reported that ultrasound-assisted extraction can induce structural modification and depolymerization of fucoidan due to cavitation effects, potentially reducing molecular weight and altering its bioactivity. Therefore, although this study demonstrates high extraction efficiency, the results highlight an important consideration that maximizing yield does not necessarily ensure optimal product quality. This emphasizes the need to balance extraction efficiency with the preservation of fucoidan structural integrity and bioactivity, which represents a critical aspect and strengthens the novelty of the present study.

The extraction yield was empirically developed and statistically modelled as a function of the process variables. The model that includes quadratic and interaction terms for yield, Y_{ext} (wt%), has been successfully developed and presented in Eq. 1.

$$Y_{ext} = 8{,}86 + 2{,}5625A - 0{,}05B + 0{,}6875C - 0{,}15AB + 0{,}575AC - 0{,}15BC + 0{,}8325A^2 - 0{,}2925B^2 + 0{,}1825C^2 \quad (1)$$

The model indicates that each variable, both individually and through its interactions, contributes to the overall extraction yield (Y_{ext}). The model is valid over a range of ultrasonic extraction time (10-20 minutes), ultrasonic power (60%-70% of the maximum power), and the ratio of *Sargassum sp.* to solvents (0,03-0,05 g/mL). A good agreement between the model and the experimental data was observed, as is shown in the parity plot provided in Fig. 1.

Fig. 1 illustrates the interactive effects of UAE extraction time and UAE power on fucoidan yield at different material-to-solvent ratios. Overall, the three response surface plots demonstrate that both variables play a synergistic role in enhancing extraction performance, although the magnitude of their effects varies with the extraction ratio. This is consistent with the mechanism of ultrasound-assisted extraction, where increased power enhances cavitation intensity, leading to cell wall disruption and improved mass transfer. Previous studies reported that UAE can significantly increase extraction yield (20–50%) due to enhanced cavitation and solvent penetration [58,59,60,61,62].

Fig. 2 shows that fucoidan yield increases with increasing extraction time and power, reflecting higher cavitation intensity and prolonged solvent contact with the algal matrix. Similar findings were reported in a study on tropical brown seaweed, where extraction time significantly influenced fucoidan yield due to extended diffusion and solubilization processes [63]. Moreover, UAE has been shown to produce higher fucoidan yield compared to conventional extraction methods, mainly due to mechanical disruption and faster mass transfer [64].

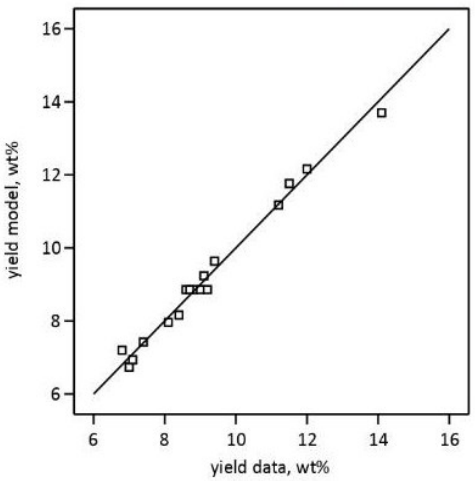

Fig. 1. Parity plot between the modelled and experimental yield of extraction fucoidan

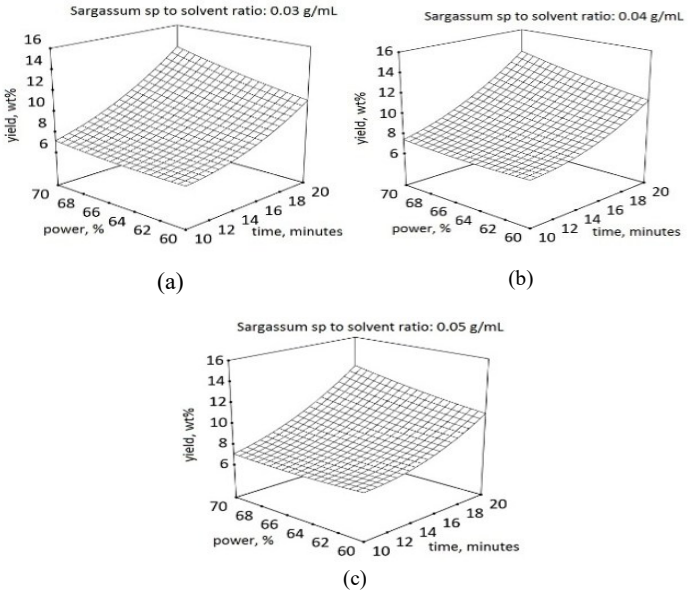

Fig. 2. Modelled yield of fucoidan versus power on various *Sargassum sp.* to solvent ratio

Fig. 2(a) shows that the surface slope is relatively moderate, suggesting that at this lower ratio, solvent availability limits mass transfer, thereby constraining the overall effectiveness of ultrasound even at higher power and longer extraction times. This observation is supported by studies indicating that insufficient solvent volume restricts diffusion and reduces extraction efficiency despite increasing ultrasonic intensity [46,65]. In Figure 2(b), corresponding to a ratio of 0,04, the response surface becomes steeper, indicating a more substantial combined effect of extraction time and UAE power on fucoidan yield. This condition reflects an optimal balance between cavitation energy and solvent capacity. A recent study on fucoidan extraction from *Sargassum sp. s*ecies also reported that

UAE conditions significantly affect yield (2.82–3.93%) and are strongly dependent on extraction parameters such as time and solvent conditions [66]. The increased availability of solvent enhances cavitation efficiency and the diffusion of fucoidan into the liquid phase.

This condition appears to provide a more favourable balance between mechanical disruption and solvent capacity, resulting in a greater improvement in extraction efficiency compared to the lower ratio. Figure 2(c) presents the interaction at a ratio of 0.05. Although fucoidan yield continues to increase with longer extraction time and higher UAE power, the surface slope becomes more gradual at higher operating conditions, indicating diminishing returns. This phenomenon can be attributed to the reduction in ultrasonic energy density at larger solvent volumes, as well as the possible onset of system saturation. Under these conditions, further increases in extraction time or power do not result in proportional improvements in yield.

This behaviour indicates a transition from a diffusion-controlled regime to a near-equilibrium condition, where further increases in extraction time or ultrasonic power no longer significantly enhance mass transfer. Under such conditions, the extraction process becomes thermodynamically limited rather than kinetically controlled [67]. Similar findings have been reported in comparative extraction studies, where excessive extraction conditions not only fail to significantly enhance yield but may also alter the structural composition of fucoidan [68]. This suggests the onset of diminishing returns, as excessive solvent volume reduces effective cavitation energy density or leads to partial saturation of the extraction system.

Consequently, further increases in power or time do not proportionally enhance yield. These results indicate that the *Sargassum sp.*-to-solvent ratio strongly influences the interaction between UAE extraction time and power. An intermediate ratio optimises ultrasonic cavitation and mass transfer, whereas ratios that are too low or too high limit extraction efficiency. Meanwhile, increasing the extraction time led to the highest yield, as the solvent had a longer contact time to diffuse into the algal cell matrix, thereby enhancing the release of active compounds into the solvent [69].

3.3. HPLC analysis

The operating principle of HPLC is to separate analytes. Analytes are chemical compounds formed after the sample is split and injected into the column, and their separation depends on polarity, molecular size, and interaction with the stationary phase. Differences in their affinities determine the separation of analytes [70]. The HPLC analysis in Figure 3 indicates that fucoidan elutes at 1,382 minutes. The appearance of fucoidan in this short sequence is consistent with the literature, which reports that fucoidan generally elutes early in the range of 1.3-1.5 minutes at reversed-phase HPLC separations [54,70,71]. In addition to retention time analysis, quantitative evaluation of fucoidan composition is essential to ensure product quality rather than merely confirming its presence. In this work, the highest fucose and sulfate contents were 38.59% and 17.38%, respectively, achieved at an extraction time of 20 minutes, a Sargassum sp-to-solvent ratio of 0.04 g/mL, and a UAE power of 70%. These findings are consistent with the commonly reported. In general, fucose content in Sargassum sp is above approximately 15%, and sulfate levels typically range from about 5% to 30%, although higher sulfate content may also occur depending on species and extraction conditions. The similarity of the obtained values to the typical compositional ranges of fucoidan supports the identification of the extracted compound as fucoidan[72,73]. Sulfate groups contribute to its hydrophilicity and biological activity, while fucose constitutes the main backbone of the polysaccharide [74]. Therefore, these compositional parameters, together with the observed retention time, strongly indicate that the extracted polysaccharide exhibits the characteristic features of fucoidan. The presence of sulfate ester groups increases the hydrophilicity of fucoidan, resulting in weaker interactions with the nonpolar stationary phase and consequently faster elution [75].

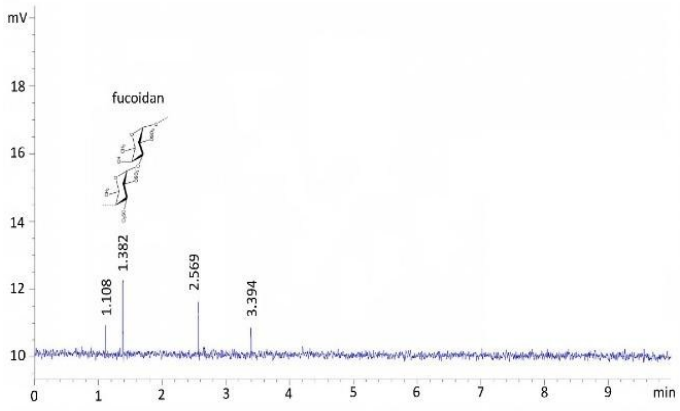

Fig. 3. Chromatogram profile of extracted fucoidan

In addition, lower-molecular-weight fucoidan fractions elute faster due to reduced steric hindrance and weaker interactions with the stationary phase [76]. Therefore, the observed retention time (1.382 min) suggests that the extracted fucoidan likely consists of relatively low-molecular-weight fractions or has undergone partial degradation during extraction. Retention time is influenced by HPLC conditions such as column type, mobile phase, and flow rate, so it alone cannot confirm compound identity [75,77]. Although the observed value falls within the reported range, fucoidan's heterogeneous nature and possible co-elution with other polar compounds may affect accuracy [71,78] Therefore, additional analyses are required to ensure reliable identification.

3.4. FT-IR analysis

FT-IR spectroscopy was used to characterise the fucoidan compound by identifying the presence and position of sulfate ester functional groups, which are key features in its structure and biological activity. The symmetric stretching vibration of the sulfate ester group (O=S=O) appeared as a strong absorption band in the range of 1240–1260 cm^{-1}, while the asymmetric stretching (O–S=O) was observed at 1030–1060 cm^{-1}, indicating the C–O stretching vibration conjugated with the sulfate group. In addition, an absorption band around 840 cm^{-1} indicated that the sulfate group occupied an axial position. When compared with literature, the FT-IR absorption pattern obtained in this study shows good agreement with typical fucoidan spectra, particularly in the regions around 3400 cm^{-1} (O–H stretching), 1600–1650 cm^{-1} (O–H bending or C=O stretching), and 1000–1200 cm^{-1} (C–O–C and S=O vibrations), confirming the presence of sulfated polysaccharide structures [79]. In contrast, the band at 820 cm^{-1} corresponded to an equatorial position on the fucoidan sugar chain [80]. These characteristic sulfate-related bands are widely reported as key indicators of sulfated polysaccharides, particularly fucoidan, and confirm the presence of esterified sulfate groups [8,81].

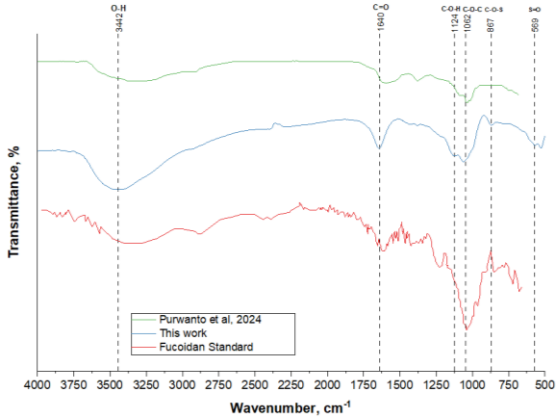

Fig. 4. FT-IR spectral profile of extracted fucoidan

The FT-IR spectrum of the fucoidan sample extracted from *Sargassum sp.* shows several prominent absorption peaks indicative of functional groups characteristic of sulfated polysaccharides. In the low wavenumber region, around 526,57 cm^{-1} and 569,00 cm^{-1}, absorption bands appear corresponding to the stretching vibrations of S–O and S=O groups from sulfate esters ($–OSO_3^-$), which are the main structural features of fucoidan. Furthermore, the peaks at 781,17 cm^{-1} and 867,97 cm^{-1} are associated with C–O–C or C–O–S vibrations, indicating the presence of glycosidic linkages between monosaccharide units in the polysaccharide chain. The presence of glycosidic linkages in this region confirms the polysaccharide backbone structure, which is consistent with previous studies on brown algae-derived fucoidan [82]. Firm peaks at 1062,78 cm^{-1} and 1124,50 cm^{-1} correspond to C–O–C and C–O–H stretching vibrations, confirming the polysaccharide backbone structure and the possible sulfation of hydroxyl groups bound to oxygen atoms. In addition, the peaks at 1379,10 cm^{-1} and 1427.32 cm^{-1} correspond to C–H and O–H bending vibrations, which originate from methyl and hydroxyl groups of fucose, the main monosaccharide component of fucoidan. These findings are in agreement with previous reports stating that fucose-rich sulfated polysaccharides typically exhibit characteristic C–H and O–H bending vibrations in this region [83]. The absorption at 1643,35 cm^{-1} is attributed to O–H bending of bound water molecules or to C=O stretching of uronic acid groups, which are commonly found in natural polysaccharides. Weak peaks around 2289,50 cm^{-1} and 2341,58 cm^{-1} are likely not from the fucoidan structure but from CO_2 interference during measurement. Meanwhile, the broad band at 3442,94 cm^{-1} is characteristic of O–H stretching vibrations of polysaccharide molecules, indicating a high content of hydroxyl groups in the fucoidan structure. Similar broad O–H absorption bands have been consistently observed in fucoidan extracted from various brown seaweed species, confirming the hydrophilic nature of the polysaccharide [8].

These results are consistent with the reference fucoidan spectrum reported in the literature [84], which exhibits similar absorption patterns at 3400 cm^{-1}, 1640 cm^{-1}, and 1000–1200 cm^{-1}. In the literature, both the extracted fucoidan and the commercial fucoidan standard display strong absorption bands around 3400 cm^{-1} (O–H stretching), 1640 cm^{-1} (O–H bending or C=O stretching), and 1000–1200 cm^{-1} (C–O–C, C–O–H, and S=O vibrations), indicating the presence of sulfate and polysaccharide structures. However, several studies have highlighted that FT-IR spectra of fucoidan may vary depending on the algal source, degree of sulfation, and extraction method, which can influence peak intensity and position [81,82]. Additionally, weak peaks in the 500–600 cm^{-1} range in both spectra correspond to S–O stretching vibrations, further supporting the compound's sulfated nature. Overall, the comparison between the fucoidan extracted from *Sargassum sp.* and the standard fucoidan demonstrates an almost identical FT-IR spectral profile. Nevertheless, due to the heterogeneous nature of fucoidan and possible overlap in the fingerprint region (1000–1200 cm^{-1}), FT-IR analysis alone may not be sufficient for definitive identification, and complementary techniques such as HPLC or molecular weight analysis are recommended [83].

3.5. Antioxidant activity

In this work, antioxidant activity was expressed as the IC50 value. DPPH assay was performed to determine the IC50 value. The IC50 was 52.27 µg/mL, confirming its antioxidant potential. This finding is approximately in line with Tsou et al, who reported the DPPH scavenging activity of 57.32%. Furthermore, fucoidan from Sargassum ilicifolium exhibited up to 92% antioxidant activity at 1 mg/mL when heated to 80 °C [91].

3.6. Kinetic study

The kinetics of fucoidan extraction from *Sargassum sp.* based on the diffusion model in spherical coordinates demonstrates a strong relationship between extraction time (t) and fucoidan yield (y_{fuc}), as depicted in Figure 5. In this study, a 12-term (n) series was performed to investigate the kinetics of fucoidan extraction from *Sargassum sp.* powder (R = 0,000177 m, 80 mesh) as the particle size. Based on the optimisation results, the optimal value of β was 0,044896, granting an effective diffusion coefficient (D_e) of 1,425118 × 10^{-2} m^2/s.

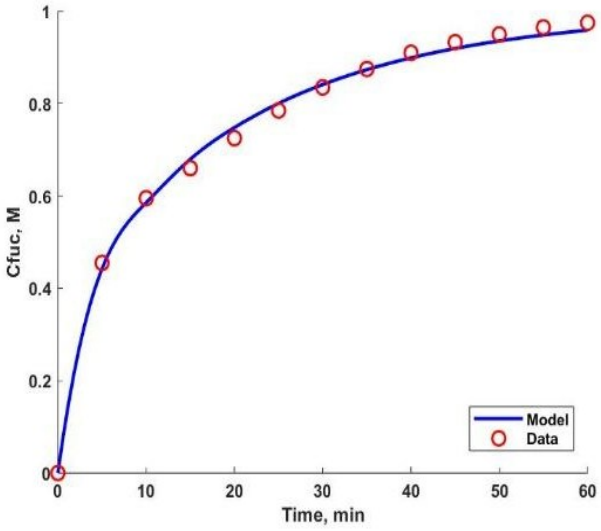

Fig. 5. Relationship between fucoidan yield and extraction time

The fitted value of β = 0.044896 is well aligned with the broader literature, indicating that diffusion-controlled mechanisms are significant in the solid–liquid extraction of fucoidan from brown seaweed, and that enhanced mass transfer, influenced by effective diffusivity, correlates with improved extraction kinetics, as captured by diffusion models. The inclusion of diffusion modelling, as supported by these studies, strengthens the validity of the kinetic analysis and the interpretation of optimised parameters in this work.

Increasing extraction time (t) is positively correlated with the rise in fucoidan concentration (C_t), as illustrated in Figure 5. In

the early extraction period (0–20 minutes), C_t increases significantly due to the high concentration gradient between the inner particle region and the solution. After around 40–60 minutes, the concentration increase slows and eventually approaches equilibrium, at which point the diffusion rate of active compounds from the algal matrix to the solvent decreases because of the reduced concentration difference between the particle surface and the solution [1].

The effective diffusion coefficient (D_e = 1,425118 × 10^{-2} m^2/s) indicates the ability of the solvent to transfer fucoidan compounds from within the cell walls to the liquid medium. This relatively high value compared to the average passive diffusion processes in solid–liquid systems. This suggests that the ultrasonic cavitation mechanism used in the extraction process plays a significant role in enhancing mass transfer by increasing tissue porosity and disrupting algal cell walls [29]. Studies on ultrasound-assisted extraction have demonstrated that ultrasonic cavitation increases the effective diffusion coefficient and accelerates internal mass transfer, thereby enhancing extraction efficiency compared with conventional methods [85]. Specifically, experimental and simulation results showed that increasing the acoustic energy density under ultrasonic conditions consistently elevated effective diffusivity, indicating a more rapid diffusion process and improved solute transport into the solvent phase [85]. This supports the interpretation that the relatively high D_e value obtained in this study reflects a fast diffusion regime, enabled by ultrasound-induced weakening of internal mass transfer resistance and improved solvent penetration. This work successfully formulated the kinetic model, as expressed in eq. 2.

$$C_{r,t} = \frac{2.C_0.R}{\pi}\sum_{n=0}^{n=\sim} \frac{(-1)^n}{n}\frac{sin\left(\frac{n\pi r}{R}\right)}{r} e\left(\frac{n\pi}{R}\right)^2 . 1{,}425118 \times 10^{-2}.t \qquad (2)$$

The sum of squared errors (SSE) of 0.004857 indicates the model fits the experimental data. It shows the minimal deviation between the model predictions (y_{cal}) and the experimental data (y_{data}). Therefore, the diffusion model in spherical coordinates effectively represents the fucoidan extraction process.

The kinetics of fucoidan extraction from *Sargassum sp.*. modeled using diffusion in spherical coordinates shows a strong correlation between extraction time and fucoidan yield, with a 12-term series fitting the data well and yielding an effective diffusion coefficient (D_e) of about 1,4 × 10^{-2} m^2/s. This relatively high D_e aligns with literature indicating that diffusion-controlled mechanisms are significant in solid-liquid extraction of fucoidan, especially when ultrasound-assisted extraction is used, as ultrasonic cavitation enhances mass transfer by disrupting cell walls and increasing porosity [86, ,87,88]. The model's good fit (low SSE) supports the validity of using diffusion models to describe the process, capturing the initial rapid increase in concentration due to a high concentration gradient and the later approach to equilibrium as diffusion slows [86]. However, comparison with other ultrasound-assisted extraction studies reveals a substantial difference in effective diffusivity values. For instance, a study on fucoidan extraction from Ecklonia maxima reported D_e values only in the range of 0.863–3.46 × 10^{-12} m^2/s, even under ultrasonic conditions, and concluded that the extraction process remained controlled by internal diffusion resistance despite the application of ultrasound. This indicates that, in that system, ultrasound primarily enhanced mass transfer moderately (approximately up to fourfold) without fundamentally altering the dominant diffusion-controlled mechanism [41].

Although this D_e value is higher than typical passive diffusion coefficients reported for many solid-liquid systems (often ranging from 10^{-14} to 10^{-9} m^2/s), ultrasound can significantly increase effective diffusivity by accelerating internal mass transfer, consistent with findings in recent studies on ultrasound-assisted extractions [87,89]. The much higher D_e obtained in this study, however, suggests a stronger intensification effect, likely due to more pronounced cavitation phenomena. Ultrasonic cavitation produces collapsing microbubbles that generate localised microjets, shockwaves, and interparticle collisions, which are known to cause severe cell wall disruption, fragmentation, and erosion of biomass structures [41]. As a result, the *Sargassum sp.* matrix may experience a drastic increase in porosity and a significant reduction in diffusion path length, thereby minimising internal resistance and accelerating solute release into the solvent phase.Factors such as particle size, temperature, and solvent properties also influence D_e and should be considered in kinetic modelling to avoid overestimation [79,86,90]. Overall, the reported kinetic model and effective diffusivity are consistent with the current understanding that enhanced mass transfer mechanisms like ultrasound can produce higher apparent diffusion coefficients in solid-liquid extraction processes [86,87,89].

4. Conclusion

Fucoidan was successfully extracted from *Sargassum sp.* using the ultrasound-assisted liquid biphasic system, achieving a maximum yield of 14,1% under optimal conditions of 20 minutes of extraction time, 70% ultrasonic power, and a material-to-solvent ratio of 0,04 g/mL. HPLC analysis showed a characteristic fucoidan peak at approximately 1,38 minutes, confirming its presence, while FT-IR spectra verified the typical functional groups of sulfated polysaccharides. The extraction kinetics followed the controlled-diffusion model, with strong agreement between calculated and experimental values, indicating that ultrasonic cavitation significantly enhanced mass transfer. The extracted fucoidan also exhibited antioxidant activity with an IC50 value of 52.27 µg/mL, indicating its potential as a natural antioxidant. The diffusion coefficient (D_e) of 1,425118 × 10^{-2} m^2/s reflects the efficiency of mass transfer of bioactive compounds from the *Sargassum sp.*. cellular matrix into the extraction solvent, and its magnitude indicates relatively rapid diffusion under the applied extraction conditions. The UAE–LBS method provided an efficient, selective, and structurally safe approach for isolating fucoidan from *Sargassum sp.*

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