Vol. 2, No. 1, April 2023, pp. 75-84
p-ISSN: 2963-8577
e-ISSN: 2964-3511
DOI: 10.57102/jescee.v2i1.60

JESCEE
Journal of Emerging Supply Chain, Clean Energy, and Process Engineering

# FLAVONOID EXTRACTION FROM PAPAYA (CARICA PAPAYA L.) SEED USING ULTRASOUND – ASSISTED EXTRACTION METHOD AND DETERMINATION OF ITS SPF VALUE

**Eduardus Budi Nursanto[1,2,*] , Rachel Wijaya[1], Alifiana Permata Sari[1,2]**
[1]Department of Chemical Engineering, Faculty of Industrial Engineering, Universitas Pertamina, Jakarta, Indonesia
[2]Central of Downstream Chemical Industry, Universitas Pertamina, Jakarta, Indonesia

***Abstract***
*Synthetic compounds with photoprotective property have their limited concentration in sunscreen formulation. Therefore, reaching the maximum UV protection by themselves is difficult. Natural compounds are good consideration to include in sunscreen formulations. Papaya seeds contain large amounts of nutraceutical compounds. However, their presence is often considered as waste. One of many benefits it has is due to the presence of flavonoids, phenols, alkaloids, saponins, and tannins. Flavonoid is one of the alternative compounds that provide beneficial effects on skin UV-protection. Therefore, this study aimed to extract the flavonoid compounds in papaya seeds and test its sun protection factor (SPF) value. Extraction was carried out by varying the mass ratio of the solid/solvent (1:10, 1:20, and 1:30), and the solvent concentration of ethanol (50%, 70%, and 96%) at 45°C for 45 minutes. The results of this study indicate the presence of these compounds in papaya seed extract which was extracted using the ultrasound-assisted extraction method with the maximum extraction yield (11.888%) obtained at 1:30 mass ratio with a 50% ethanol concentration; the highest total flavonoid content was 2.854 mg quercetin equivalent (QE)/g papaya seed at 1:30 ratio with 96% ethanol concentration, and the highest SPF value was at a 50% ethanol concentration which was 12.0775 (at 300 ppm).*



***Keywords:***
*Papaya seed; ultrasound-assisted extraction; total flavonoid content; mass transfer coefficient; sun protection factor*

***Article History:***
*Received: March 22nd, 2023*
*Revised: April 8th, 2023*
*Accepted: April 26th, 2023*
*Published: April 30th, 2023*

***Corresponding Author:***
*Eduardus Budi Nursanto*
*Department of Chemical Engineering, Universitas Pertamina, Indonesia*
*Email:*
eduardus.bn@universitaspertamina.ac.id

## 1. Introduction

Ultraviolet (UV) radiation exposure to human is closely unavoidable. Unfortunately, UV is considered carcinogenic and being the cause of numbers of skin disorders [1]. UV radiation is classified based on the wavelength: UVA (320-400 nm), UVB (290-320 nm), and UVC (200-290 nm) [2].

Sunscreen is designed to protect human from sun's UV rays. Nowadays, commercial sunscreen consists of inorganic compound (physical sunscreen) and organic compound (chemical sunscreen). However, these sunscreens each have concentration limitation in formulating sunscreen to reach optimum, yet safe SPF value based on regulation concern [3]. Therefore, we need other organic compounds derived from natural sources so that they are safe for daily use. Flavonoid has been studied to be compounds that can counteract UV-induced radicals, act as antioxidant & anti-inflammatory agent, provide protective effect and absorb UV rays which make it able to protect skin from sun's UV [3].

Papaya seed was found containing phenolic compounds, phenolic acids, and carotenoid with one of which is flavonoids [4]. Ironically, approximately 20% of the total weight of papaya is papaya seeds and account for 30-35% of the waste from papaya which is usually disposed of [4]. There have been previous studies on flavonoid extraction from papaya seed with the variation of extractant used with microwave-assisted extraction method [5], flavonoid extraction on different parts of papaya plant with water as extractant [6], optimizing flavonoid extraction from papaya seed using ultrasound-assisted extraction method [7], and flavonoid extraction from papaya seed with varying drying pre-treatment method with maceration method [8]. By this time, there have not been any studies

 p-ISSN: 2963-8577
e-ISSN: 2964-3511

on flavonoid extraction from papaya seed with ethanol concentration variation, its mass transfer coefficient, and SPF value. Furthermore, the utilization of papaya seeds will highlight its potential and reduce environmental pollution.

Flavonoid extraction of papaya seeds in this study was carried out using the ultrasound-assisted extraction (UAE) method since compared to other methods, especially conventional methods, UAE required low amount of solvent, energy, temperature, and process time [9]. The mechanism of UAE fundamentally consists of the cavitation phenomenon [10]. When the bubbles created from ultrasonic waves collapse near the surface of the plant solute, they will cause the fragmentation, erosion, and destruction of plant structures that leads to solvent entry into the matrix, decreasing particle size, penetrating solvent better, and releasing the extract from the matrix [11].

In this study, we did the optimization for ultrasound assisted extraction of antioxidant from papaya seed. The optimization in this study is related with ratio of papaya seed with solvent amount and the concentration of solvent. From the best sample, we conducted the experiment to calculate the mass transfer coefficient. Furthermore, analysis for the SPF ability of extract papaya has been investigated in our study.

## 2. Experimental Section

*A. Plant material preparation*

Fresh papaya (*Carica papaya* L.) seeds were dried by air-drying method at room temperature in well-ventilated room with no direct contact with sunlight for 5 days. The seeds were then ground using an electric blender.

*B. Ultrasound-assisted extraction*

Finely ground and dried papaya seeds that had been weighed were then put into Erlenmeyer flask and mixed with the solvent. Ethanol, the solvent used, was varied in concentration by 96%, 70%, and 50% with the amount of each being based on the ratio of solvent/solute that had been determined, which were 1/10, 1/20, 1/30 (g/ml).

Extraction was carried out using an ultrasonic water bath at atmospheric pressure with a temperature of 45°C for 45 minutes. The extract obtained was then filtered using a vacuum filter. The filtrate was separated from the solvent with a vacuum oven afterward at 40-50°C and 0.2 atm. The extract yield of each variation is calculated as % (wt/wt) using the equation:

$$\%yield = \frac{dried\ papaya\ seed\ extract\ mass}{dried\ \&\ ground\ \ papaya\ seed\ mass} \times 100\% \qquad (1)$$

*C. Phytochemical screening*

*Flavonoid Test*. 1 ml of extract was mixed with 1 ml of 96% ethanol and 0.1 gram of Mg powder followed by 10 drops of concentrated HCl. Red, yellow, or brownish orange colour indicates the presence of flavonoids.

*Tannin Test*. 2 ml of extract was mixed with 2 ml of aquadest and few drops of 1% $FeCl_3$. Blue or blackish green colour indicates the presence of tannin.

*Phenolic Compound Test*. 1 ml of extract was mixed with 3 drops of 1% $FeCl_3$. Green, red, violet, blue, or black colour indicates the presence of polyphenols.

*Triterpenoid Test*. 2 ml of extract was mixed with 10 drops of glacial acetic acid and 2 drops of concentrated $H_2SO_4$. The mixture was shaken well and allowed to stand for a few minutes. The red or violet colour indicates the presence of triterpenoid.

*Alkaloid Test*. 10 ml of extract was mixed with 1.5 ml of 2 M HCl, then heated for 5 minutes followed by the addition of 5 drops of Dragendroff's reagent. The orange colour and formation of precipitate indicate the presence of alkaloid.

*Saponin Test*. 2 ml of extract was mixed with 10 ml of hot aqua dest, then shaken for 15 minutes followed by the addition of few drops of 2 M HCl. The formation of stable and persistent froth indicates a positive test for saponin.

*D. Determination of total flavonoid content (TFC)*

TFC of papaya seed was determined by using the $AlCl_3$ colorimetric method, and the results were expressed as µg quercetin (QE)/g papaya seed. Quercetin was used to make the standard calibration curve.

5 mg of quercetin was dissolved in 5 ml of 96%, 70%, and 50% ethanol then diluted to 40, 60, 80, 100, and 120 µg/ml. 0.5 ml of standard solution of each concentration and 0.5 ml of each extract solution were put separately into vials. To each vial, 0.1 ml of 10% $AlCl_3$, 0,1 ml of 1 M potassium acetate, and 2.8 ml of aquadest were added and mixed well. Each mixture was incubated for 30 minutes at 25°C. The absorbance of each mixture was measured at 438 nm with ethanol 96%, 70%, and 50% as blank. Absorbance data of the vials with standard solution was then

plotted as standard curve calibration, while the absorbance data of the vials with extract solution was used to calculate the TFC using the equation:

$$TFC = \frac{c \times V \times f}{m} \tag{2}$$

where TFC is the total flavonoid content (μgQE/mg dry weight), c is quercetin equivalent (μg/ml), V is extracted total volume (ml), f is dilution factor (1), and m is papaya seed mass (mg).

*E. Determination of sun protection factor (SPF)*

Dried papaya seed extract of 96%, 70%, and 50% ethanol was dissolved in each ethanol concentration to the concentration of 300 ppm. SPF value was determined by firstly calculated the area under the curve (AUC) of absorbances at 280-400 nm with 5 nm intervals using the equation:

$$[AUC] = \frac{A_a + A_b}{2} \times (dP_{ab}) \tag{3}$$

with $A_a$ is absorbance at wavelength an nm, $A_b$ is the absorbance at wavelength b nm, and $dP_{ab}$ is a difference in wavelengths and b. The AUC of each wavelength segment is summed up to calculate the SPF value using the equation:

$$\log SPF = \frac{\sum AUC}{(\lambda_n - \lambda_1)} \tag{4}$$

with $\lambda_n$ is the longest wavelength (400 nm), and $\lambda_1$ is the shortest wavelength (290 nm).

*F. Determination of mass transfer coefficient*

Mass transfer coefficient determination was done for the highest TFC extract. Extraction was done in 5 minutes, 15 minutes, 30 minutes, 45 minutes, and 60 minutes. The extracts were put into 5 different Erlenmeyer flask for easy sampling every extraction time mentioned before. Each sample was then vacuum filtered followed by calculating the total flavonoid content by the $AlCl_3$ method for its concentration. The mass transfer coefficient was then calculated by the following equation:

$$k_L a.t = \ln \frac{C_s}{(C_s - C_L)} \tag{5}$$

where $k_La$ is volumetric mass transfer coefficient ($min^{-1}$), t is time (min), $C_s$ is a concentration of flavonoid at equilibrium (ppm QE), and $C_L$ is a concentration of flavonoid at time t (ppm QE). The mass transfer coefficient was obtained from the slope of the plot of $\ln(C_s/(C_s-C_L))$ versus t.

## 3. Result and Discussion

The result showed that as the solute-solvent ratio or solid to liquid ratio (SLR) improved from 1/10 to 1/30, the higher yield obtained as seen on Fig. 1. This is occurred due to an increase in solvent diffusivity into plant cells, thereby accelerating the solute dissolution and mass transfer [12]. The improved solute-solvent ratio also makes the ultrasonic wave intensity higher, causing more fragmentation, erosion, and pore formation effects, thereby increasing yield [13]. In addition, the large difference in ratio increases the contact area between the solute and solvent so that it also increases the yield [13].

Table 1. Yield determination in papaya seeds correspond with ethanol concentration and SLR variation

| Ethanol Conc. | Solid-Liquid Ratio (SLR) | Yield (%) |
|---|---|---|
| 96% | 1/30 | 9.7282 |
| | 1/20 | 8.3825 |
| | 1/10 | 5.9288 |
| 70% | 1/30 | 10.6689 |
| | 1/20 | 9.4443 |
| | 1/10 | 6.9779 |
| 50% | 1/30 | 11.8888 |
| | 1/20 | 10.8839 |
| | 1/10 | 8.0250 |

Meanwhile, the higher the ethanol concentration, the lower the yield. This shows that increasing the concentration of water in the solvent increases the extraction yield, in accordance with previous studies [14],[15],[16]. This is because compounds other than flavonoids, and other polar compounds were also extracted and contributed to this higher yield, which are flavonoid glycosides [17], tannin, saponin [18], and ferulic acid [19].

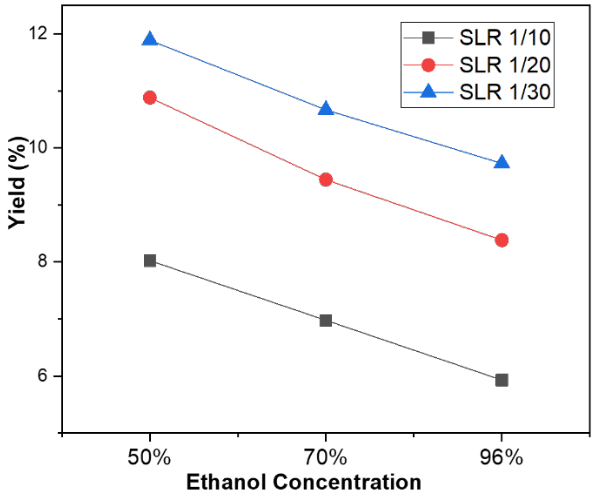


Figure 1. Effect of ethanol concentration and solid to liquid ratio on extraction yield of papaya seed

Phytochemical screening of papaya seed extract is shown on Table 2. From phytochemical screening test, extract of papaya seed contains mixture of flavonoid, phenolic compound, tannin, alkaloid, saponin and triterpenoid.

Table 2. Phytochemical screening results of papaya seed extract

| **Phytochemical** | **Result** | **Compound Example** |
|---|---|---|
| Flavonoid | Brownish orange (+) | Quercetin, kaempferol [20], naringenin [21], quercetin-3-o-galactoside, quercetin-3-o-glycoside [6] |
| Phenolic Compound | Green (+) | Caffeic acid, p-hydroxybenzoic acid, ferulic acid, coumaric acid [20], gallic acid [22] |
| Tannin | Dark green (+) | Tannin [21] |
| Alkaloid | Orange + precipitate (+) | Quinine, ribalidine [21] |
| Saponin | Stable froth (+) | Sapogenin [21] |
| Triterpenoid | No changes (+) | |

Table 3. Calibration curve equation of quercetin

| **Ethanol Concentration** | **Equation** | **$R^2$** |
|---|---|---|
| 96% | $y = 0.0040x – 0.0103$ | 0.9915 |
| 70% | $y = 0.0048x – 0.0184$ | 0.9932 |
| 50% | $y = 0.0050x – 0.0183$ | 0.9935 |

Equation of calibration curve of quercetin standard is as seen on Table 3. The result of papaya seed extract total flavonoid content (TFC) showed that 96% ethanol extraction with solid to liquid ratio (SLR) of 1:30 had the highest TFC compared to other variation. The units for represent TFC is mg quercetin (QE) per gram papaya seed. From Fig 2., higher value of SLR resulting in higher the TFC obtained. This could be due to the increasing diffusivity of the solvent into the cell and supporting the dissolution of flavonoids [12]. As the SLR increases, the viscosity and concentration of the extractant will also decrease thereby increasing the cavitation effect in the UAE method [13] and maximizing the extraction process.

Table 4. TFC determination in papaya seeds correspond with ethanol concentration and SLR variation

| Ethanol Conc. | Solid-Liquid Ratio (SLR) | TFC (mg QE/g-papaya seed) |
|---|---|---|
| 96% | 1/30 | 2.8540 |
| | 1/20 | 2.4388 |
| | 1/10 | 1.9009 |
| 70% | 1/30 | 2.5632 |
| | 1/20 | 2.0955 |
| | 1/10 | 1.7229 |
| 50% | 1/30 | TF |
| | 1/20 | 2.0199 |
| | 1/10 | 1.4070 |

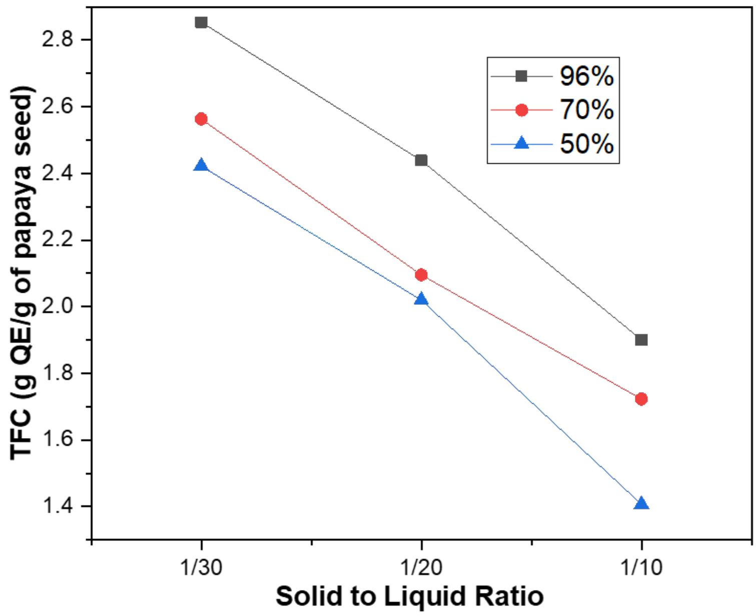


Figure 2. Effect of ethanol concentration and solid to liquid ratio on total flavonoid content (TFC) of papaya seed extract

Meanwhile, the increase in TFC along with the increase in ethanol concentration occurred due to the same level of polarity of ethanol and flavonoids (like-dissolves-like). Solvent with low viscosity and surface tension such as ethanol can also provide good cavitation effects in the UAE process [23].

To design and analyse the extraction process on a large scale, relevant kinetic studies are required. In the extraction process, no chemical reaction is involved, so the mass transfer kinetic model is used to represent the experimental data [24]. Based on the mass transfer theory, during the extraction process of the desired compound, the highest mass transfer resistance in the whole process is involved with the rigid structure of the plant cell wall used and the extraction is considered an irreversible process so it can be concluded that the first order extraction kinetics can be used [25]. The use of first-order kinetics is also determined by the external mass diffusion rate (lumped model) from papaya seeds to the bulk solvent phase with the following assumptions [26]:

- Flavonoids were uniformly distributed in papaya seeds, so that there is no concentration gradient in papaya seeds,
- Samples of papaya seeds are in spherical shape,
- The effective diffusion coefficient of flavonoids remains constant throughout the extraction process,
- Since the ultrasonic process can cause convection in the liquid medium, the extraction solvent was assumed to be well mixed in the extractor and the external resistance to mass transfer in the liquid phase is negligible,
- Mass transfer resistance in the liquid phase is negligible,
- The transfer of flavonoids from solid particle to the liquid phase takes place by diffusion,

There is no chemical reaction or ultrasonic degradation of flavonoids during the extraction process [27].

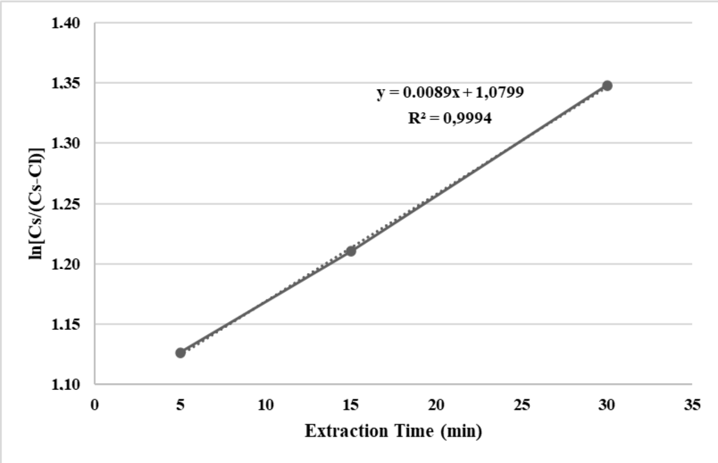


Figure 3. First-order kinetic model of papaya seed extraction

From several research, the mass transfer kinetic model for the extraction of fruit seed is following first order kinetic model that mentioned in equation (5). By using the first-order kinetic model that is approached based on Fick's law [28], the plotted result is shown on Fig. 3 above. The concentration at equilibrium ($C_s$) used was when the extraction reached the highest TFC which was 71.7 ppm QE with 45 minutes extraction time. After calculating and plotting, the result shown that first-order kinetic was proven as fitted model for the experimental data with $R^2$ of 0.9994 with the $k_La$ reach 0.0089 $min^{-1}$ or 8.9 mg QE/(g-ethanol. minute).

SPF value of papaya seed extract at 300 ppm was the highest in 50% ethanol extract as shown in Table 4. The results showed that the higher the ethanol concentration, the lower the SPF value obtained. The same result was also obtained for the yield which the lower the ethanol concentration, the higher the extract yield. Meanwhile, the result of the SPF value was contrary to the trend of the TFC value obtained. Although flavonoids have been widely studied and are more responsible for providing protection against UV radiation [31], some phenolic compounds also have the potential for photoprotection [3]. From this research, the obtained TFC content was small so that the SPF value obtained might because of the high total phenolic content (TPC) value which was not tested quantitatively in this study. This result is similar to few studies before, where the SPF value was parallel to the TPC in the *Crataegus pentagyna* extract using methanol as the extractant with UAE method [29], and in the *G. versteegii* leaves extract using various ethanol solvents by maceration where the highest SPF value was at 50% ethanol extract with the highest TPC value [30].

On the other hand, the higher the ethanol concentration, the lower the TPC value, and the maximum TPC achieved in 50% ethanol solvent [32]. This means that the TPC in papaya seed extract had higher polarity than the TFC, so that at 50% ethanol, there were more phenolic compounds, and at 96% ethanol, there were more flavonoid compounds. In addition, according to [4],[6],[20], the TPC in papaya seeds was indeed far more than the TFC content, thereby possibly in this extract, TPC was more influential and had good correlation with the SPF value. Although the one that is known to be more potent with its photoprotective potential is flavonoids. The compounds in papaya seed that are proven more soluble in 50% ethanol are caffeic acid, coumaric acid, p-hydroxybenzoic acid, and ferulic acid [33] which are the most phenolic content in papaya seed [20]; rutin, naringin, quercetin rhamnoside, quercetin glycoside, and kaempferol rhamnoside (flavonoid glycosides) as studied in [6],[34],[35].

The increase in the SPF value which is not proportional to the TFC value in this study might be due to the $AlCl_3$ method for TFC test is only able to detect flavonoids from flavones and flavonols subgroup, while the anthocyanidins (cyanidins), flavanols (catechin), flavanones (naringenin) [36] which also contained in papaya seeds were not detectable [37].

The highest SPF value in this research was 12,0775 of papaya seed extract with 50% ethanol. The value was considered as maximum protection to the classification based on Wilkinson & Moore [38], and based on EU guidelines, approximately considered as low category [39]. The low SPF value of the extract does not mean that papaya seed extract cannot be utilized as sunscreen. According to previous studies, mixing flavonoids from natural sources with synthetic compounds can be used to support an adequate and safe SPF value, for example: a mixture of 0.1% rutin and 6.0% benzophenone increased the SPF from 24.3 to 33.3 when flavonoids were involved, as well as when 10% of rutin and quercetin were combined with $TiO_2$ and ZnO, the SPF value became around 30 [40].

Table 5. IR spectrum interpretation of papaya seed extract

| Bond | Wavelength frequency ($cm^{-1}$) | 50% Ethanol Extract ($cm^{-1}$) | 70% Ethanol Extract ($cm^{-1}$) | 96% Ethanol Extract ($cm^{-1}$) | Identification Result |
|---|---|---|---|---|---|
| -OH | 3200-3500 | 3392.1730 | 3415.3140 | 3411.4570 | Phenols, Flavonoids, Tannin, Alkaloid, Saponin |
| -OH water | 3100-3700 | 3392.1730 | 3415.3140 | 3411.4570 | Hydrate |
| C-H aliphatic | 2700-3000 | 2838.7030 | 2842.5600 | 2838.7030 | Ethanol, Tannin, Saponin |
| -OH alcohol | 2700-3000 | 2950.5500 | 2954.4110 | 2952.4820 | Ethanol |
| C=O | 1650-1900 | 1650.7670 | 1658.4810 | 1650.7670 | Flavonoids, Tannin, Phenols, Saponin |
| C=C aromatic | 1475-1500 | 1454.0640 | 1450.2970 | 1411.6380 | Flavonoids, Tannin, Phenols, Alkaloids, Saponin |
| C-O alcohol | 1000-1260 | 1022.0870 | 1112.7250 | 1110.7970 | Alcohol, Flavonoids, Tannin, Alkaloids, Saponin |
| C-O ether | 1085-1150 | 1110.7970 | 1025.9440 | 1110.7970 | Flavonoids, Tannin, Phenols |
| C-H aromatic | 650-1000 | 636.3940 | 688.4626 | 673.0349 | Flavonoids, Tannin, Phenols, Alkaloids |
| C-OH aromatic | 375-450 | 431.9766 | 437.7620 | 408.8350 | Phenols |
| C-N | 1020-1250 | 1022.0870 | 1025.9440 | 1022.0870 | Alkaloids |
| C-O-C dan carboxylic ester group | 1062-1256 | 1110.7970 | 1112.7250 | 1110.7970 | Saponin |
| Fingerprint region of flavonoid | 900-1300 | 1110.7970 | 1025.9440 | 1110.7970 | Flavonoids |
| Fingerprint region of tannin | 950-1500 | 1110.7970 | 1112.7250 | 1022.0870 | Tannin |

From the result of the FTIR analysis as seen on Table 5 and Fig. 4, it shows that the papaya seed extract contains groups of compounds of the phytochemical compounds tested before, which were flavonoids, phenols, alkaloids, saponin, and tannin.

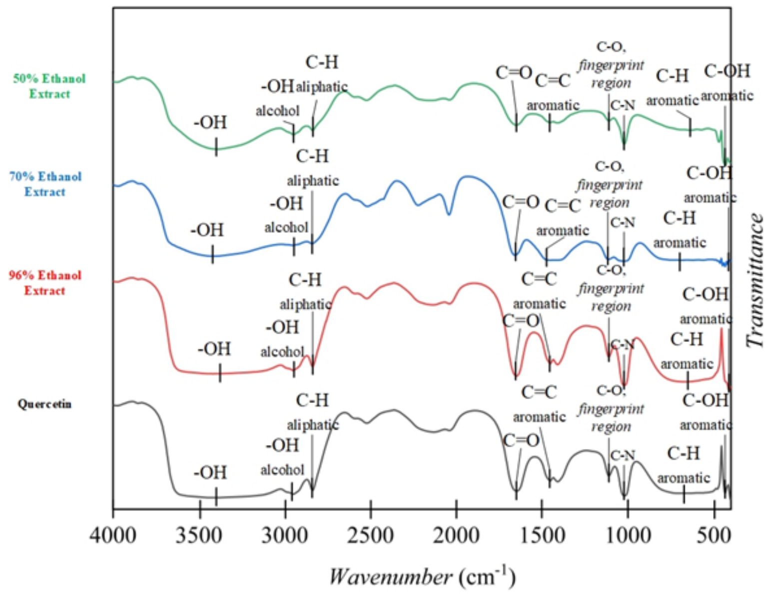


Figure 4. FTIR transmittance spectra of papaya seed extract

## 4. Conclusion

In the present work, extraction of flavonoid from papaya seed extract is carried out using ultrasound-assisted extraction method with varying the solvent concentration (ethanol) and ratio. It can be concluded that the smaller the ethanol concentration, the greater the yield value, but the smaller the value of the total flavonoid content obtained. According to recent studies, it was found that by using higher concentration of ethanol (more polar), more other photoprotective compounds were dissolved (ferulic acid, rutin, p-hydroxybenzoic acid, flavonoid glycosides, etc.)

The optimum condition to obtain the highest yield is at a ratio of 1:30 solid to solvent and 50% ethanol concentration, which was 11.8888%wt. Meanwhile, the optimum condition for obtaining the highest TFC was at a solid to liquid ratio of 1:30 and 96% ethanol concentration, which was 2.8540 mg QE/g papaya seed. By using the optimum condition to get the highest TFC, the mass transfer coefficient ($k_La$) was 0.0089/min or 8.9000 mgQE/(g-ethanol. minute). Furthermore, the highest SPF value of papaya seed extract was obtained at SLR of 1:30 and 50% ethanol concentration with a value of 12.0775.

## References

[1] D'Orazio, J., Jarrett, S., Amaro-Ortiz, A., & Scott, T. (2013). UV Radiation and the Skin. International Journal of Molecular Sciences, 12222–12248.
[2] United States Environmental Protection Agency. (2010, June). UV Radiation. Retrieved from Air and Radiation: https://www.epa.gov/sites/production/files/documents/uvradiation.pdf
[3] Saewan, N., & Jimtaisong, A. (2015). Natural products as photoprotection. Journal of Cosmetic Dermatology, 47-63.
[4] Kumoro, A. C., Alhanif, M., & Wardhani, D. H. (2020). A Critical Review on Tropical Fruits Seeds as Prospective Sources of Nutritional and Bioactive Compounds for Functional Foods Development: A Case of Indonesian Exotic Fruits. International Journal of Food Science, 1-15.
[5] Kothari, V., & Seshadri, S. (2010). Antioxidant activity of seed extracts of Annona squamosa and Carica papaya. Nutrition & Food Science.
[6] Zunjar, V., Mammen, D., & Trivedi, B. (2014). Antioxidant activities and phenolics profiling of different parts of Carica papaya by LCMS-MS. Natural Product Research.
[7] Kee, H. M., Anuar, A., Samat, A. F., Salleh, N. H., & Mohamed, A. R. (2019). Optimization Studies by Ultrasound Assisted Solvent Extraction and Screening Of Phenolic Compounds In Papaya Seeds. Journal of Advanced Research in Fluid Mechanics and Thermal Sciences, 8-16.
[8] Irondi, A., Anokam, K., & Ndidi, U. (2013). effect of drying methods on the phytochemicals compositionand antioxidant activities of Carica papaya Seed. International Journal of Biosciences, 1-7
[9] *Idris, N. A., & Sulaiman, A. Z. (2017). Comparison between Conventional Extraction and Ultrasound Assisted Extraction of Labisia Pumila Sp. in 25-L Mobile Extractor using Water as Solvent of Extraction. CHEMICAL ENGINEERING TRANSACTIONS, 781-786.*
[10] Lavilla, I., & Bendicho, C. (2017). Fundamentals of Ultrasound-Assisted Extraction. In Water Extraction of Bioactive Compounds (pp. 291-317). Vigo: Elsevier Inc.
[11] Rutkowska, M., Namie´snik, J., & Konieczka, P. (2017). Ultrasound-Assisted Extraction. Gda ´ nsk: Elsevier.
[12] Zhou, T. X.-P.-J.-J.-B. (2017). Ultrasound-assisted extraction and identification of natural antioxidants from the fruit of Melastoma sanguineum. Molecules, 1-15.
[13] *Kumar, K., Srivastav, S., & Sharanagat, V. S. (2021). Ultrasound assisted extraction (UAE) of bioactive compounds from fruit and vegetable processing by-products: A review. Ultrasonics Sonochemistry*
[14] Do, Q., Angkawijaya, A., Tran-Nguyen, P., Huynh, L., Soetaredjo, F., Ismadiji, S., & Ju, Y. (2014). Effect of extraction solvent on the total phenolic content, total flavonoid content, and antioxidant activity of Limnophilaarmatica. J. Food Drug Ana., 296-302
[15] Mujtaba, A., Masud, T., Ahmad, A., Naqvi, S. M., Qazalbash, M. A., & Levin, R. E. (2016). Effect of Solvents on Extraction Yield, Total Flavonoid, Total Phenolic Contents, DPPH Scavenging Activity and Antibacterial Potential of Three Apricot Cultivars. Transylvanian Review: Vol XXIV, No. 10, Special Issue, 1662-1677
[16] Zielinski, H., & Kozłowska, H. (2000). Antioxidant activity and total phenolics in selected cereal grains and their different morphological fractions. J Agric Food Chem, 2008-2016
[17] Ferreira, O., & Pinho, S. P. (2012). Solubility of Flavonoids in Pure Solvents. Industrial & Engineering Chemistry Research, 6586-6590

[18] Widyawati, P. S., Budianta, T. D., Kusuma, F. A., & Wijaya, E. L. (2014). Difference of Solvent Polarity to Phytochemical Content and Antioxidant Activity of Pluchea indicia Less Leaves Extracts. International Journal of Pharmacognosy and Phytochemical Research, 850-855
[19] Shakeel, F., Salem-Bekhit, M. M., Haq, N., & Siddiqui, N. A. (2017). Solubility and thermodynamics of ferulic acid in different neat solvents: Measurement, correlation, and molecular interactions. Journal of Molecular Liquids, 144-150
[20] Kadiri, O., Akanbi, C. T., Olawoye, B. T., & Gbadamosi, S. O. (2017). Characterization and antioxidant evaluation of phenolic compounds extracted from the protein concentrate and protein isolate produced from pawpaw (Carica papaya Linn.) seeds. International Journal of Food Properties, 2423-2436
[21] Nna, P., Egbuje, O., & Don-Lawson, D. (2019). Determination of Phytoconstituents and Antimicrobial Analysis of the Ethylacetate Extract Carica Papaya Seed. International Journal of Research and Innovation in Applied Science (IJRIAS), 2454-619
[22] S, N., I, S. Z., K, M. S., MR, A., & K, K. R. (2010). Antioxidant Levels and Ativities of Selected Seeds of Malaysian Tropical Fruits. *Mal J Nutr*, 149-159
[23] Lee, C. H., Lee, T. H., Ya'akob, H., Wong, S., & Janne, H. B. (2019). Optimization of Ultrasound-Assisted Extraction of Total Flavonoids Content from the White Flowering Variety of Melastoma Malabathricum. Jurnal Kejuruteraan SI, 91-102
[24] Tajane, S., Dadhe, P., Mandavgane, S., & Mehetre, S. (2017). Kinetic and thermodynamic azadirachtin extraction from whole neem fine powder formulation. Indian Journal of Chemical Technology, 218-222.
[25] Wei, M., Zhao, R., Peng, X., Feng, C., Gu, H., & Yang, a. L. (2020). Ultrasound-Assisted Extraction of Taxifolin, Diosmin, and Quercetin from Abies nephrolepis (Trautv.) Maxim: Kinetic and Thermodynamic Characteristics. molecules, 1-19
[26] Makris, D. P. (2016). Kinetics of Ultrasound-Assisted Flavonoid Extraction from Agri-Food Solid Wastes Using Water/Glycerol Mixtures. resources, 1-10
[27] Tao, Y., Zhang, Z., & Sun, D.-W. (2014). Kinetic modeling of ultrasound-assisted extraction of phenolic compounds from grape marc: Influence of acoustic energy density and temperature. Ultrasonics Sonochemistry, 1461-1469
[28] LIN, C. B., JINGWEN, P., & ALI, A. (2016). EXTRACTION KINETIC OF ZIZIPHUS JUJUBA FRUIT USING SOLID-LIQUID EXTRACTION. Journal of Engineering Science and Technology, 27 - 39
[29] Ebrahimzadeha, M. A., Enayatifard, R., Khalili, M., Ghaffarloo, M., Saeedi, M., & Charati, J. Y. (2014). Correlation between Sun Protection Factor and Antioxidant Activity, Phenol and Flavonoid Contents of some Medicinal Plants. Iranian Journal of Pharmaceutical Research, 1041-1049
[30] Sari, R. K., Wahyuningrum, M., Rafi, M., & Wientarsih, I. (2020). Effect of ethanol polarity on extraction yield, antioxidant, and sunscreen activities of phytochemicals from Gyrinops versteegii leaves. Materials Science and Engineering.
[31] Morais, D. V., Costa, M. A., Ba´rbara, M. F., Silva, F. d., Moreira, M. M., Delerue-Mato, C., . . . Lopes, C. A. (2018). Antioxidant, photoprotective and inhibitory activity of tyrosinase in extracts of Dalbergia ecastaphyllum. PLOS ONE, 1-16
[32] Muhamad, N., Muhmed, S. A., Yusoff, M. M., & Gimbun, J. (2014). Influence of Solvent Polarity and Conditions on Extraction of Antioxidant, Flavonoids and Phenolic Content from Averrhoa bilimbi. *Journal of Food Science and Engineering 4*, 255-260
[33] Galanakis, C., Goulas, V., Tsakona, S., Manganaris, G., & Gekas, V. (2012). A Knowledge Base for The Recovery of Natural Phenols with Different Solvents. *International Journal of Food Properties*, 382-396.
[34] Li, H., Zhou, X., Wu, M., Deng, M., Wang, C., Hou, J., & Mou, P. (2016). The cytotoxicity and protective effects of Astragalus membranaceus extracts and butylated hydroxyanisole on hydroxyl radical-induced apoptosis in fish erythrocytes. *Animal Nutrition*, 1-7
[35] Emejulu, A., Nwufo, K., Ene, A., & Obasi, U. (2017). GC-FID Phytochemical Analysis and Intraperitoneal Lethal Dose, Determination of Ethanol Root Extract of Mueuna pruriens. *International Journal of Research in Pharmacy and Biomedicines*, 23-28
[36] Csepregi, K., Neugart, S., M. S., & Hideg, É. (2016). Comparative Evaluation of Total Antioxidant Capacities of Plant Polyphenols. *molecules*, 1-16
[37] Desmiaty, Y., Ratnawati, J., & Andini, P. (2009). PENENTUAN JUMLAH FLAVONOID TOTAL EKSTRAK ETANOL DAUN BUAH MERAH (PANDANUS CONOIDEUS LAMK.) SECARA KOLORIMETRI KOMPLEMENTER. *POKJANAS TOI XXXVI*
[38] Wilkinson, J. B., & Moore, R. J. (1982). *Harry's Cosmeticology (7th edition).* New York: Chemical Publishing Company
[39] M.S. Latha, M., Jacintha Martis, M., Shobha V, M., Shinde, R. S., Sudhakar Bangera, M., Binny Krishnankutty, M., . . . B.R. Naveen Kumar, M. (2013). Sunscreen Agent: A Review. *Clinical and Aesthetic*

[40] Nunes, A. R., Vieira, I. G., Queiroz, D. B., Leal, A. L., Morais, S. M., Muniz, D. F., . . . Coutinho, H. D. (2018). Use of Flavonoid and Cinnamates, the Main Photoprotectors with Natural Origin. *Advances in Pharmacological and Pharmaceutical Sciences*

**Biographies of Authors**

**Eduardus Budi Nursanto** graduated his doctoral degree majoring in clean energy and chemical engineering from Korea University of Science and Technology, South Korea. Currently, he is active faculty member at Chemical Engineering Department, Universitas Pertamina, Indonesia.

**Rachel Wijaya** graduated her bachelor's degree from Chemical Engineering Department, Universitas Pertamina, Indonesia.

**Alifiana Permata Sari** graduated her master's degree from School of Chemical Engineering, University of Birmingham, United Kingdom. Currently, she is active faculty member at Chemical Engineering Department, Universitas Pertamina, Indonesia.