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Enhancement of Dissolution Rate of Piperine Using Solid Dispersion Approach and Evaluation of Its Antioxidant Activity

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Abstract

Piperine is a phenolic compound in black pepper (*Piper nigrum* Linn) and *Piper longum*. It has been used in traditional medicine and has many pharmacological properties. However, its poor solubility in water has hindered the development of drugs with piperine as the main ingredient. In this study, solid dispersions of piperine were formulated using hydrophilic polymer (PVP) and hydrophobic polymer (Eudragit) to improve its dissolution rate and antioxidant activity. The solid dispersions were prepared using solvent evaporation techniques with various ratios of pure piperine to polymer (2:1, 1:1 and 2:1, w/w). FESEM, DSC, XRD, and FT-IR characterized the resulting solid dispersions of piperine. The dissolution rates were measured in distilled water, and antioxidant activity was evaluated using DPPH and FRAP free radical scavenging assays. The physicochemical characterization results indicated that solid dispersions with PVP and Eudragit had properties different from those of pure piperine. The dissolution test results showed that the solid dispersions with PVP (2:1) and Eudragit (1:1) exhibited the best dissolution rates, at 40.32 and 38.02 %, respectively. Furthermore, PVP and Eudragit solid dispersions (2:1, 1:1) demonstrated a higher antioxidant capacity in scavenger DPPH and FRAP free radicals than other formulations. These findings suggest that both polymers can increase piperine solubility, leading to increased antioxidant activity. However, further studies are needed to understand the underlying mechanisms.

Keywords: Piperine, Solid dispersion, PVP, Eudragit, Dissolution, Antioxidant

Introduction

Indonesia is one of the largest tropical countries producing black pepper (*Piper nigrum* Linn) in the world, besides Vietnam, India, China, and Brazil [1]. This ingredient has been used for centuries and is known worldwide as a food ingredient and traditional medicine for various purposes. Piperine is an alkaloid compound found in black pepper and *P. longum*, which gives a

distinctive spicy taste. It is the first pharmacologically active chemical substance found in plants of the Piperaceae family [2], which shows various pharmacological effects, including antioxidant, anti-inflammatory, anticancer, neuroprotective, antimicrobial, hepatoprotective, antidepressant, antiobesity, cardioprotective, antiaging, which are increasingly in demand worldwide [3-5].

Despite its various benefits, drug development with piperine as the main ingredient has yet to be well developed due to its poor solubility in water [6]. This issue of poor solubility is not just a technical challenge, but a significant barrier that hampers the potential of piperine in pharmaceutical applications. Various approaches to enhance piperine solubility and dissolution rates have been investigated to improve the water solubility property of piperin [7]. These include structure modification, co-crystallization, co-amorphous, inclusion complexes, nanoparticles, and solid dispersions (SD) [8].

Solid dispersion (SD), as a practical method to improve the bioavailability of poorly water-soluble drugs, has been effectively used to improve the pharmacokinetic performance of poorly water-soluble drugs [9]. Studies have revealed that drugs in solid dispersions do not necessarily need to be in a micronized state. The carrier dissolves when solid dispersions are exposed to aqueous media, and the drug is released as fine colloidal particles [10]. Therefore, solid dispersions (SDs) are becoming a primary focus in research and development, especially regarding the dosage forms used to establish water-insoluble active pharmaceutical ingredients [11]. This method involves the distribution of active ingredients in various forms within the polymer matrix and water-soluble carriers, including molecular, amorphous, and microcrystalline created by melting (fusion), solvent, or melting solvent generating inclusion complexes, and reducing particle size to the nanoscale level, thus increasing the available surface, so that wetting, and dissolution can occur more rapidly [12-14].

The polymeric carriers used in these solid dispersion formulations are expected to induce supersaturation, positively impacting the drug's hygroscopicity, water solubility, and particle size reduction. Conversion of a drug from its crystalline form to its amorphous form is an important route to increase the solubility of the drug [14]. Carriers play a significant role in the formulation of solid dispersion. They can be hydrophilic, hydrophobic, or water-soluble. Depending on their characteristics, they can be used as release retardants or release enhancers [15]. Selection of the appropriate SD carrier to achieve the desired SD type and physics is critical. Some types of polymers or carriers used in the preparation of solid dispersions of piperine are eudragit, hydroxypropyl methylcellulose acetate succinate (HPMCAS), and polyvinylpyrrolidone (PVP) [16].

In this study, the hydrophilic polymer polyvinyl pyrrolidone (PVP) and the hydrophobic polymer Eudragit 100 were chosen as matrices to prepare amorphous solid dispersions (SD) of piperine (Pip). Both polymers have the proven ability to enhance the properties of the active ingredient. PVP, for instance, is used extensively in stabilizing nanoparticles. It is an amphiphilic polymer with an alkyl hydrophobic side group and a hydrophilic pyrrolidone group, soluble in water and many organic solvents because of the formation of hydrogen bonds between the carbonyl group in PVP and the solvent [17]. Additionally, other earlier research demonstrated that PVP can increase the dissolution rate by improving wettability and elevating the dispersibility of piperine [6]. On the other hand, prior studies showed that Eudragit yielded the most significant enhancement in solubility caused by acid-base interaction between their carboxyl groups in Eudragit and piperine, leading to improved piperine dissolution and maintenance of a supersaturated solution [18]. Moreover, the potential of solid dispersions to

enhance the solubility and bioavailability of complex drugs in water and increase the antioxidant activity of compounds is a promising avenue. For instance, quercetin, an antioxidant compound, demonstrated increased antioxidant activity when formulated as a solid dispersion [19]. Similarly, the solid dispersion of usnic acid also showed enhanced antioxidant activity based on the solubility results [20]. However, the effect of Pip-SD with PVP and Eudragit on improving the antioxidant properties of piperine through free radical scavenging has not been reported. This research, therefore, holds the promise of expanding our understanding and potentially revolutionizing the application of piperine in pharmaceutical and drug development research, instilling hope and optimism in the potential of piperine in pharmaceutical and drug development research.

This study aimed to determine the effect of PVP and Eudragit as dispersant polymers on their solubility and antioxidant activity compared to pure piperine. We prepared the Pip-SD samples using a solvent evaporation method and characterized them using field emission surface electron microscopy (FESEM), X-ray diffraction (XRD), DSC, and FTIR. We then conducted a dissolution test to study the dissolution of Pip-SDs. Finally, we determined the antioxidants in the samples through DPPH free radical scavenger activity and FRAP assay.

Materials and methods

Material

Piperine was isolated from *P. ningrum* collected from a local market in Bogor-West Java. Dry material (2 kg) was extracted with 96 % ethanol (1:10) for 24 h at room temperature. The extract was concentrated under reduced pressure to form a dry extract, which was then dissolved successively in n-hexane and ethyl acetate to obtain pale yellow crystals identified as piperine based on NMR spectroscopy analysis. 2, 4, 6-tri(2-pyridyl)-s-triazine (TPTZ), 1,1-Diphenyl-2-picryl-hydrazyl (DPPH), 6-Hydroxy-2,5,7,8-tetramethychroman-2- carboxylic (Trolox), and Folin-Ciocalteu were all purchased from Sigma Company (USA). Eudragit L 100, PVP K30, and analytical grade of organic solvent (ethanol (Merck 1.00983), Ethyl acetate (Fulltime 6801-04), hexane (Fulltime 6711-04) was purchased from local suppliers.

Preparation of piperine solid dispersion (SD-Pip)

The solid dispersion process was carried out using polyvinylpyrrolidone (PVP), and eudragit (E) polymers were prepared using solvent evaporation Kathavarayan and Yoo [7] with slight modification. Solid formulations were made with piperine: Polymer ratios: 2:1, 1:1, and 2:1 (w/w). The dispersion process started by dissolving 1 g of piperine and polymer powder, each in 50 mL of ethanol. After complete dissolution, the 2 solutions are combined and evaporated until the solvent is wholly evaporated and dried. Subsequently, all the Pip-SD samples were carefully ground using a mortar, sieved through a #80 mesh, and stored in a dry condition for subsequent characterization Kathavarayan and Yoo [7] and antioxidant assays [21,22].

Characterization piperine solid dispersion (Pip-SD)

Field emission scanning electron microscopy (FE-SEM)

The surface morphology of the piperine, matrix, and Pip-SD was observed at various magnifications using SEM (Jeol JSM-7900F, Tokyo, Japan) with 20 kV and 12 mA evaluated. The powder samples were put into an aluminum holder and then coated with gold with a thickness of 10 nm.

Powder x-ray diffraction (PXRD)

The diffraction patterns of the piperine and Pip-SD were analyzed at room temperature (± 25 °C) using a diffractometer (AERIS Panalytical). The measurements

were then carried out under particular conditions involving a Cu metal target, a Kα filter, a voltage of 40 kV, and an electric current of 40 mA. Analyzes were carried out in the range of 5 - 50 °C.

Infrared spectroscopy's fourier transform

The piperine and Pip-SD were analyzed using an infrared spectrophotometer Bruker-Tensor II, ATR. The sample was placed in an ATR crystal, and the cover tip was positioned parallel to the sample hole. The absorption spectra were recorded at a wavenumber of 4000 - 500 cm^{-1}.

Differential scanning calorimetry (DSC)

Differential scanning calorimetry was carried out with a heating rate of 10 °C/min using TA Instruments DSC Perkin Elmer 8000 for piperine, PVP, eudragit, and their solid dispersion. About 2 mg of the samples were placed in sealed aluminum pans and then heated from 25 to 170 °C (to 220 °C for PVP samples) under nitrogen purging.

Dissolution test

A dissolution test was conducted using polymer to determine the difference in solubility of piperine and Pip-SD (PVP and Eudragit). This experiment was conducted using a dissolution apparatus (COPLEY Dis 6000), and the dissolution medium used was distilled water (900 mL), according to Thenmozhi, 20017 with slight modification. The equivalent of 10 mg of piperine samples were weighed and taken to a dissolution vessel for 1 h with constant stirring at 50 rpm and 37 °C. Aliquot (3 mL) was withdrawn from dissolution media using a syringe and put into a vial using a 0.45 um filter syringe at a predetermined time interval (5, 10, 15, 30, 45, and 60 min). The same volume of distilled water was added to the vessel to maintain the same condition. The concentration of dissolved piperine was evaluated spectrophotometrically at λ 343 nm.

Antioxidant assay

DPPH assay

The antioxidant activity of piperine and Pip-SD was determined using 2,2-diphenyl-1-picrylhydrazyl (DPPH), according to Tzeng *et al.* [21]. A stock solution of pure piperine (10 mg/mL) was prepared in methanol (as positive control). Next, SD-Pip (equivalent to 10 mg piperine), the polymer (PVP and Eudragit), and pure piperine are all dissolved in distilled water. 500 µL of each sample was collected and mixed with 500 µL DPPH (0.1 mM), and then MeOH was added to the sample to a total volume of 2500 µL. The mixture was homogenized, kept in a dark place at room temperature for 30 min, and evaluated by a Cary 60 UV-Vis spectrometer at 517 nm. The scavenging effect on the DPPH radical of the samples was calculated as the Trolox equivalent's antioxidant capacity from the calibration curve: $y = 4.7513x - 2.5904$. $R^2 = 0,9973$.

FRAP assay

The FRAP assay was evaluated by observing the color change of Fe3+ tripiridyltriazine (colorless) to Fe2+ -tripyrydyltriazine (blue) [22]. The absorbance results were measured with a spectrophotometer at 593 nm. FRAP reagent was prepared with 300 mM acetate buffer (pH 3.6), 10 mM 2,4,6-tri (2- pyridyl)-s-triazine, and 20 mM FeCl3 in a 10:1:1 ratio. Sample pure piperine, polymers matrics, and SD- Pip (40 µL) were mixed with 1,200 µL FRAP reagent and incubated at 37 °C for 30 min. The FRAP calculation was based on the standard Trolox calibration curve: $y = 0.2845x - 0.3862$, $R2 = 0.991$. FRAP values were based on the standard Trolox calibration curve and expressed in mg TE/g.

Statistical analysis

The result of the solubility test and *in vitro* dissolution test of piperin, physical mixture, and solid dispersions were presented as mean ± SD. The statistical

analysis was investigated by One-way ANOVA using Minitab Software. p-value < 0.05 was determined as a significant difference. Tukey's test was applied to determine the significant level. The same letter expressed no significant difference between the values.

Results and discussion

Piperine possesses numerous biological activities, including its potential as antimicrobial, antioxidant, anti-inflammatory, antitumor, antidepressant, and analgesic [3-5]. Piperine also enhances the bioavailability of several medicinal compounds, magnesium, and nutrients [23]. Our previous study reported that piperine could significantly increase magnesium absorption in the lungs when administered intraperitoneally compared with controls in mice [24]. However, the activity is lower when piperine is administered orally than intraperitoneal administration. Therefore, piperine was formulated as a solid dispersion so that its solubility in water increased with the help of PVP and eudragit matrices.

In this study, the solid dispersion method and the solvent evaporation method were used. This method is carried out by dissolving the piperine and its carrier in ethanol solvent, followed by evaporation until an amorphous solid dispersion (Pip-SD) is obtained. Characterization of solid dispersions involves various methods such as dissolution efficiency calculations, stability studies, thermal analysis (e.g., differential scanning calorimetry), X-ray diffraction, Fourier transforms infrared spectroscopy, and release kinetic studies. This characterization helps evaluate the physical state, interactions between drug and carrier, crystal form, and release behavior of solid dispersion formulations [25,26]. This technique provides a way to reduce particle size to near the molecular level, resulting in rapid dissolution and increasing the therapeutic efficacy of the dosage form [25].

Characterization piperine solid dispersion (Pip-SD)

The FESEM (Scanning electron microscopy) images revealed distinct differences between piperine, Pip-SD PVP, and Pip-SD Eudragit solid dispersion, as shown in **Figure 1**. Pure piperine exhibited a random or irregular crystal shape with a rough surface featuring varying lengths and widths. In contrast, in the SD Pip-PVP, the irregular shape of piperine crystals was still noticeable. However, in the SD Pip-PVP solid dispersion with a ratio of 2:1, a more uniform shape with smaller particles was observed, indicating that within the PVP polymer, some piperine crystals had transitioned into an amorphous form, showing a relatively effective dispersion of piperine in the PVP polymer. In the solid dispersion of piperine with eudragit at a ratio of 1:1, the irregular crystals of piperine were less apparent. At the same time, some particles were presumed to be microparticles of eudragit with a smoother surface.

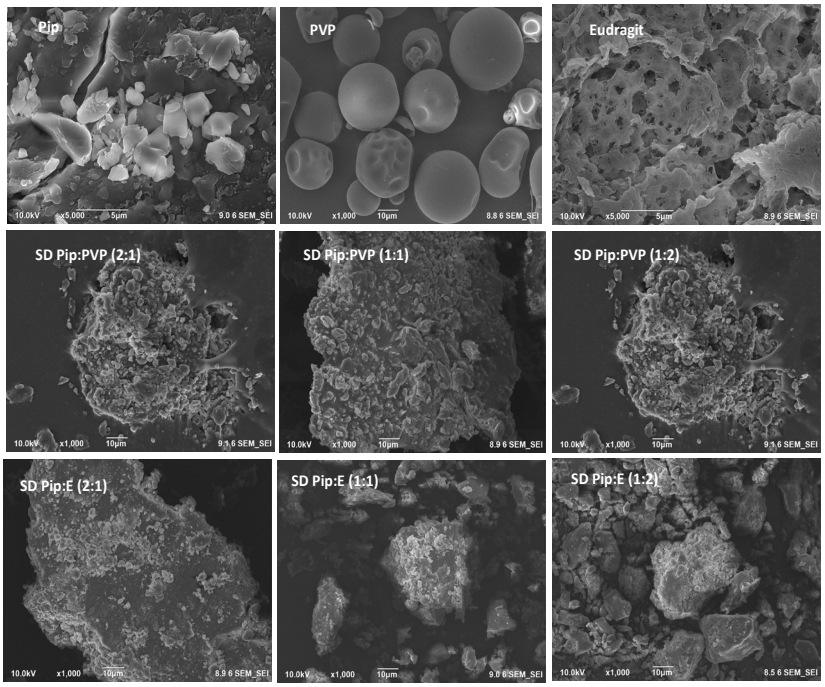

Figure 1 FESEM micrographs of Piperine, matrix, and Pip-SD.

Furthermore, smaller particles became more prominent as the ratio of eudragit to piperine increased in the solid dispersion. This observation suggested that eudragit can effectively disperse piperine crystals, potentially leading to an enhanced dissolution rate of piperine. The presence of a crystalline phase in the sample, which is essential for understanding the physical properties of the dispersion and potential interactions between components, can be seen from the results of the XRD analysis. Diffraction is one of the most accurate methods for determining diffraction patterns in manufacturing solid dispersion systems. The XRD pattern in the crystalline form will show a sharp diffraction pattern, whereas, in the amorphous form, it will not show a peak diffraction pattern. The identified piperine peaks may decrease intensity or disappear in the solid dispersion. The diffraction pattern of SD-pip with PVP and Eudragit is shown in **Figure 2**. Various characteristics of piperine crystals can be seen from the diffraction peaks with high and sharp intensity at specific 2θ values, including 12.8; 14.6; 15.46; 19.58; 21.2; 22.16; 24.07; 25.7; 28.13; and 36.3 ° in the 2θ region, and these peaks can later be used to identify the presence of piperine in solid dispersions[5]. Based on **Figure 2**, it can be seen that the diffraction peaks are still similar to the piperine diffraction pattern, but the intensity decreases as the matrix concentration increases. Indicating that adding PVP and Eudragit polymers as carriers and the evaporation dispersion technique have not entirely changed the crystal form to amorphous in a solid dispersion. However, complete amorphization does not guarantee increased dissolution of the amorphous solid dispersion system [27].

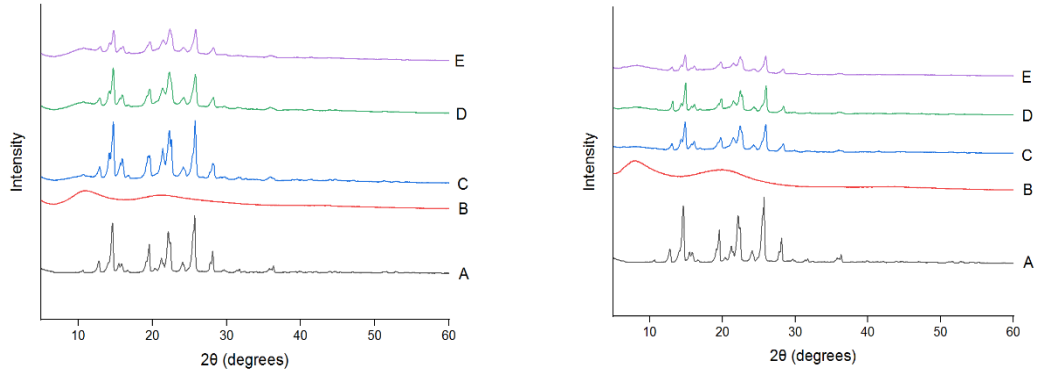

Figure 2 X-Ray Powder diffractions of piperine (A) and Pip-SD PVP (I): PVP (B), 2:1 (C), 1:1 (D), 2:3 (E) and Pip-SD-Eudragit (II): Eudragit (B), 2:1 (C), 1:1 (D), 2:3 (E).

DSC analysis can determine solid dispersion samples' melting point and enthalpy [20]. Understanding thermal stability and potential interactions with the dispersion medium is critical. The melting point value of a dispersed solid sample from DSC measurements indicates the temperature at which the sample undertakes a phase transition from solid to liquid. In dispersed solid samples, the melting point value can explain the interaction between the dispersed material and the dispersion medium.

DSC measurements of SD-Pip (**Figure 3**) show a shift in the melting point of the SD-Pip sample compared to pure piperine (**Table 1**). This indicates that dispersion has lower molecular mobility than pure compounds because, in solid dispersions, strong interactions are formed between components, such as ionic and hydrogen bond interactions, which can reduce the mobility of drug molecules [28]. A lower melting point value can also indicate that the drug is more soluble in the dispersion medium, increasing its bioavailability [29].

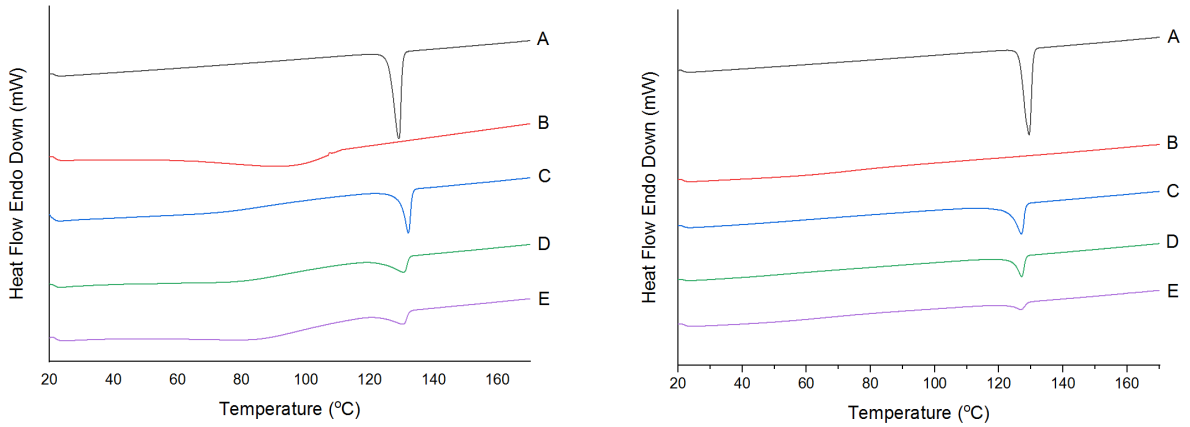

Figure 3 DSC thermograms of piperine (A) and Pip-SD PVP (I): PVP (B), 2:1 (C), 1:1 (D), 1:2 (E) and Pip-SD-Eudragit (II): Eudragit (B), 2:1 (C), 1:1 (D), 1:2 (E).

Table 1 Melting points of piperine and the solid dispersion (SD-Pip).

Samples	Melting point (°C)
Piperine	133.83
PVP	158.00
Eudragit	49.50
SD Pip-PVP 2:1	131.40
SD Pip-PVP 1:1	129.98
SD Pip-PVP 1:2	129.81
SD Pip-E 2:1	131.46
SD Pip-E 1:1	131.56
SD Pip-E 1:2	131.36

In the FTIR study, PVP exhibited a peak transmission of existing functional groups, such as C=O amide groups, at 1680 - 1630 cm^{-1} wavelengths. Additionally, a broad band at a wavelength of 3400 cm^{-1} indicated the N-H stretching vibrations of the amide functional group, signifying both moisture and the hygroscopic nature of PVP (**Figure 4**). Based on the FTIR spectra of Pip-SD PVP (10:1), it was known that there was a broad band around the wavelength of 3340 cm^{-1}. This band was also present in other solid dispersions. However, the transmittance was not as pronounced as in the case of the Pip-SD PVP with a ratio of 10:1. Moreover, strong IR spectra within the 1632 - 1629 cm^{-1} wavenumber were observed in all comparisons of Pip-SD PVP, indicating the presence of C=O stretching vibrations of amide functional groups. Based on its molecular structure, eudragite has several functional groups that can be identified using FTIR [7], such as carboxyl groups characterized by the presence of O-H stretching vibrations at 3400 - 2400 cm^{-1} and C=O stretching vibrations at 1730 - 1700 cm^{-1}. There were also ester groups characterized by C=O stretching vibrations at 1750 - 1735 cm^{-1} and C-C(O)-C stretching vibrations at 1210 - 1160 cm^{-1}. In this study, the IR spectra of Pip-SD eudragit with various ratios did not reveal any corresponding peaks indicative of interactions between the functional groups in eudragite and the previously described wavenumbers (**Figure 4**). Furthermore, no alterations in peak shape or significant shifts in wavenumbers were observed when comparing the IR spectra of piperine with those of Pip-SD eudragit. Consequently, it can be inferred that piperine did not interact significantly, or at most, only slightly exhibited with the eudragite polymer.

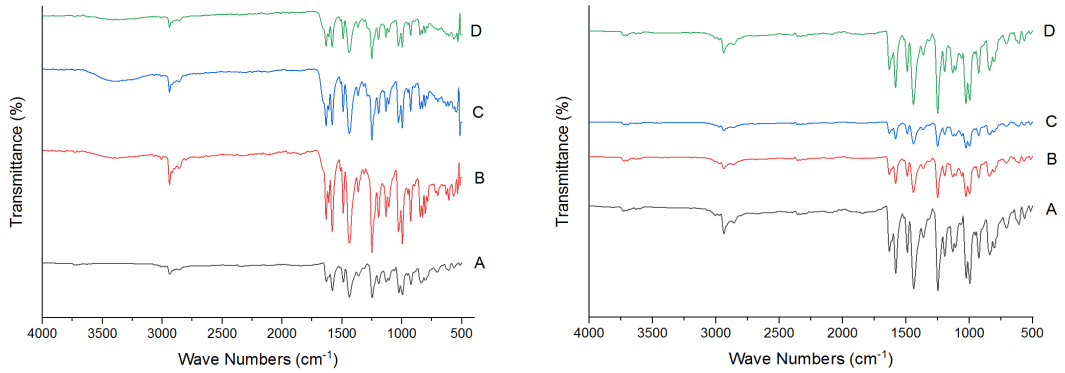

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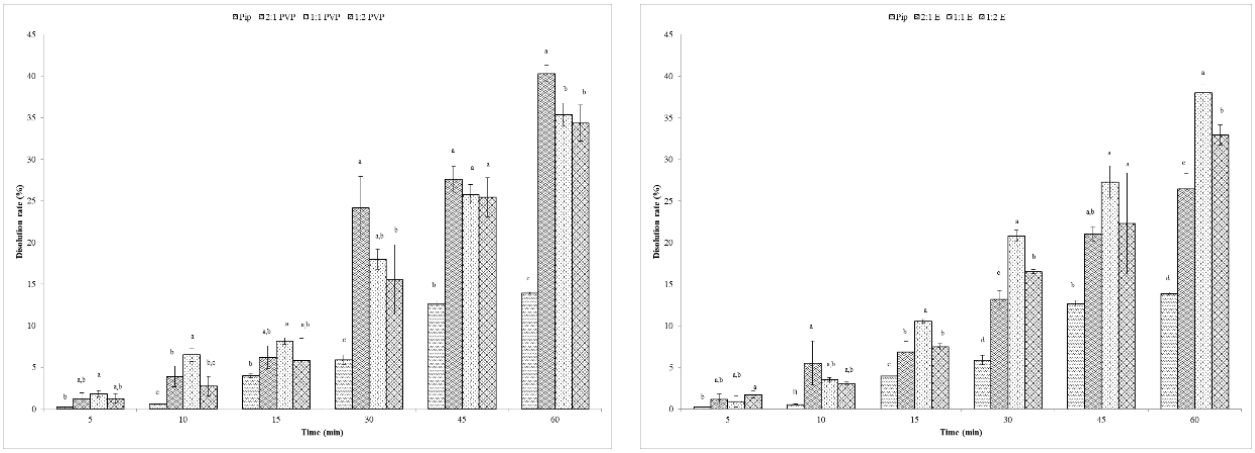
Figure 4 FTIR Spectra of piperine piperine (A) and Pip-SD PVP (I): PVP (B), 2:1 (C), 1:1 (D), 1:2 (E) and Pip-SD-Eudragit (II): Eudragit (B), 2:1 (C), 1:1 (D), 1:2 (E).

The aqueous solubility of a drug for an oral formulation is significant because it strongly influences the drug's bioavailability. Therefore, increasing the solubility of piperine will increase its bioavailability, and its activity will also increase [14]. The dissolution test results of pure piperine and Pip-SD are presented in **Figure 5**. In this study, all piperine solid dispersion tended to have a higher dissolution rate than piperine. These results indicated that the polymer carriers enhance the wettability of Piperine and improve Piperine release [18]. In the dissolution test of all samples at 60 min, the Pip-SD PVP (2:1) significantly had the best dissolution rate (40.32 %) ($p < 0.05$). Meanwhile, Pip-SD Eudragit with a ratio of 1:1 showed a significantly high dissolution rate (38.02 %) among the other SD eudragit ratios ($p < 0.05$); this indicates that this solid dispersion is the most soluble in distilled water media.



(A) (B)

Figure 5 Dissolution profile of piperine and Pip-SD PVP (A) and Pip SD-Eudragit (B).

The use of PVP and eudragit matrices in the piperine solid dispersion process has been studied to increase the solubility and dissolution rate of the hydrophobic drug piperine. Hydrophilic carriers such as PVP have been shown to increase the solubility of piperine, thereby enhancing dissolution [7]. In addition,

using the Eudragit matrix has shown promising results in increasing the solubility of piperine in solid dispersions. These studies demonstrate that PVP and Eudragit matrices can effectively increase the solubility of piperine, a hydrophobic drug, via solid dispersion techniques [15]. Therefore, hydrophilic and hydrophobic matrices play an essential role in increasing the solubility of hydrophobic drugs via solid dispersion techniques [30]. PVP is a hydrophilic polymer that can form hydrogen bonds with drug molecules, increasing solubility and dissolution rate [31]. Molecular interactions between PVP and drug molecules can suppress phase separation and subsequent recrystallization of amorphous drugs. In contrast, the Eudragit matrix is often used as an enteric coating and can increase the solubility of hydrophobic drugs in water [32]. Using the Eudragit matrix has shown promising results in increasing the solubility of piperine in solid dispersions [15,32].

Antioxidant activities of piperine solid dispersion (Pip-SD)

Antioxidant activity in foods and drugs has received attention due to its association with beneficial health effects against various degenerative diseases. A sample can have antioxidant activity if a specific mechanism involves free radical scavenging reactions such as hydrogen atom transfer, single electron transfer, and targeted scavenging [33]. Colorimetric assays are widely used to measure antioxidant activity due to their simplicity, cost-effectiveness, and ability to provide reliable results in a relatively short time frame [34]. The most common colorimetric assays are DPPH, FRAP, and ABTS, which change color due to electronic transitions in atoms or molecules [35]. These colorimetric assays are widely used due to their simplicity, cost-effectiveness, and ability to provide reliable results in a relatively short time. They are commonly used to evaluate the antioxidant activity of various biological samples, such as serum, plasma, whole blood, tissues, cells, culture supernatants, and other foods [33].

Trolox has been commonly used as a standard to calculate the antioxidant capacity of a pure compound or extract in TEAC, DPPH, ORAC, and FRAP assays [36]. Antioxidant test results are usually expressed in Trolox equivalent units so that standard values can be used for by/ in comparison. As presented in **Table 2**, PVP Pip-SD (2:1) and Pip-SD Eudragit (1:1) exhibited the highest free radical scavenging and a higher trolox equivalent value than other formulas. The results corresponded well with their dissolution, which showed the best dissolution rate compared to another comparison. Research has shown that various approaches, such as piperine-loaded drug delivery systems, novel multicomponent crystals of piperine with succinic acid, and amorphous systems of piperine, have been effective in improving the aqueous solubility, dissolution rate, and antioxidant activity of piperine [13,30]. Additionally, the amorphization of piperine has been found to considerably improve its dissolution rate, apparent solubility, permeability, and antioxidant activity [33]. Therefore, increasing the dissolution rate of piperine through various formulation approaches can enhance its bioavailability and antioxidant activity, which is crucial for its potential health benefits.

Table 2 Comparative Inhibition activity of pure piperine and Pip-SD.

Sample	DPPH scavenging (mg TE/g)	FRAP (mg TE/g)
Piperin	4.09 ± 0.01[d]	1.42 ± 0.03
PVP	1.98 ± 0.01 [e]	0.01 ± 0.01
Pip-SD PVP 2:1	**6.50 ± 0.07[a]**	**4.51 ± 0.02**
Pip-SD PVP 1:1	4.87 ± 0.03 [c]	4.18 ± 0.12
Pip-SD PVP 1:2	5.42 ± 0.01 [b]	3.16 ± 0.04
Piperin	4.09 ± 0.01[c]	1.42 ± 0.03
Eudragit	1.80 ± 0.02[d]	0.13 ± 0.04
Pip-SD E 2:1	5.11 ± 0.02 [a,b]	2.39 ± 0.11
Pip-SD E 1:1	**5.30 ± 0.23 [a]**	**3.94 ± 0.01**
Pip-SD E 1:2	4.79 ± 0.01[b]	2.95 ± 0.06

Conclusions

In the present study, dissolution enhancement of piperine was achieved by the solid dispersion technique using PVP and Eudragit showed good characterization in the diffraction peak intensity in the XRD analysis, lower melting point, and diminished endothermic peaks in the DSC analysis. FTIR spectroscopy analysis demonstrated no chemical interactions between pure piperine and the polymers, while FESEM analysis revealed significant changes in crystal morphology. Increasing piperine's dissolution rate can improve bioavailability and enhance antioxidant activity. However, the mechanism of hydrophilic and hydrophobic polymers in solid piperine dispersion still needs further research.

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