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Formulation And Evaluation of Solid Dispersions to Improve the Aqueous Solubility of Piperine

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Abstract
The aim of this study was formulation & evaluation of solid dispersions to improve the aqueous solubility of piperine. Piperine the active compound found in black pepper has poor aqueous solubility, which limits its bioavailability when administered orally. Piperine has several therapeutic benefits including anti-inflammatory, antioxidant, antidiabetic, Digestive stimulant & anticancer effect. Improving its solubility & bioavailability through solid dispersions van make it more effective as a therapeutic agent broaden its [potential applications. Solid dispersions were prepared by solvent evaporation method using poloxamer 188 & polyethylene glycol 6000 as polymer & methanol as a solvent. Solid dispersions were evaluated for FTIR, drug content, solubility, % yield. In vitro drug release & stability test. The F1 formulation was found to be best formulation as it possesses high drug content 87.7%, solubility 4470.64, % yield 98.24% & in vitro drug release was 76.86%. Thus, solid dispersions approach can be used successfully enhance solubility, dissolution rate & bioavailability of piperine.

Keywords
Piperine, solid dispersion, Bioavailability, Aqueous solubility, FTIR

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I. Introduction

The alkaloid and secondary metabolite piperine (1-piperoylpiperidine) is present in long pepper (Piper longum), black pepper (Piper nigrum), and other pepper plants that are members of the Piperaceae family (Gorgani et al., 2017). In many Asian nations, this substance has been used extensively in traditional medicine to treat ailments like rheumatism, muscle soreness, dyspepsia, flatulence and indigestion, as well as coughing and sore throat. It also functions as a digestive tonic and has antipyretic, antiseptic, bactericidal, insecticidal, and diuretic properties (Smilkov et al., 2019). Piperine has been shown in studies to block drug-metabolizing enzymes and improve the bioavailability of foods, medications, anticarcinogens, and phytochemicals. Numerous research have also looked at piperine's pharmacological effects, including its antioxidant, cytoprotective, anti-inflammatory, analgesic, antidepressant, and antileukemic qualities (Ashour et al., 2016).

However, piperine's use in creating medicinal doses is restricted due to its low solubility in aqueous fluids and melting point of 135°C. After oral administration, the majority of active pharmaceutical ingredients (APIs) with low water solubility probably have a poor absorption profile. The physicochemical characteristics of piperine provide obstacles to its development as a pharmaceutical molecule, limiting its clinical application despite its broad and prospective bioactivity. With a log P value of 2.25, piperine is extremely lipophilic despite having a low water solubility of 0.04 mg/ml, placing it in the virtually insoluble category according to the US Pharmacopoeia. This leads to dissolution as the rate-limiting phase in the gastrointestinal tract's absorption process of piperine, which results in low in vivo pharmacological efficacy and inconsistent oral bioavailability. Because piperine is prone to isomerization from UV radiation, which also alters its concentration in preparation during manufacturing, storage, and administration, piperine photostability is another issue (Ahmad et al., 2016). Therefore, improving these medications' solubility is one of the most important strategies to boost drug bioavailability, which is thought to be the biggest obstacle facing the pharmaceutical sector (Alshehri et al., 2020). Piperine's solubility and release profile have been enhanced by a number of methods, such as its integration into solid dispersion systems, multicomponent crystals, inclusion complexes, nanosuspensions, and microparticles (Zaini et al., 2020).

1.1 Solid Dispersions

Solid dispersion (SD) technology has become a key tactic for improving the bioavailability and solubility of medications that are not very soluble in water. Two components are usually included in an SD system: a hydrophilic matrix and a hydrophobic medication. As a carrier, the hydrophilic matrix helps the hydrophobic medication spread throughout its structure. Solid dispersions are eutectic mixes or solid solutions of

pharmaceuticals and water-soluble carriers that, as a result of molecular dispersions and/or polymer solubilization effects, improve drug solubility by causing amorphous formation or supersaturation (Dewi et al., 2024). The high energy of the amorphous state and the thermodynamics or kinetics of supersaturated solution tend to cause nucleation and recrystallization, which polymer matrices help to prevent. It has been shown that solid dispersions methods can effectively improve the solubility and bioavailability of piperine (Zhu et al., 2020).

II. Solubility

A material's solubility is defined as the quantity that has entered the solution when the equilibrium between the excess, or undissolved substance, and the solution is attained at a specific temperature and pressure. The term "solvent" refers to the material that has been dissolved, the solvent is the dissolving fluid in which the solute is dissolved, and the combination of the two is called the solution (Shinkar et al., 2017).

The definitions of various solubility terms:

Description Form	Parts of solvent required for one part of solute	Solubility (mg/ml)	Solubility assigned (mg/ml)
Very Soluble	<1	>1000	1000
Freely soluble	1-10	100-1000	100
Soluble	10-30	33-100	33
Sparingly soluble	30-100	10-33	10
Slightly soluble	100-1000	1-10	1
Very slightly soluble	1000-10000	0.1-1	0.1
Practically insoluble	>10000	<0.1	0.01

III. Biopharmaceutical Classification System (BCS)

The BCS is the Biopharmaceutical Classification System. The BCS is a scientific framework that is used to categorize drug substances based on intestinal permeability and equilibrium aqueous solubility as summarized in Figure1.1. The BCS considers three main factors: intestinal permeability, dissolution rate, and solubility when combined with a drug product's in vitro dissolution characteristics (Tran et al., 2019). For immediate-release solid oral dosage forms, these three factors control the rate and extent of oral drug absorption. Based on the solubility and permeability properties of drug substances, the BCS classifies them into four categories.

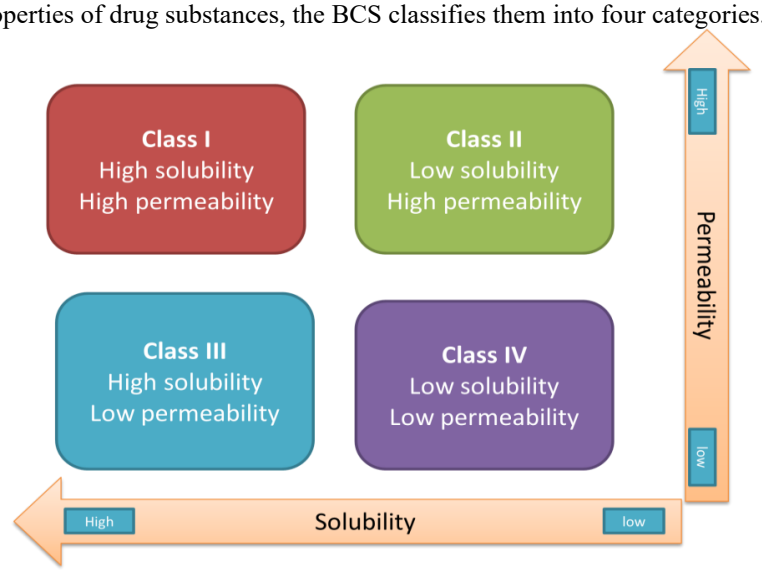


Figure 1.1: Biopharmaceutical Classification Systems (BCS)

IV. Materials & Methods

Piperine was obtained from Kshipra Biotech Private Limited, Indore,Madhya Pradesh. Polyethylene glycol 6000, poloxamer 188, Poly viny pyrrolidone K 30 from Central drug house Pvt. Ltd. Distilled water was used in the study was prepared fresh for each experiment. All other materials used were of analytical grade.

4.1 Preparation of Solid Dispersion

The selection of carrier and optimum drug: carrier ratio for the preparation of solid dispersion of Piperine was established on the basis of the solubilizing potential of carriers towards the enhancement of solubility of the Piperine during the screening of carriers.

A solid dispersion of piperine with two different polymers (polaxamer 188 and PEG 6000) was prepared by the solvent evaporation method. The ratios of piperine/polymers are shown in Table 1. Briefly, the prescribed

amounts of piperine and polymer were separately dissolved in a certain volume of methanol. The two solutions were mixed with glass rod while putting on hot plate to remove the solvent. Then the dried samples were crushed and screened through a mesh size of 80. Prepared solid dispersions were kept in a desiccator until further investigation(Wang et al., 2022).

Table 1: Composition of Solid Dispersion

Formulations	Polymer	Drug: carrier Ratio
F1	Polaxamer 188	1:2
F2	Polaxamer 188	2:1
F3	Polaxamer 188	1:5
F4	Polaxamer 188	5:1
F5	Polaxamer 188	1:1
F6	PEG 6000	1:2
F7	PEG 6000	2:1
F8	PEG 6000	1:5
F9	PEG 6000	5:1
F10	PEG 6000	1:1

V. Pre formulation studies

5.1 Organoleptic evaluation

Piperine evaluated for various organoleptic parameters namely nature, color, and odor, Melting point determination

Melting point of Piperine was determined by the capillary fusion method using melting point apparatus. Fill a capillary tube with the powdered sample, ensuring it occupies 2-3 mm of the tube. The capillary tube was tied of the thermometer and the thermometer was kept in the tube of the apparatus then slowly increased temperature of the apparatus and recorded the temperature at which drug completely melted. The temperature at which the sample starts melting was noted down(Unde & Kurup, 2021).

UV-Vis spectrophotometric study

5.2 Determination of maximum wavelength λmax in Distilled water

Piperine powder (10mg) was accurately weighed and transferred in a 10 ml volumetric flask. then dissolved in 5ml of methanol and diluted to 10 ml with distilled water to obtain the final concentration of 1000µg/ml. Take 1ml from 1000µg/ml and was diluted 100 ml with distilled water to obtain the final concentration of 10µg/ml and scanned for λmax in the range of 200-400 nm to determine the maximum wavelength(Prakash et al., 2008).

5.3 Determination of maximum wavelength λmax in phosphate buffer (pH 6.8)

Piperine powder (10mg) was accurately weighed and transferred in a 10 ml volumetric flask thendissolved in 5ml of methanol and diluted to 10 ml with phosphate buffer (pH 6.8) to obtain the final concentration of 1000µg/ml. Take 1ml from 1000µg/ml and was diluted 100 ml with phosphate buffer (pH6.8) to obtain the final concentration of 10µg/ml and scanned for λmax in the range of 200-400 nm determined the maximum wavelength(Tambe et al., 2021).

5.4 Calibration Curve of drug in phosphate buffer (pH 6.8)

10 mg of the drug weighed with accuracy and transferred to the volumetric flask of 10ml. It was dissolved in 5 ml of methanol and made the volume up to mark with (pH 6.8) to get 1000µg/ml solution and then take 1ml from 1000µg/ml and transferred to the volumetric flask of 100ml and diluted with (pH 6.8) to get 10µg/ml solution and then dilute with (pH 6.8) to get 1,2,3,4,5 µg/ml solution. The absorbance values were plotted against concentrations to get a standard calibration curve of piperine in (pH 6.8). The calibration curves were prepared to determine the concentration of piperine in samples(Machui et al., 2011).

5.5 Determination of maximum wavelength λmax in 0.1N HCL (pH 1.26)

Piperine powder (10mg) was accurately weighed and transferred in a 10 ml volumetric flask thendissolved in 5ml of methanol and diluted to 10 ml with 0.1N HCl (pH 1.26) to obtain the final concentration of 1000µg/ml. Take 1ml from 1000µg/ml and was diluted 100 ml with 0.1N HCl (pH 1.26) to obtain the final concentration of 10µg/ml and scanned for λmax in the range of 200-400 nm to determine the maximum wavelength(Colombo et al., 2017).

5.6 Calibration Curve of drug in 0.1N HCL (pH 1.26)
10 mg of the drug weighed with accuracy and transferred to the volumetric flask of 10ml. It was dissolved in 1 ml of methanol and made the volume up to mark with 0.1N HCl (pH 1.26) to get 1000µg/ml solution and then take 1ml from 1000µg/ml and transferred to the volumetric flask of 100ml and diluted with 0.1N HCl (pH 1.26) to get 10µg/ml solution and then dilute with 0.1N HCl (pH 1.26) to get 1,2,3,4,5 µg/ml solution. The absorbance values were plotted against concentrations to get a standard calibration curve of piperine in 0.1N HCl (pH 1.26). The calibration curves were prepared to determine the concentration of piperine in samples.

5.7 Determination of Solubility
The saturation solubility of piperine was determined in distilled water, phosphate buffer pH 6.8, and 0.1N HCl (pH 1.26). Solubility studied were carried out by taking an excess amount of drug in different media(Douroumis et al., 2007).

5.7.1 Solubility of a drug in phosphate buffer (pH 6.8)
50 mg of the drug weighed with accuracy and transferred to the volumetric flask of 10ml after dissolving the sample with phosphate buffer (pH 6.8) for 5min then filter the sample with Whatman filter paper. Then take 1ml and dilute it with phosphate buffer (pH 6.8) up to 10 ml. Theabsorbance of the resultant solution was measured at 335nm.

5.7.2 Solubility of a drug in 0.1N HCL (pH 1.26)
50 mg of the drug weighed with accuracy and transferred to the volumetric flask of 10ml after dissolving the sample with 0.1N HCl (pH 1.26) for 5min then filter the sample with Whatman filter paper. Then take 1ml and dilute it with 0.1N HCl (pH 1.26) up to 10 ml. The absorbance of the resultant solution was measured at 334nm.

5.8 Screening of carriers
The aqueous solubility of piperine was tested in aqueous solutions of different carriers (PVP K30, Polaxamer188, PEG 6000) to select the ideal carrier. An excess quantity of piperine was added to the aqueous solutions of various carrier in different ratio (0.4, 0.6, 0.8). The vials were closed and shaken for 10 min using vortex shaker and sample were filtered through Whatman filter paper. The filtrate was suitably diluted and analyzed by UV spectrophotometer for the dissolved drug at λmax 336.20.

5.9 Drug- excipients compatibility
Infrared spectrophotometry is a useful analytical technique for determining the chemical interaction of pharmaceuticals and excipients in formulations. The sample was pulverized and intimately mixed with 10 mg of potassium bromide (KBr). The powdered combination was collected in a diffuse reflectance sampler and measured with a Fourier transform infrared spectrophotometer in the 4000-400/cm wavelength range. The drug's IR spectra were compared to those of the physical combination to find potential drug- excipient interaction(Okonogi et al., 1997).

5.10 Saturation Solubility studies
In this method, an excess amount of pure drug piperine (100mg), and solid dispersions (containing an equivalent amount of piperine, 100mg) were taken in volumetric flask of 10 ml diluted with distilled water. The flasks were shaken for 5 min in vortex shaker. The solutions were filtered using Whatman filter paper. The filtrate obtained was suitably diluted with respective buffer and the amount of drug was estimated UV spectrophotometrically at their relevant λ_{max}.

5.11 Drug Content
The solid dispersion containing 10 mg of piperine were accurately weighed. The powder was transferred in 10ml of volumetric flask, and the volume was made up to 10 ml by 0.1 N HCl, for 24 hours. The drug content in the filtrate was measured using a UV-spectrophotometer at 200- 400nm against a blank. The drug content (DC%) of prepared solid dispersion was determined using the formula below-

- The formula to calculate drug content in a solid dispersion is: (Actual amount of drug in the solid dispersion / Theoretical amount of drug in the solid dispersion) * 100%.

5.12 Fourier transform infrared spectroscopy study
The powdered form of piperine solid dispersion was added to potassium bromide, blended homogeneously, filled in the sample holder, and analyzed by FTIR spectrometer for distinctive peaks in the range of 400-4000 cm^{-1}.

5.13 Determination of Percentage yield

The percentage yield of a solid dispersion is used to evaluate the efficiency of the preparation procedure. The weight of solid dispersion, measured by weighing the final product, is the amountof solid dispersion obtained after the preparation process. To calculate the percentage yield, divide the weight of solid dispersion by the weight of drug and weight of polymer then multiply by 100.

5.14 Particle size measurement

Particle size analysis of solid dispersion was performed by microscope method. small amount of the solid dispersion placed on a clean glass slide. Place the sample slide under a microscope, focusing on the particles, and use the appropriate magnification level for clear observation, starting with lower and gradually increasing to higher levels. Measured approximately hundred particles of each formulation to get a representative sample size was counted and examined.

VI. Result and Discussion

6.1 Organoleptic evaluation

The drug was evaluated for various organoleptic parameters namely nature, color, and odor. The obtained results were summarized in Table 2. The result for organoleptic parameter of piperine.

Table 2: Organoleptic Parameters of Piperine

S. No.	Physical Characteristics	Inference
1	Nature	Amorphous powder
2	Color	Off white to Creamish
3	Odor	pungent

6.2 Melting point

The melting point of piperine was determined using capillary fusion method and recorded in Table 3. The observed melting point lies in the range of literature value which indicated that drug was piperine.

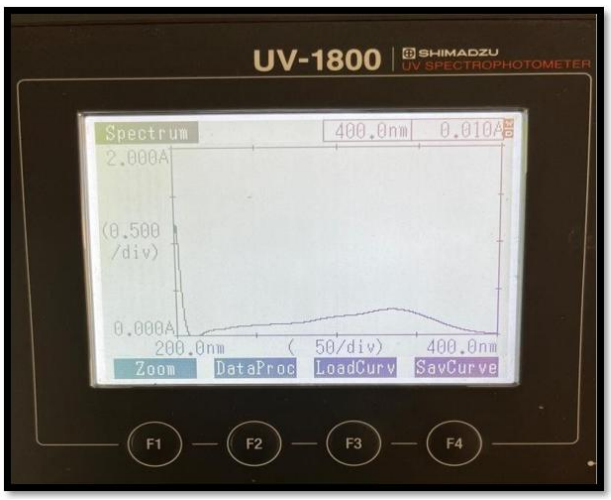
Table 3: Melting Point of Piperine

S.No.	Drug	Observed Average Melting point	Reference Melting point
1	Piperine	129°C	128-130°C

6.3 UV-Vis spectrophotometric characterization

Determination of maximum wavelength (λ_{max}) of Piperine

The maximum wavelength (λ_{max}) of piperine was found at 336.20 nm in distilled water shown in Figure 3.1, at 333.50 nm in the pH 1.2 (0.1N HCl) shown in Figure1.2, and at 335.70 nm in the pH 6.8 shown in Figure 1.3.



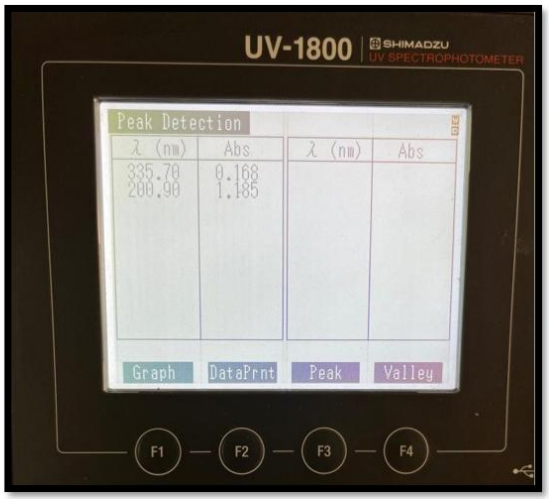


Figure 1.2: Maximum wavelength (λ_{max}) of piperine in the pH 1.2 (0.1N HCl)

Figure 1.3: Maximum wavelength (λ_{max}) of piperine in the pH 6.8

6.4 Calibration curves of Piperine

Calibration curve in pH 1.2 (0.1N HCl)

The reading for the calibration curve of piperine in pH 1.2 (0.1N HCl) have been provided and the calibration curve has been depicted in Figure 1.4

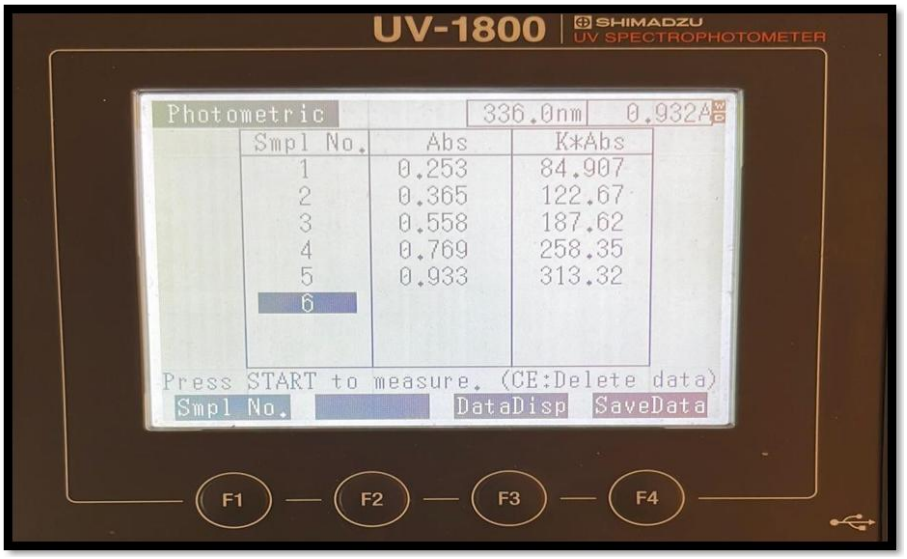


Figure 1.4: Calibration curve of piperine in pH 1.2 (0.1N HCl)

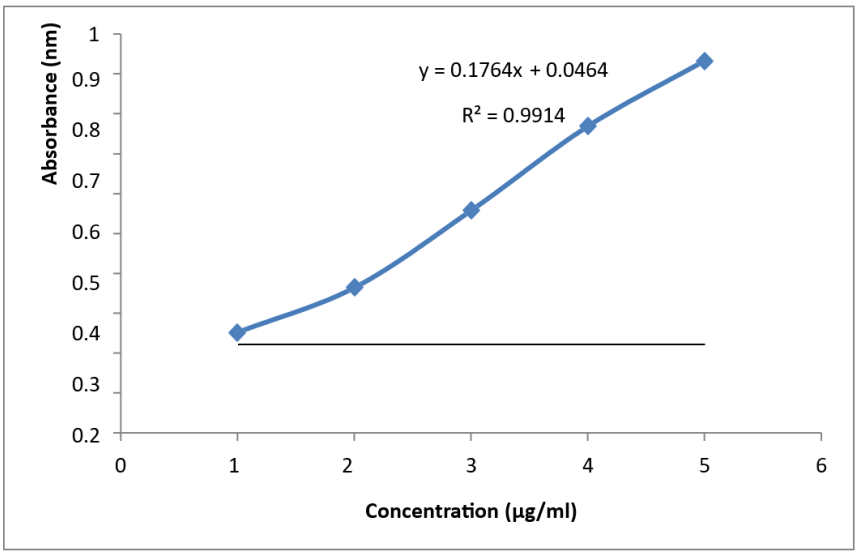


Figure 1.5: Calibration curve of piperine in pH 1.2 (0.1N HCl)

Calibration curve in pH 6.8

The reading for the calibration curve of piperine in pH 6.8 have been provided in Figure 3.6 andthe calibration curve has been depicted in Figure 1.6

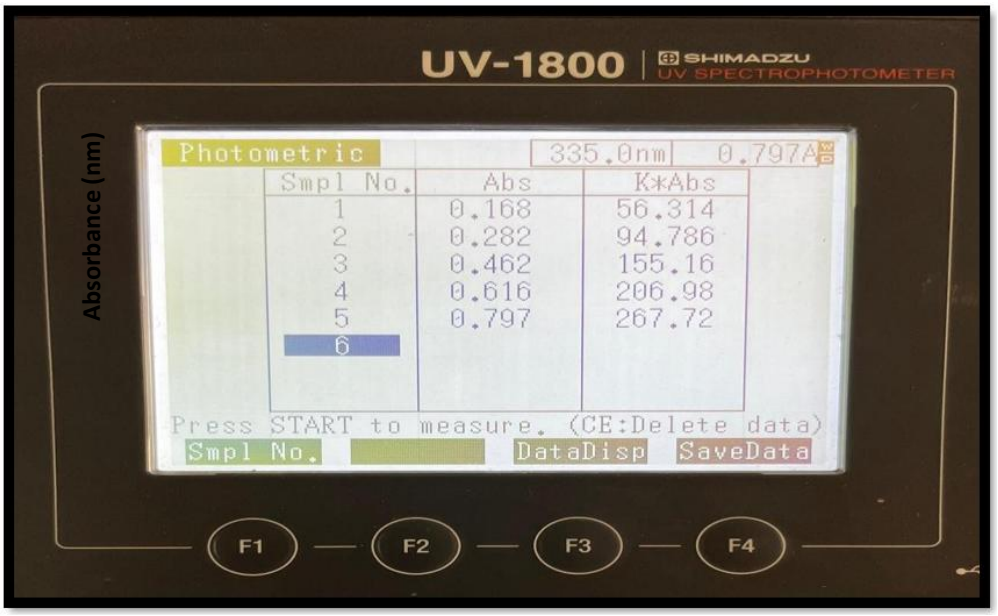


Figure1.6: Calibration curve of piperine in pH 6.8

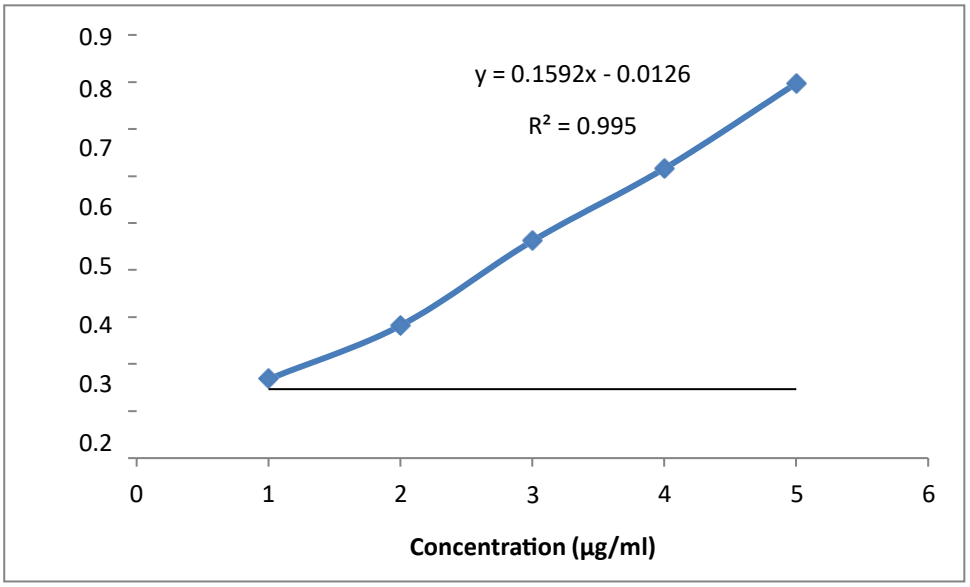


Figure 1.7: Calibration curve of piperine in pH 6.8

Table 4: R2 & Regressed equation obtained for Piperine in various Solvents

Solvent	Concentration(µg/ml)	R^2	Regression equation
In Distilled water	1-5	0.9996	y = 0.1609x - 0.0017
In 0.1N HCl	1-5	0.991	y = 0.1764x + 0.0464
In Phosphate Buffer (Ph6.8)	1-5	0.995	y = 0.1592x - 0.0126

1.5 Determination of solubility

The determination of solubility in different medium, such as water, 0.1N HCl, and phosphatebuffer pH 6.8 is shown in Table 3.4

Table 5: The solubility of Piperine was determined in Different Media

Different Media	Solubility (µg/ml)
Distilled water	29.85
0.1N HCl	190.27
Phosphate buffer pH 6.8	42.73

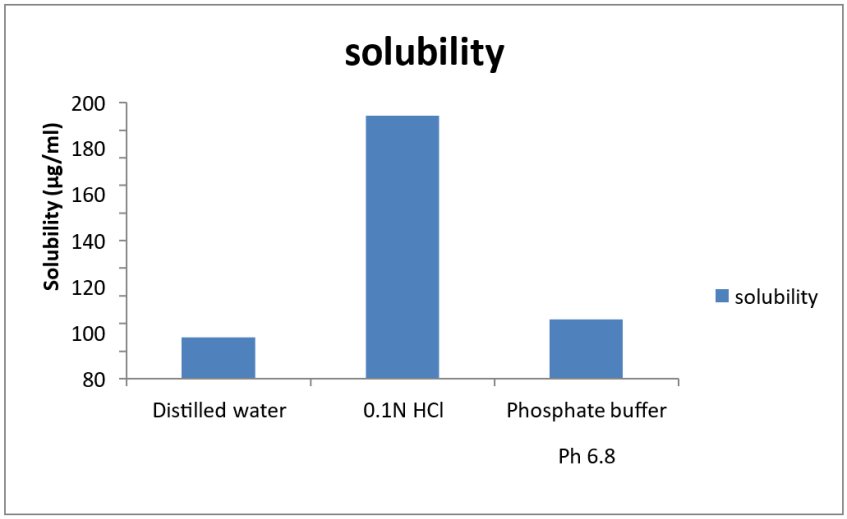


Figure 1.8: Solubility of piperine in different media

6.6 Screening of carriers

The aqueous solubility of piperine was tested in aqueous solutions of different carriers (PVPK30, Polaxamer 188, PEG 6000) to select the ideal carrier shown in Table 6

Table 6: Solubility Profile in Different Concentration of Polymer

Media (Distilled water)	Solubility(µg/ml)
PVP K30	
0.4	238.84
0.6	241.95
0.8	269.47
Polaxamer 188	
0.4	286.69
0.6	423.43
0.8	558.91
PEG 6000	
0.4	252.33
0.6	341.82
0.8	425.91

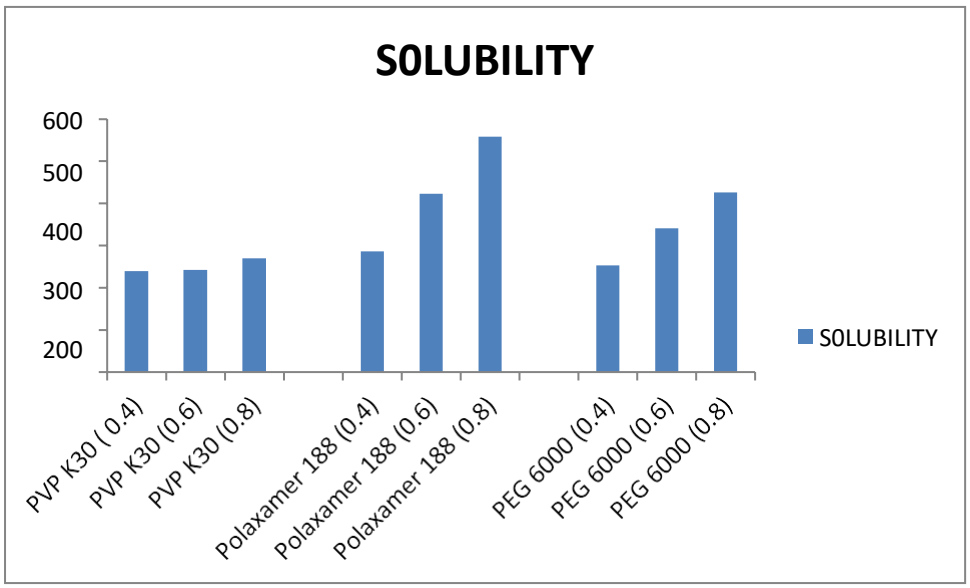


Figure 1.9: Solubility of piperine in different concentration of polymer

Fourier Transform Infrared (FTIR) Spectroscopy

6.7 Drug interaction

FTIR analysis was performed to analyze the physiochemical interaction of drug, physical mixture of drug and polymers. The result of the FTIR spectrum of the piperine in Fig1. The main peak of FTIR spectrum of the pure piperine were at 2938 cm^{-1} (Aromatic C-H stretching); 2916 cm^{-1} (Aliphatic C-H stretching); 1676 cm^{-1} (-CO-N stretching); 1250 cm^{-1} (-O-CH_2-O symmetric stretching); 1132 cm^{-1} (-O-CH_2-O asymmetric stretching); 1632cm^{1}(symmetric stretching and conjugated diene); 1610cm^{-1} (asymmetric stretching and conjugated diene); 1028cm^{-1} (-C-H bending). The values of FTIR spectrum matched with the data given in the literature as given in the Table 7 From the FTIR analysis it was confirmed that the drug was pure and the physical mixture (i.e drug and polymers) are compatible to each other and there wasno interaction between drug polymers. The peaks were also observed indicating the stable nature of drug and polymers.

Table 7: FTIR Spectra of Drug & Physical Mixture

FunctionalGroup	Reference Wavenumber (cm^{-1})	Observed Wavenumber (cm^{-1}) (piperine)	Observed (Drug+polaxamer188)	Observed (Drug+ PEG6000)
Aromatic C-Hstretching	3008 cm^{-1}	2938 cm^{-1}	2939 cm^{-1}	2939 cm^{-1}
Aliphatic C-Hstretching	2920 cm^{-1}	2916 cm^{-1}	2882 cm^{-1}	2939 cm^{-1}
-CO-N stretching	1699 cm^{-1}	1676 cm^{-1}	1669 cm^{-1}	1632 cm^{-1}
-O-CH_2-O asymmetric	1253 cm^{-1}	1250 cm^{-1}	1248 cm^{-1}	1250 cm^{-1}
stretching				
-O-CH_2-O asymmetricstretching	1134 cm^{-1}	1132 cm^{-1}	1194 cm^{-1}	1132 cm^{-1}
symmetric stretching and conjugated diene	1633 cm^{-1}	1632 cm^{-1}	1633 cm^{-1}	1632 cm^{-1}
asymmetric stretching and conjugateddiene	1612 cm^{-1}	1610 cm^{-1}	1582 cm^{-1}	1582 cm^{-1}
-C-H bending	1018 cm^{-1}	1028 cm^{-1}	1030 cm^{-1}	1028 cm^{-1}

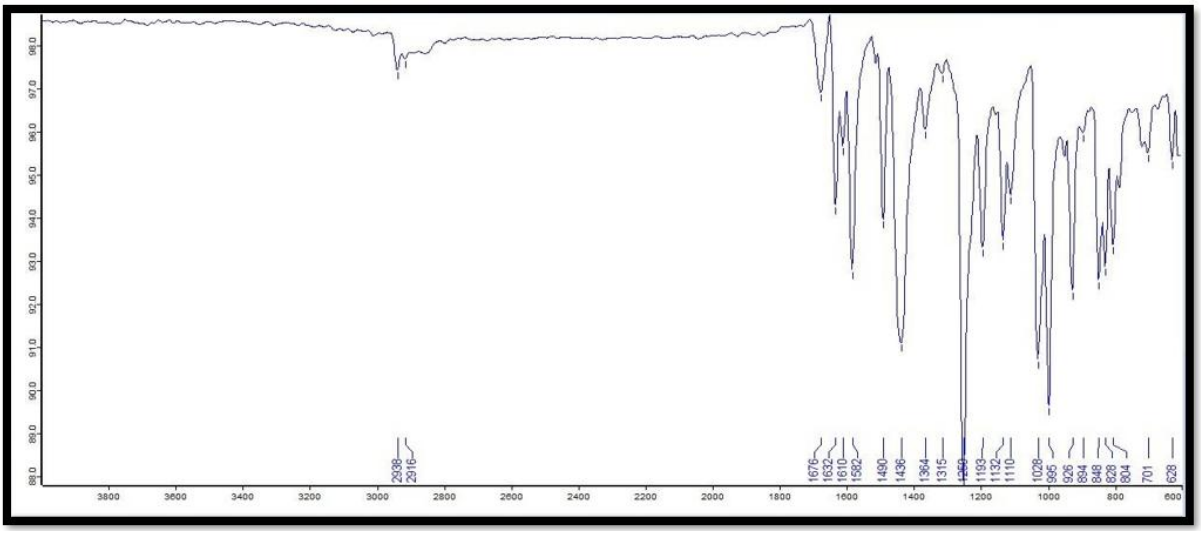


Figure 1.10: FTIR spectrum of drug (piperine)

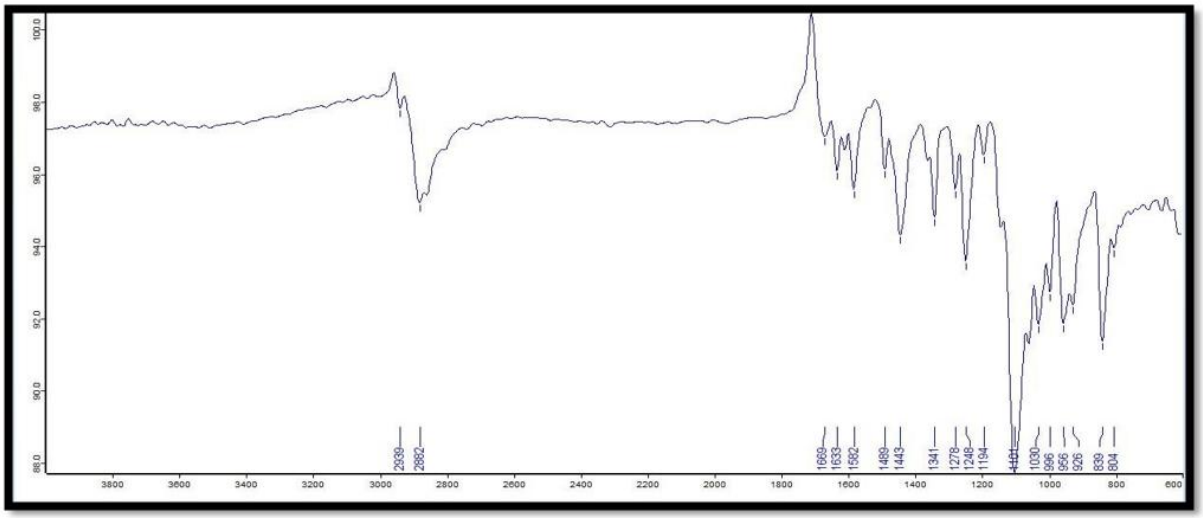


Figure 1.11: FTIR spectrum of physical mixture (piperine and polaxamer188)

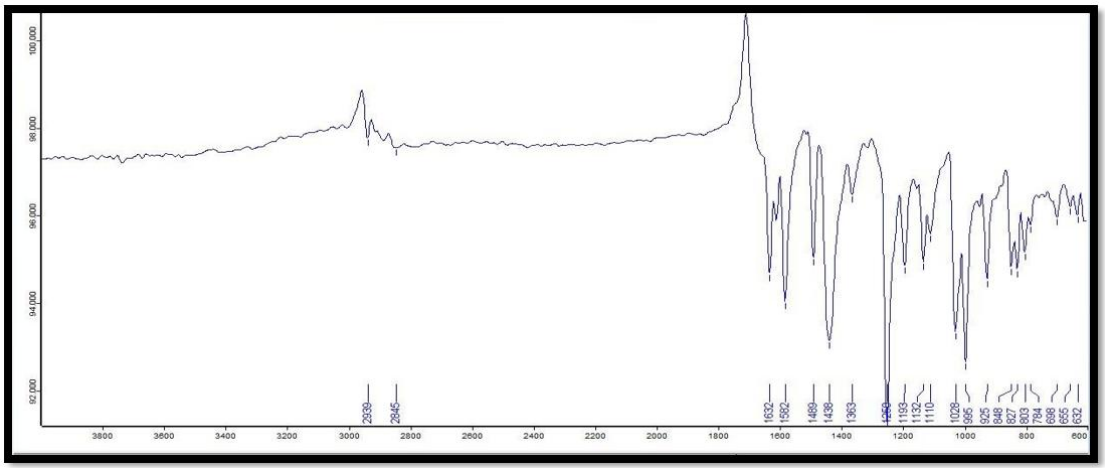


Figure 1.12: FTIR spectrum of physical mixture of piperine and PEG 600

6.8 Polymer Interaction

The main peak of FTIR spectrum of the poloxamer 188 was at a wavenumber of 1100 cm^{-1} (C– O–C symmetric stretching vibration); 1145 cm^{-1}(C–O–C asymmetric stretching vibration); 956 cm^{-1} (CH2rocking/CO stretching) and 840cm^{-1}(–CH2–CO– rocking/stretching); 2880 cm^{-1} (symmetric stretching of –CH2and wagging); 1341 cm^{-}

[1] (twisting of –CH2). The values of FTIR spectrum matched with the data given in the literature as given in the Table3.7 From the FTIR analysis it was confirmed that the polymer was pure.

Table 8: FTIR Spectra of Polaxamer 188

Functional Group	Reference Wavenumber(cm^{-1})	Observed Wavenumber (cm^{-1}) of polaxamer 188
C–O–C symmetric stretchingvibration	1100 cm^{-1}	1100 cm^{-1}
C–O–C asymmetric stretchingvibration	1150 cm^{-1}	1145 cm^{-1}
CH2rocking/CO stretching	960 cm^{-1}	956 cm^{-1}
–CH2–CO– rocking/stretching	845 cm^{-1}	840 cm^{-1}
symmetric stretching of –CH2and wagging	2883 cm^{-1}	2880 cm^{-1}
twisting of –CH2	1345 cm^{-1}	1341 cm^{-1}

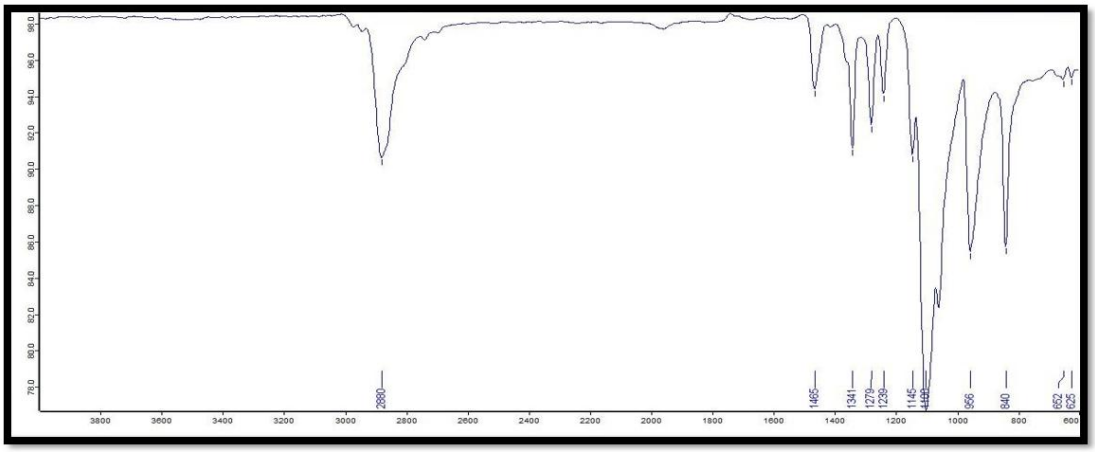


Figure 1.13: FTIR Spectrum of poloxamer 188

6.9 Preparation of solid dispersion

Solid dispersion of piperine was prepared by solvent evaporation method using polymer polaxamer 188 and PEG 6000 as a carrier in various ratios. Dissolve a Drug (piperine) and a polymer (polaxamer 188) in a solvent (methanol) to form a homogeneous solution. Then put the homogeneous solution on a hot plate and stir with a glass rod so that solvent is removed by evaporation. The solid residue obtained after evaporation of solvent is collected. Then the mass was pulverized and sieved through mesh no.80 This residue contains the drug dispersed within the carrier matrix. The solid dispersion is then dried at room temperature for 24 hours (Figure3.13), 10 formulation were prepared.

Figure 1.14: Piperine solid dispersion

Characterization

6.10 Saturation Solubility

The saturation solubility of pure drug and solid dispersion in Table3.8. The solubility of piperine was determined to be 29.85 µg/mL and the highest solubility determined for piperine solid dispersion is 4470.64 µg/mL,of formulation F1 and the lowest solubility determined is 1866.37 µg/mL of formulation F10. however, the solubility of prepared solid dispersion was improved compared to pure drug powder (Table3.8).

Table 9: Solubility of Pure Drug & Solid Dispersion

Pure Drug	**Solubility (µg/ml)**
Piperine	29.85
Formulation code	**Solubility(µg/ml)**
F1	4470.64
F2	1878.80
F3	2463.02
F4	2139.83
F5	1592.91
F6	2376.00
F7	2150:40
F8	2394.65
F9	2326.28
F10	1866.37

6.11 Drug content

The amount of drug content in formulations was analyzed at 333.50 nm. The drug content was found in the range 58.2-87.7 % indicating the acceptability of solvent evaporation method for preparation of solid dispersion. Drug content was found to be uniform among all solid dispersion. Drug content of solid dispersion indicated uniform drug distribution in all the prepared formulations. The percentage of drug content of the prepared solid dispersion is shown in Table3.9.

Table 10: Determination of Drug Content

Solid Dispersion	**Drug content (%)**
F1	87.7
F2	64.5
F3	82.2
F4	70
F5	61.3
F6	85.9
F7	78.1
F8	74
F9	65.8
F10	58.2

Fourier transform infrared spectroscopy study

The FTIR spectra of the optimized formulation (F1) was found 2880cm^{-1}, 1631cm^{-1}, 1279cm^{-1}, 1145 cm^{-1}, 1609 cm^{-1} and 2920cm^{-1} due to C-H stretching, 1699cm^{-1} due to -CO-N stretching, 1253^{-1} due to -O-CH_2-O stretching, 1633cm-1 due to symmetric stretching and conjugated diene respectively. The same peaks were also observed indicating the stable nature of drug and formulation as shown in Figure3.14. The obtained spectra of polaxamer 188, 1100cm^{-1} due to C- O-C symmetric stretching vibration, 1145cm^{-1} due to C-O-C asymmetric stretching vibration, 957cm^{-1} due to CH_2 rocking/ CO stretching, 840cm^{-1} due to –CH_2-CO- rocking/stretching, 1341cm-1 twisting of –CH_2 groups.

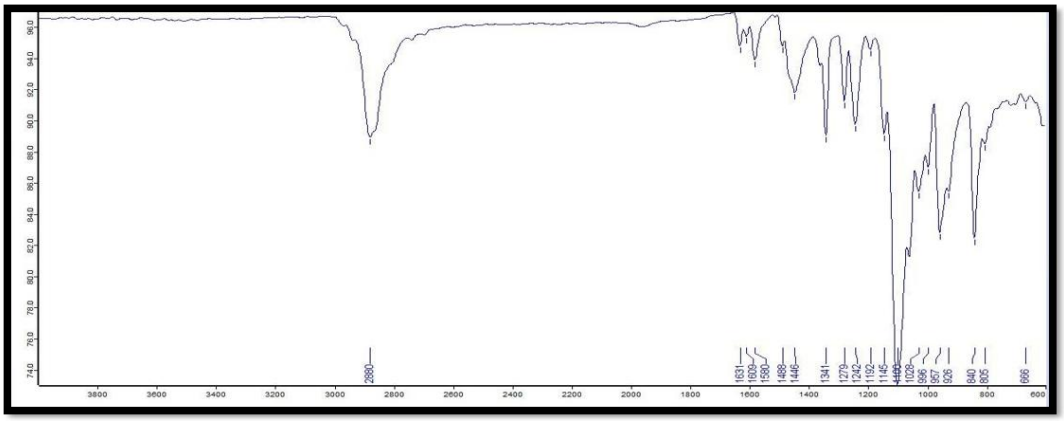


Figure 1.15: FTIR spectra of formulation F1

Percentage yield

The percentage yield of the solid dispersion is shown in table3.10. The percentage yield wasfound 17.6-98.24%. The highest percentage yield of formulation code F1 was obtained.

Table 11: Determination of Percentage Yield

Formulation code	Percentage yield (%)
F1	98.24
F2	92
F3	82.12
F4	75
F5	70.6
F6	89.42
F7	81.61
F8	92.02
F9	90.71
F10	87

6.12 *In-Vitro* Drug Release Study

In Vitro drug release studies for solid dispersion were conducted for 2 hours using 0.1N HCl (pH 1.2) as a release medium by using USP type-I dissolution apparatus. After 2 hours, the cumulative drug release of all 10 formulations shows that formulation F3 had the lowest cumulative drug release and F1 had the highest cumulative drug release was shown in Table 3.11.

Table 12: In Vitro Drug Release Studies of Optimized Formulations

Time (min)	Puredrug	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
5	1.06	0.04	0.08	0.08	0.16	0.45	0.48	0.52	0.12	0.25	0.46
10	1.92	1.48	2.57	7.98	8.56	2.02	4.61	5.86	6.88	1.99	3.83
20	3.3	9.69	4.03	18.12	9.22	7.31	8.97	7.04	8.84	5.87	5.86
30	5.78	30.94	15.09	27.61	10.49	9.73	12.84	17.24	16.83	7.83	8.17
45	19.14	35.95	27.16	35.87	19.9	23.99	27.87	20.31	45.67	17.65	22.94
60	25.67	76.86	48.64	38.22	57.74	63.57	56	66.02	68.89	43.42	37.28

The formulation F1 was considered as optimized one as it is neither too slow nor too fast in releasing the drug content (Table3.12). Further the comparison of drug release from pure drug as shown in Figure 3.15.

Table 13: *In vitro* drug release studies of optimized formulation was compared with pure drug (piperine)

Cumulative drug release (%)		
Time (min)	**Optimized formulation(F1)**	**Pure Drug (Piperine)**
5	0.04	1.06
10	1.48	1.92
20	9.69	3.3
30	30.94	5.78
45	35.95	19.14
60	76.86	25.67

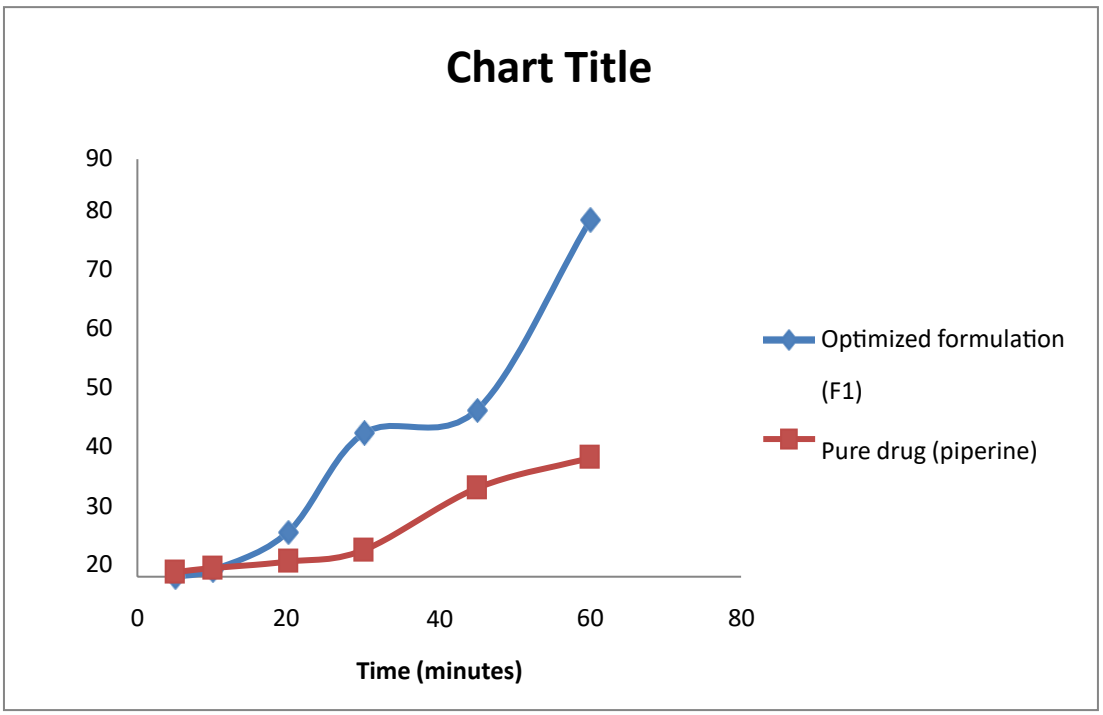
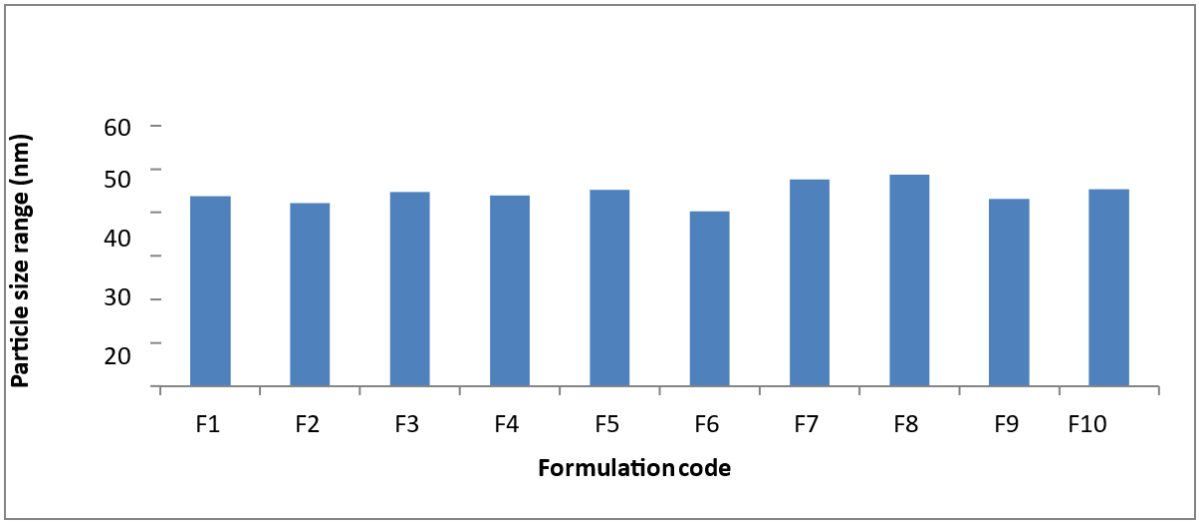


Figure 1.16: *In vitro* drug release studies of optimized (F1) was compared with piperine

6.13 Particle Size Analysis

Particles size analysis was carried out for all the solid dispersion formulations as it plays an important role in drug release. Smaller the size more will be the release. The particle size for all solid dispersion formulations was found to be in range of 43.52 - 48.65µm (Figure 3.17).



1.17: Particle size measurement

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