Original Article

ENHANCEMENT OF SOLUBILITY AND DISSOLUTION CHARACTERISTICS OF ETORICOXIB BY SOLID DISPERSION TECHNIQUE USING DIFFERENT GRADE OF PEG CARRIER USING

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Abstract

In this research work based on solubility enhancement method useful of use less water soluble drug of etoricoxib pure drug and use with water soluble carrier different PEG3350,PEG4000,PEG6000,PEG8000,PEG 20000 grade and drug and water soluble carrier ratio 1:1,1:2,1:4 and 1:6 and urea in different ratio1:1,1:2,1:4 and 1:6 and use physical fusion method and evolution of solid dispersion and I was observed drug solubility increases it useful in development of novel formulation use though solid dispersion method drugs that are poorly water soluble, which accelerates dissolving and can significantly improve bioavailability. Amorphous drug forms typically have substantially higher enthalpy than their crystalline counterparts. By transforming the medicine into an amorphous molecular dispersion using a hydrophilic carrier matrix, crystallization can be prevented. During the formulation development process, one of the most difficult aspects of drug delivery is enhancing the bioavailability of the weak aqueous drug. The pace and quantity of the drugs that leaves the dose form and enters the systemic circulation before it reaches the site of action to have the desired effect is known as bioavailability.

Key word: solid dispersion, etoricoxib, bioavailability, PEG, solubility enhancement etc.

INTRODUCTION:

During the formulation development process, one of the most difficult aspects of drug delivery is enhancing the oral bioavailability of the low aqueous medication. The bioavailability of a medicine refers to how quickly and how much of it leaves the dosage form and circulates throughout the body before it has the desired effect at the site of action. The traditional definition of a poorly water-soluble substance is one that dissolves in less than 1 part per 10,000 parts of water, which will cause a bioavailability issue and reduce the therapeutic effectiveness of a new medicine. Increasing the drug's water solubility can help with the bioavailability issue. Co-solvents, emulsified systems, solubilization, particle size reduction, amorphous drug forms, molecular complexes, techniques to increase a drug's water solubility. They are frequently used to speed up increasing the rate of drug

release the oral bioavailability of such medications. However, it has been discovered that these strategies have certain practical limits. Sekiguchi and Obi proposed a new technology in 1961 that could solve the majority of the issues highlighted above. The name "Solid Dispersion" was later given to this technology. A microcrystalline eutectic drug combination with a hydrophilic carrier form in solid dispersions. Drug that are poorly soluble in water increase dissolution and can significantly improve bioavailability amorphous drug forms typically have substantially higher enthalpy than their crystalline counterparts. By transforming the drug into an amorphous molecular dispersion using a hydrophilic carrier matrix, crystallization can be prevented.[1-3, 26]

The science of solid dispersion technology involves dispersing one or more active ingredients in an inert matrix during the solid stage in order to increase dissolution rate, achieve sustained drug release, change solid state properties, enhance drug release from ointment and suppository bases, and improve solubility[4-5]

Martial and method: drug Etoricoxib used as a slandered drug gift sample obtained from Ziess pharmaceutical industry Ltd baddi (H.P) and PEG ,urea PG lab Indore

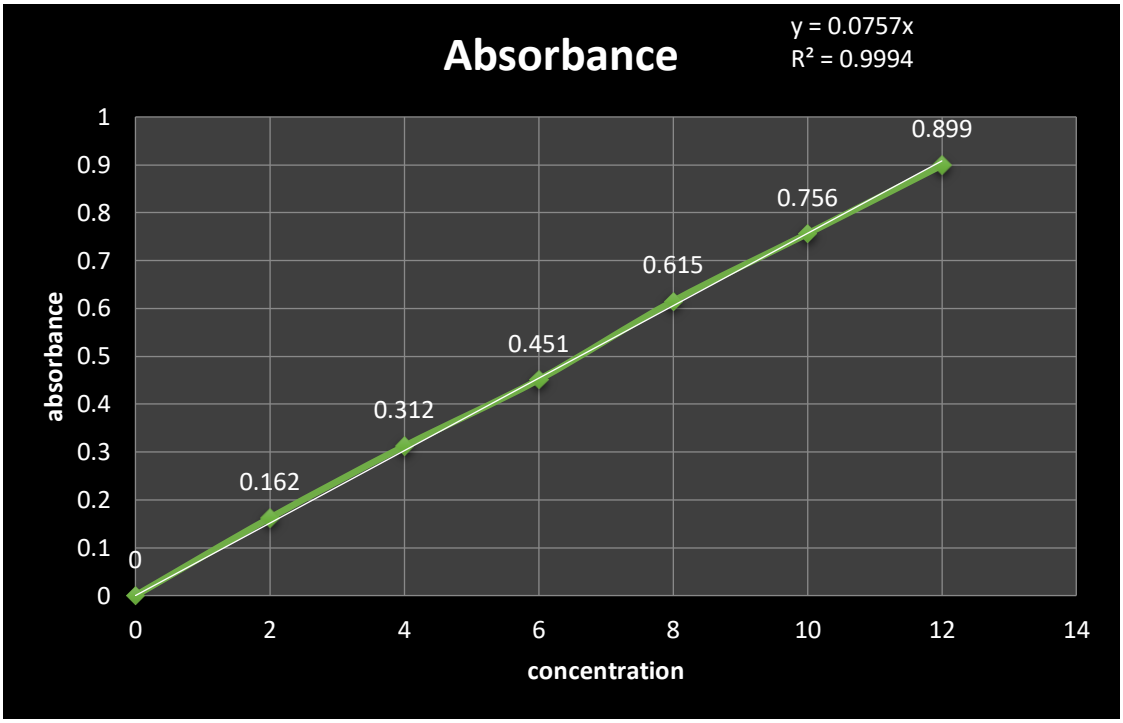
PREPARATION OF CALIBRATION CURVE OF ETORICOXIB METHANOL[6-7]

1. First taken 100 mg of etoricoxib was weighed properly and transfer to a 100 ml flask. and add 70 ml of 0.1 N HCl and dissolve the drug etoricoxib and the volume was make up to 100 ml with methanol solvent .stock solution 1 mg /ml solution was prepared
2. Then make suitable dilution concentration 2 to 12 µg/ml with same solvent system.
3. And examine absorbance uv/visible spectroscopy method at 233 nm

Table no 1. Calibration curve, concentration v/s absorbance data 233 nm

Concentration in µg/ml	Absorbance
0	0.00
2	0.162
4	0.312
6	0.451
8	0.615
10	0.756
12	0.899

Fig 1. Calibration curve of etoricoxib



FOURIER TRANSFORMS INFRA-RED SPECTRAL ANALYSIS OF DRUG SAMPLE[8]:

The compatibility of drug excipients was examined using FT-IR. Utilizing Perkin-Elmer spectrum, FT-IR was performed. All of the samples were correctly combined with KBr in a 1:3 ratio before being formed into pellets. The pellets underwent analysis. Using an FT-IR Spectrophotometer, each KBr disc was scanned throughout a wave number range of 4000-400 cm-1. The distinctive peaks in the FTIR spectra of etoricoxib (alone) were observed at 1515.0 cm-1 (C-N stretching vibration), 1445.5 cm-1, 1356.3 cm-1, 1156.6 cm-1, and 1082.3 cm-1 (S=0 stretching vibrations), and 845.4 cm-1, 776.8 cm-1, and 657.0 cm-1 (C-Cl stretching vibration), respectively.

Fig. 2 FTIR spectrum of Etoricoxib reference drug

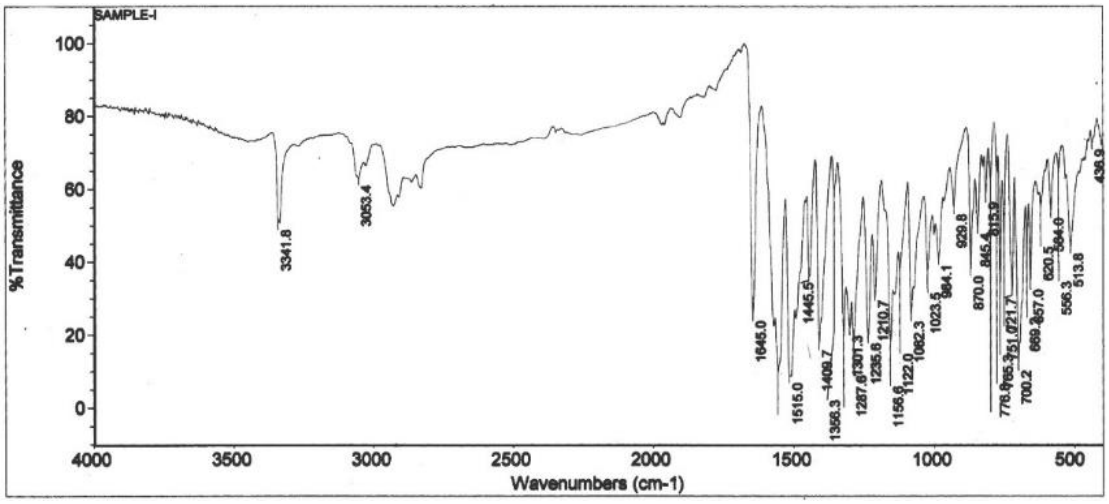
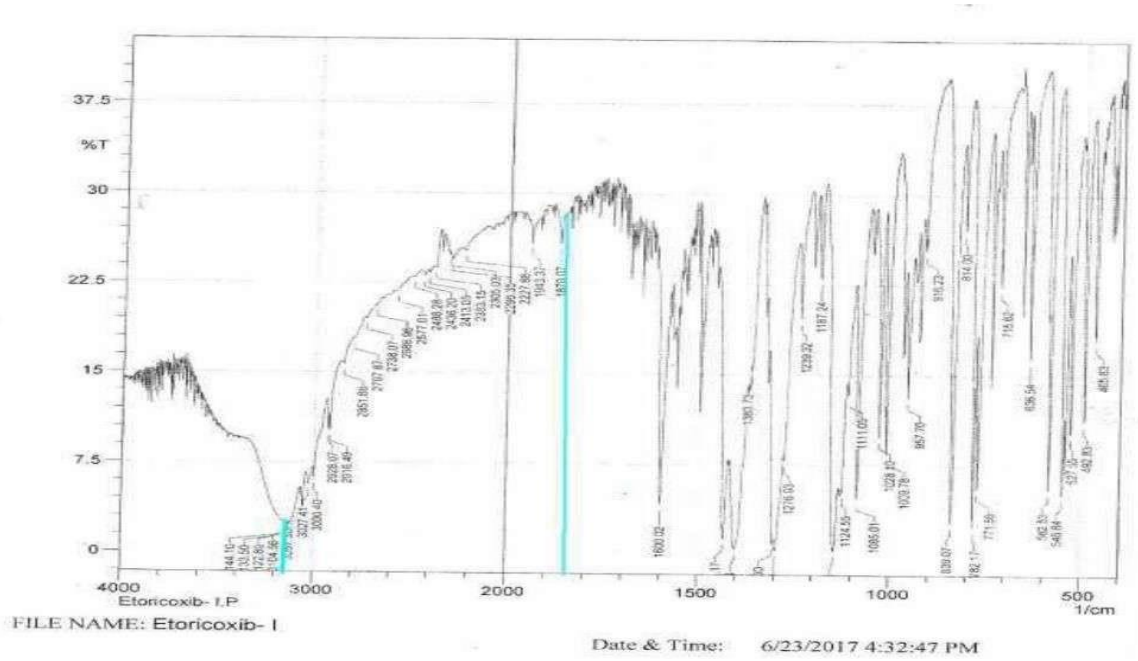


Fig. 3 FTIR spectrum of Etoricoxib pure drug sample



DETERMINATION MELTING POINT DRUG AND CARRIER[8-11]:

1. A one-sided closed capillary filled with drug was used to determine the melting point using the capillary fusion method.

2. And placed in the melting point apparatus while the temperature was raised, it was noted at what point the solid drug changed into liquid and that was the melting point.

Table 2 melting point study of drug and drug carrier

S.NO	NAME OF MARTIAL	REFERENCE M.P in ºC	OBSERVED M.P in ºC
1.	Etoricoxib drug	134-138	137
2.	PEG -3350	56± 2	57
	PEG -4000	53-58	56
	PEG -6000	58-63	59
	PEG-8000	55-60	58
	PEG-20000	57-60	59
3.	UREA	131-134	131

Three reading mean value

SOLID DISPERSION METHOD OF PREPARATION [6,7,12-13:]

1. Fusion method or melting method applied

1. Use for formulation of solid dispersion Sekiguchi was used first time melting or fusion method, also known as melting or Fusing is the process of physically combining a drug with a water-soluble carrier and heating it to melt it.
2. And then melted mixture was vigorously stirred while swiftly solidifying in an ice bath. Crushed and make fine ,
3. And sieve no 60 are used to sieved the final powder bulk.
4. And then cooled by air or water flowing on the other side of the plate. In addition, by fast cooling the melt from a high temperature, it is frequently possible to achieve a super-saturation of a solute or drug carrier in a system.

Advantage of method:

1. The simplicity and economy of the direct melting method are its key benefits.
2. Additionally, melting under a vacuum or a blanket of an inert gas, such as nitrogen, may be used to stop drug or carrier oxidation.

Table: 3 formulation table of solid dispersion of drug with water soluble carrier different grade of PEG carrier using.

S.NO	DRUG	RATIO	FORMULATION CODE
1.	ECB with PEG 3350	1:1	SDsEPEG3-1
		1:2	SDsEPEG3-2
		1:4	SDsEPEG3-3
		1:6	SDsEPEG3-4
2.	PEG4000	1:1	SDsEPEG4-1
		1:2	SDsEPEG4-2
		1:4	SDsEPEG4-3
		1:6	SDsEPEG4-4
3.	PEG 6000	1:1	SDsEPEG6-1
		1:2	SDsEPEG6-2
		1:4	SDsEPEG6-3
		1:6	SDsEPEG6-4
4.	PEG 8000	1:1	SDsEPEG8-1
		1:2	SDsEPEG8-2
		1:4	SDsEPEG8-3
		1:6	SDsEPEG8-4
5.	PEG 20000	1:1	SDsEPEG 20-1
		1:2	SDsEPEG 20-2

		1:4	SDsEPEG 20-3
		1:6	SDsEPEG 20-4
6.	Urea	1:1	SDs EU-1
		1:2	SDs EU-2
		1:4	SDs EU-3
		1:6	SDs EU-4

SOLUBILITY STUDIES[8, 25]:

1. In order to conduct studies on drug solubility in various aqueous media, excessive amounts of the drug were dissolved in 5 ml of the appropriate medium, and the solutions were then placed in screw-capped tubes, which were then shaken on a mechanical shaker at room temperature for a period of 12 hours. After that, the solutions were left to equilibrate for 24 hours.
2. Subsequently, the solutions were placed in centrifuge tubes and spun at a speed of about 1500 RPM for 5 minutes. The solutions were then filtered using a Whatman grade 41 filter.
3. The filtrate was appropriately diluted with the appropriate medium to yield one ml. On a double beam UV/Visible spectrophotometer, the solutions' absorbances were measured at 233 nm.

Table 4 Solubility study of different organic solvent: all solvent choose in analytical grade.

S.NO	SOLVENT SYSTEM	STANDERED	OBSERVED
1.	Methanol	Freely soluble	Freely soluble
2.	Ethanol	Freely soluble	Freely soluble
3.	Formaldehyde	soluble	Soluble
4.	Acetone	soluble	Soluble
5.	N haxen solvent	Spingly soluble	Spingly soluble

Table 5 solubility study of solid dispersion of drug with water soluble carrier different grade of PEG carrier

S.NO	NAME OF MATERILA	RATIO	FORMULATION CODE	SOLUBILITY WATER µg/ ml	SOLUBILITY IN O.1N HCl µg/ ml
1	ETORICOXIB DRUG	------	-------	0.312±0.01	0.328±0.01
S.NO	drug	RATIO	FORMULATION CODE	SOLUBILITY WATER	SOLUBILITY IN O.1N HCl

1.	ECB with PEG 3350	1:1	SDsEPEG3-1	0.95±0.01	0.0068±0.02
		1:2	SDsEPEG3-2	1.52±0.02	0.0098±0.01
		1:4	SDsEPEG3-3	1.68±0.01	1.38±0.01
		1:6	SDsEPEG3-4	1.60±0.01	1.850±0.01
2.	PEG4000	1:1	SDsEPEG4-1	0.54±±0.01	0.68±0.01
		1:2	SDsEPEG4-2	0.98±0.01	0.88±0.01
		1:4	SDsEPEG4-3	1.52±0.01	1.98±0.01
		1:6	SDsEPEG4-4	1.51±0.01	1.96±0.01
3.	PEG 6000	1:1	SDsEPEG6-1	0.67±0.01	0.58±0.01
		1:2	SDsEPEG6-2	0.84±0.01	0.66±0.01
		1:4	SDsEPEG6-3	0.95±0.01	0.73±0.01
		1:6	SDsEPEG6-4	1.21±0.01	0.81±0.01
4.	PEG 8000	1:1	SDsEPEG8-1	0.48±0.01	0.74±0.01
		1:2	SDsEPEG8-2	0.95±0.06	0.99±0.01
		1:4	SDsEPEG8-3	1.52±0.01	1.62±0.01
		1:6	SDsEPEG8-4	1.87±0.01	1.82±0.07
5.	PEG 20000	1:1	SDsEPEG 20-1	0.98±0.05	0.78±0.06
		1:2	SDsEPEG 20-2	1.52±0.01	0.91±0.01
		1:4	SDsEPEG 20-3	1.95±0.01	1.47±0.01
		1:6	SDsEPEG 20-4	2.25±0.08	1.85±0.03
6.	Urea	1:1	SDs EU-1	0.25±0.01	0.33±0.02
		1:2	SDs EU-2	0.32±0.02	0.35±0.01
		1:4	SDs EU-3	0.40±0.01	0.51±0.01
		1:6	SDs EU-4	0.45±0.01	0.62±0.01

Three reading mean value

DISSOLUTION PROFILE STUDY OF SOLID DISPERSION [9-11, 23]

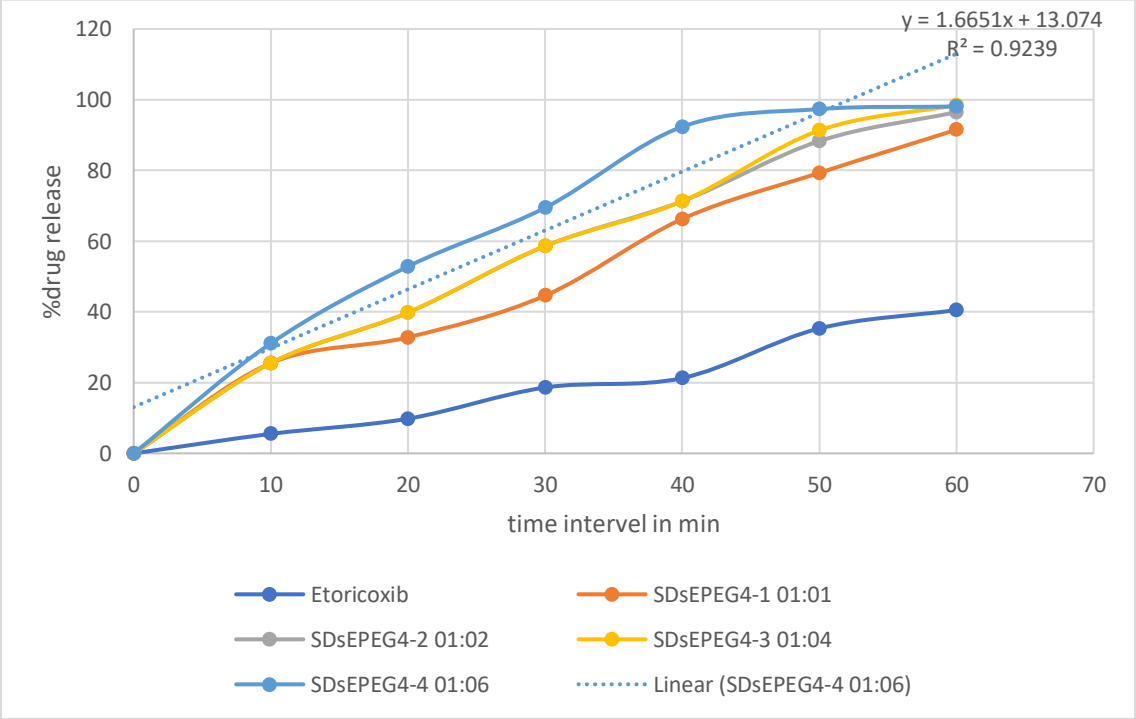
USP type I test aperture Dissolution procedure using an electro lab and a dissolution aperture by trying to place 100 mg drug equilibrium in, which contained 900 ml of the 0.1 N HCl solution dissolution medium, dissolution was started and the condition of the shank was maintained. Sample was taken pre-determined intervals, take 5 ml of each dissolution vessel's sample solution and filter it and dilution was examined in Shimadzu UV-Spectrophotometer absorbance at 233nm and % drug released.

Table 6: Dissolution data of Etoricoxib from PEG solid dispersions Drug: PEG 4000

Time Interval In Min	Etoricoxib	SDsEPEG 4-1 1:1	SDsEPEG 4-2 1:2	SDsEPEG 4-3 1: 4	SDsEPEG 4-4 1:6
0	0	0	0	0	0
10	05.51	25.51	25.51	25.51	31.11
20	09.81	32.81	39.81	39.81	52.84
30	18.62	44.6	58.62	58.62	69.46
40	21.28	66.28	71.28	71.28	92.36
50	35.32	79.32	88.32	91.32	97.35
60	40.51	91.51	96.51	98.51	98.08

Three reading mean value

Fig.4 in vitro dissolution of drug with PEG 4000



DRUG CONTENT ESTIMATION[12-16, 24]:

100 mg of solid dispersion in 100 ml of methanol should be dissolved. The solution was filtered, appropriately

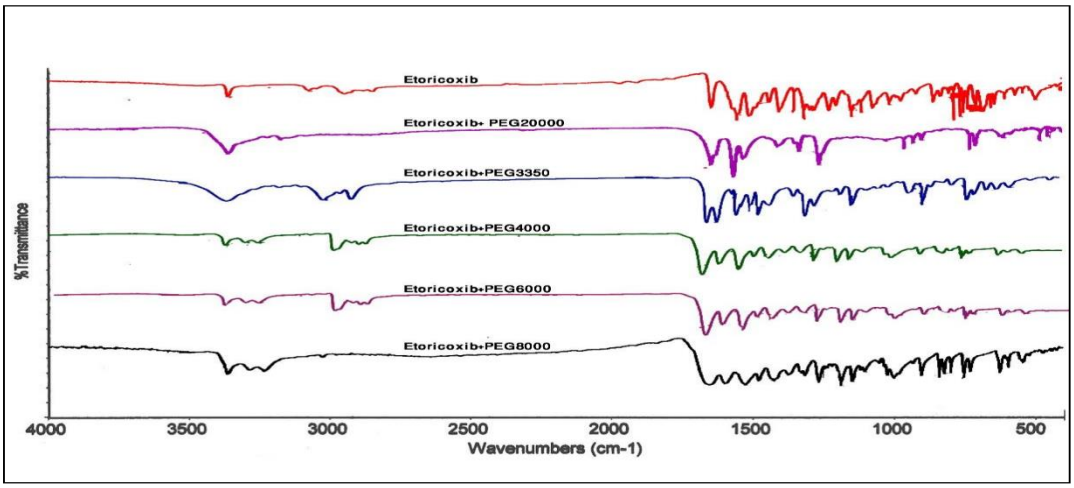
diluted, and subjected to UV spectrophotometer analysis at 233 nm. Following is how the actual drug content was determined

The actual amount of etoricoxib present in a given amount of solid dispersions multiplied by 100 gives the percent drug content.

DRUG COMPATIBILITY STUDY[17-21, 22]:

Drug compatibility study done by UV spectroscopy and it comfortable with drug and water-soluble carrier PEG and FTIR.

Fig. 5 FTIR spectrum of Etoricoxib drug with PEG water soluble carrier.



RESULT AND DISCUSSION:

This research work based on solubility enhancement method useful of use poorly water soluble drug and use with water soluble carrier different PEG3350,PEG4000,PEG6000,PEG8000,PEG 20000 grade and drug AND solubilizer ratio 1:1 ,1:2,1:4& 1:6 and urea in different ratio1:1,1:2,,1:4 & 1:6 and use physical fusion method and evolution of solid dispersion and I was observed drug solubility increases it useful in development of novel formulation use though solid dispersion method drugs that are poorly water soluble, which accelerates dissolving and can significantly improve bioavailability and solubility enhance maximum PEG 4000 solubility enhanced RSD 101.6% this method is very useful in development of novel formulation.

CONCLUSION:

Present research work is based on solid dispersion by fusion method use PEG water soluble carrier, different grade of solubility enhancer water soluble carrier PEG 4000 GRADE in drug: carrier ration 1:4 SDsEPEG4-3 in more effective for use among of PEG grade water soluble carrier and they have solubility enhance of drug (RSD =101.6%) this is very useful in novel formulation.

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