Formulation and Optimization of PVP K15-Based Solid Dispersion-Integrated Fast Dissolving Films of Domperidone

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***Abstract*—Objective The objective of this study was to enhance the solubility and dissolution rate of poorly water-soluble Domperidone by preparing solid dispersions using PVP K15 and PEG 4000 carriers.**

Methods

Preformulation studies including melting point determination, solubility analysis, UV spectrophotometry, calibration curve construction, and FTIR spectroscopy were performed. Solid dispersions were prepared using solvent evaporation and melting methods at different drug-to-carrier ratios and evaluated for solubility, drug content, dissolution, and compatibility.

Results

The drug exhibited a melting point of 243°C and λmax at 286 nm. Solubility studies showed that PVP-based solid dispersions provided greater solubility enhancement than PEG-based formulations. Drug content ranged from 85.6% to 95%, indicating uniform drug distribution. Among all formulations, SD3 (Domperidone:PVP K15, 1:5) showed the highest solubility and cumulative drug release (≈93.6% at 60 min). FTIR studies confirmed the absence of drug–polymer incompatibility and successful solid dispersion formation. Pasted text.txt

Conclusion

The solid dispersion technique effectively improved the solubility and dissolution behavior of Domperidone. PVP K15 was found to be a superior carrier compared to PEG 4000, and SD3 was identified as the optimized formulation for further development.

***Index Terms*—Domperidone, Solid Dispersion, PVP K15, PEG 4000, Solubility Enhancement, Dissolution Rate, FTIR, Drug Release, Solvent Evaporation Method, Oral Bioavailability**.

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I. INTRODUCTION

Oral drug delivery remains the most preferred route due to its simplicity, patient compliance, and cost-effectiveness. However, many therapeutic agents, including Domperidone, encounter challenges such as poor solubility and low dissolution rates, which significantly affect their bioavailability. Domperidone, a dopamine D2 receptor antagonist widely used for treating nausea and vomiting, has low aqueous solubility, limiting its therapeutic efficacy when administered orally.[1,2]

Fast-dissolving oral films (FDOFs) have emerged as a promising drug delivery platform, especially for pediatric and geriatric patients who experience difficulty swallowing conventional tablets or capsules. These films disintegrate rapidly upon contact with saliva, eliminating the need for water and providing a convenient, patient-friendly dosage form. By integrating solid dispersion technology, the solubility and dissolution rate of poorly water-soluble drugs like Domperidone can be significantly enhanced.[2,3]

Solid dispersion involves dispersing the drug in a hydrophilic polymer matrix, converting it into an amorphous state, thereby improving wettability and dissolution. This technique is particularly effective for BCS Class II drugs, where solubility is the rate-limiting step for absorption. Incorporating solid dispersion into fast-dissolving films ensures improved bioavailability while maintaining ease of administration.[4,5]

Salient Features of Fast Dissolving Oral Film:

- Ease of administration for patients who are mentally ill-disabled & uncooperative.
- Requires no water; have quick disintegration and dissolution of the dosage form.
- Leaves minimal or no residue in the mouth after administration.
- No risk of choking.
- Provide advantages of liquid medication in the form of solid preparation.
- Amenable and adaptable to existing processing and packaging machinery

Patients who suffer from vomiting cannot be administered the conventional oral formulations and need fast acting formulation. In general, emesis is preceded with nausea and in such condition it is difficult to administer drug with a glass of water; hence it is beneficial to administer drugs as mouth dissolving films with good mouth feel.[6,7]

This delivery method bypasses hepatic first-pass metabolism, potentially leading to improved bioavailability and faster therapeutic effects compared to traditional oral dosage forms. The route offers several advantages over oral route[8]. The oral cavity has a large surface area, leading to rapid dissolution and disintegration of oral dosage forms. There is no risk of choking. Oral fast-dissolving films (OFDFs) are solid unit dosage forms, providing accurate dosing and great precision. Pregastric absorption improves the bioavailability of the drug, requiring fewer doses and enhancing patient compliance.[9]

This study focuses on the formulation and optimization of Domperidone-loaded fast-dissolving films integrating solid dispersion technology. The integration of solid dispersion with FDOFs offers a novel approach to improving drug delivery and patient outcomes for water-insoluble therapeutic agents.

Pre-formulation studies [10-16]

Preformulation studies were carried out to evaluate the physicochemical properties of Domperidone prior to formulation development. These studies included melting point determination to confirm the identity and purity of the drug, solubility analysis in various solvents to assess its solubility profile, determination of the maximum absorption wavelength (λmax) for analytical estimation, and compatibility studies using Fourier Transform Infrared (FTIR) spectroscopy to investigate potential interactions between Domperidone and the selected excipients. The results of these studies provided essential information for the successful development of the formulation.

The melting point of Domperidone was determined using the capillary tube method to confirm its identity and purity. The solubility of Domperidone in different solvents was evaluated by the shake flask method to assess its solubility characteristics and support formulation development.

Drug-Excipient compatibility studies using FTIR spectroscopy

FTIR analysis was carried out using a Shimadzu FTIR spectrophotometer. After initializing the instrument and cleaning the sample holder with acetone, the software was opened and the scan range set to 650–4500 cm^{-1}. A background spectrum was collected, then the sample was placed on the holder and scanned. The obtained spectrum was labeled, saved in ASCII format, and the instrument was turned off after analysis.

Determination of λmax

Domperidone 10 µg/ml concentration was prepared by using mixture of phosphate buffer 6.8 and methanol. The solution was scanned from 200-400 nm by UV Spectrometer and a spectrum was observed for absorption maxima.

II. METHOD OF PREPARATION OF SOLID DISPERSION

Preparation by Solvent Evaporation Method (F1–F3)

The required quantity of domperidone (0.1 g) and the specified amount of PVP K15 (0.1 g, 0.3 g, or 0.5 g) were accurately weighed according to the formulation design. PVP K15 was dissolved in 10 mL of methanol to obtain a clear polymer solution. Domperidone was dissolved separately in 5 mL of dichloromethane. The drug solution was then added slowly to the polymer solution under continuous magnetic stirring to obtain a homogeneous solution.

The resulting solution was stirred for approximately 30–60 minutes to ensure complete mixing of the drug and polymer. The organic solvents were then removed by evaporation at room temperature or under reduced pressure until a dry solid mass was obtained. The dried mass was further kept in a hot air oven or vacuum desiccator at 40°C for 24 hours to remove any residual solvents. The dried solid dispersion was pulverized

gently using a mortar and pestle and passed through sieve No. 80 to obtain a uniform powder. The prepared solid dispersion was stored in an airtight container in a desiccator until further evaluation.[17]

Table No: 01: Formulation Design of Domperidone loaded Solid Dispersion

Polymer &solventsC	F1	F2	F3
Drug(gm)	0.1	0.1	0.1
PVPk15(gm)	0.1	0.3	0.5
PEG4000(gm)	-	-	-
Methanol(ml)	10	10	10
Dichloromethane	5	5	5
Method	SE	SE	SE

SE= Solvent evaporation method

Formulation code	Run	Factor A	Factor B	Factor C
		A (Crosspovidone)	B (sodium starch glycolate)	C (Poly ethylene glycolate-400)
F1	1	-1	-1	-1
F2	2	+1	-1	-1
F3	3	-1	+1	-1
F4	4	_+1	+1	-1
F5	5	-1	-1	+1
F6	6	+1	-1	+1
F7	7	-1	+1	+1
F8	8	+1	+1	+1

2^3 Factorial Design:

Factor	Low Level (-1)	High Level (+1)
A = Crospovidone	40 mg	120 mg
B = Sodium starch glycolate	40 mg	120 mg
C = PEG 400	0.6 mL	1.2 mL

Preparation of solid Dispersion incorporated Fast Dissolving oral film:

Solvent Casting Method

The required quantity of film-forming polymer is dissolved in distilled water and allowed to hydrate completely.Plasticizer and other excipients are added with continuous stirring to obtain a uniform solution. The prepared solid dispersion containing the drug is then dispersed uniformly into the polymeric solution.The mixture is stirred to remove air bubbles and poured onto a petriplate or casting surface. The solution is dried at room temperature or in a hot air oven until a thin film is formed. The dried film is carefully peeled off and cut into required sizes for evaluation[18]

Evaluation Of Solid Dispersion:

The prepared solid dispersions were evaluated for various physicochemical parameters, including solubility, drug content, and in vitro dissolution studies, to assess their performance and potential for enhancing the solubility and dissolution rate of Domperidone.

Determination of Drug Content

An accurately weighed quantity of prepared solid dispersion equivalent to 10 mg of Domperidone was

transferred into a 100 mL volumetric flask containing phosphate buffer pH 6.8. The volume was made up to 100 mL and shaken thoroughly to obtain a clear solution. The solution was filtered through Whatman filter paper. From the filtrate, 1 mL was withdrawn and diluted to 10 mL with phosphate buffer pH 6.8. The diluted solution was analyzed using a UV spectrophotometer at 284 nm to determine drug content.[19]

In vitro Dissolution Studies

Accurately weigh solid dispersion equivalent to 10 mg of solid dispersion. Fill 500ml of phosphate buffer pH 6.8 into dissolution vessel and maintain temperature at 37±0.5∘C and 50 rpm for 1hr.Add the weighed solid dispersion sample into the Dissolution medium.Withdraw 5ml sample at specific time intervals such as 5,10,15,20,30,45 and 60min.After each withdrawl ,replace with equal volume of fresh dissolution medium maintained at some temperature.Filter the collected sample using whtatsman filter paper to remove undissolved particle.Measure absorbance using uv spectrometer at 286nm.Calculate cumulative % drug release using calibration curve.[20]

III. RESULT AND DISCUSSION

Preformulation studies of Domperidone were performed to assess its physicochemical properties and suitability for formulation development. The melting point of the pure drug was found to be **243°C**, which is close to the reported value, confirming its purity and identity. The narrow melting range indicated the absence of significant impurities. Solubility studies showed poor solubility in water and phosphate buffer (pH 6.8) but better solubility in methanol and ethanol. These results indicate the hydrophobic nature of Domperidone and its potential for low dissolution and bioavailability. The solubility study of Solid Dispersion showed that drug solubility increases with increasing carrier ratio in both PVP and PEG formulations. PVP solid dispersions exhibited higher solubility compared to PEG at all ratios. The PVP 1:5 formulation showed maximum solubility, indicating better enhancement efficiency. PEG formulations showed only slight improvement, remaining mostly in slightly to sparingly soluble range. Overall, PVP is a more effective carrier for improving drug solubility than PEG .

The UV spectrum of Domperidone exhibited a maximum absorbance (λmax) at 286 nm, which was selected for quantitative analysis. The calibration curve showed a linear relationship between concentration and absorbance with y=0.025x $R^2 = 0.999$, confirming adherence to the Beer–Lambert law.

FTIR analysis revealed characteristic peaks corresponding to aromatic C–H, aliphatic C–H, amide carbonyl, C–N, and C–O functional groups. The observed peaks matched reported values and confirmed the chemical identity of the drug and its purity. The FTIR spectrum of the solid dispersion (PVP K15, 1:5) shows characteristic peaks confirming the presence of functional groups such as C=O (1650 cm^{-1}), C–N (1284 cm^{-1}), and C=C (1422 cm^{-1}). A broad peak in the higher region indicates O–H stretching, suggesting hydrogen bonding. The spectrum retains all major drug peaks, indicating no chemical incompatibility with the polymer. Slight peak broadening and reduced intensity confirm interaction between drug and carrier. Overall, the results indicate successful formation of a stable solid dispersion with improved molecular interaction.

The drug content study indicates that all formulations show acceptable drug content ranging from 85.6% to 95%. Among them, F3 exhibited the highest drug content (~95%), suggesting efficient drug incorporation. PVP formulations (F1–F3) showed slightly better uniformity compared to PEG formulations (F4–F6). The values confirm minimal drug loss and good mixing during formulation. Overall, all batches meet acceptable limits, indicating uniform drug distribution and formulation reliability.

The comparative drug release profile shows a steady increase in % cumulative drug release for all formulations over time. Among them, F3 exhibited the highest drug release (≈93.6% at 60 min), indicating superior dissolution performance. F2 and F6 also showed good release, while F4 exhibited comparatively lower release throughout the study.

Table no 1: Melting Point of the Drug

Trials	Melting Point	Average
1	244◦C	243.3◦C
2	242◦C	
3	244◦C	

Table no :02 Solubility Analysis of Domperidone:

Solvents	Solubility(gm/ml) gm	Volume of Solvents ml/gm (ml)	Solubility Crireria
Water	0.0852	11737	Practically insoluble
Methanol	99.9500	10005	Freely soluble
Ethanol	43.5013	22980	Soluble
Chloroform	54.5200	18348	soluble
Phosphate buffer 6.8	0.40123	2492	Very slightly soluble

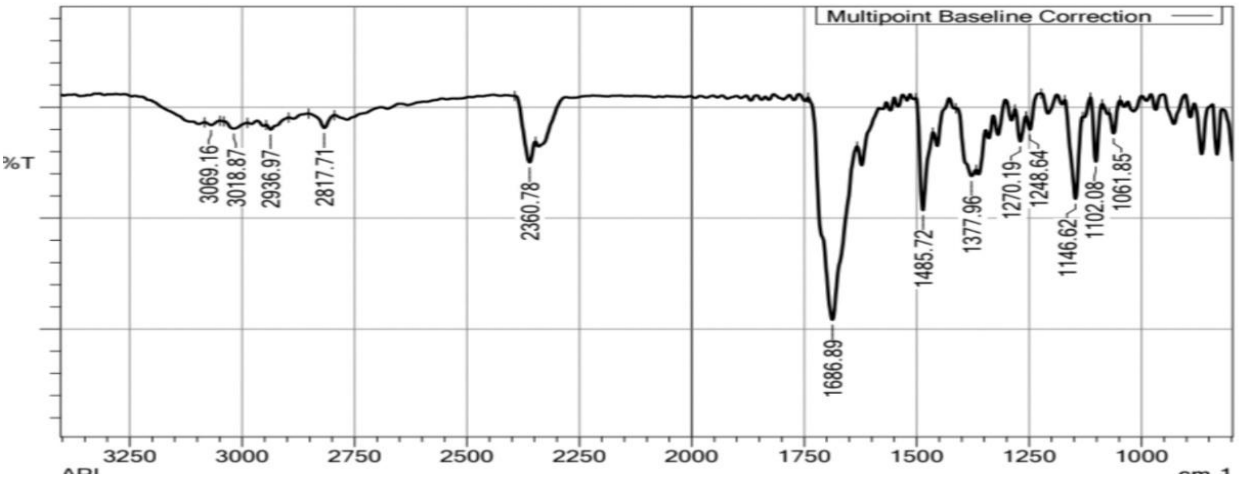

Fig01:FTIR Spectra of Domperidone

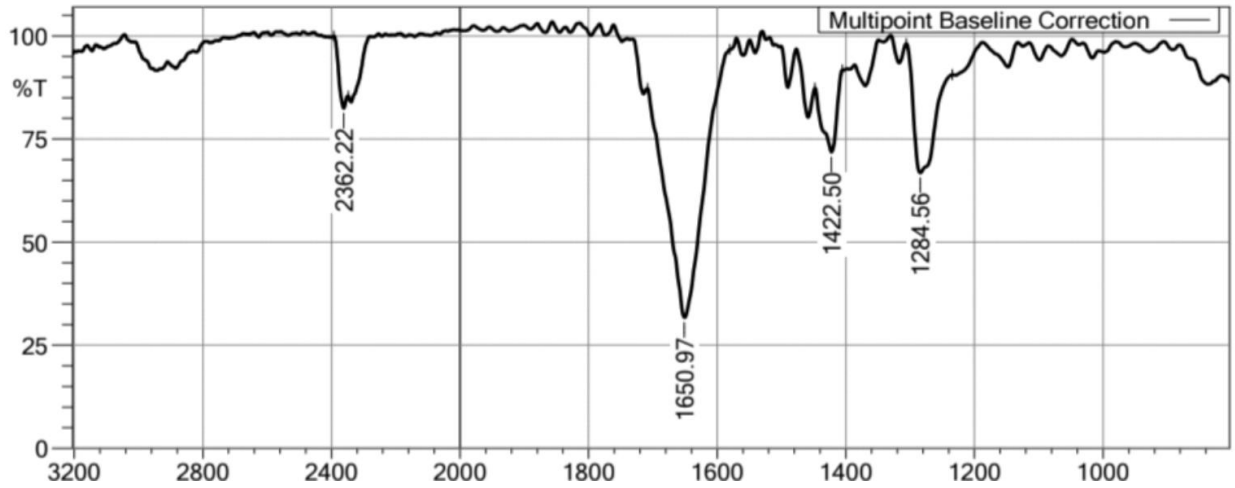

Fig02:FTIR Spectra of PVP K15: Drug(1:5)

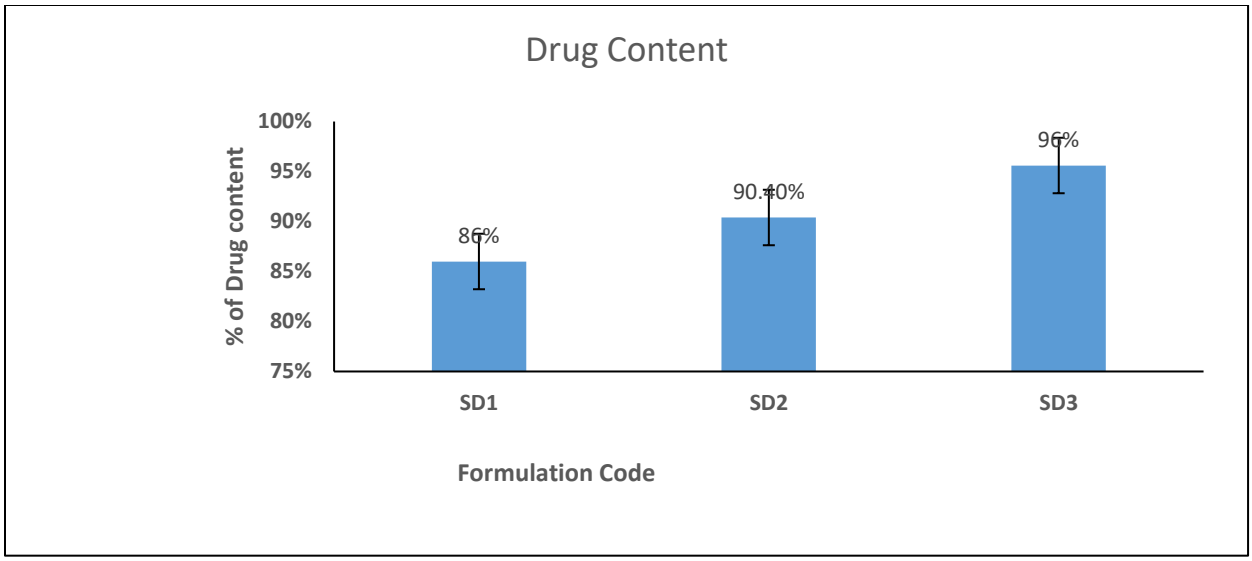

Fig 03: % of Drug Content of Solid Dispersion

Table no : 04 Solubility Analysis Of PVP K15 Solid Dispersion

PVP k15 Ratio	Solvents	Solubility(mg/ml)	Volume of Solvent in ml/1gm(ml)	Solubility Criteria
1:1	Phospahte buffer 6.8	8.413	118863	Slightly soluble
1:3		12.502	79991	Sparingly soluble
1:5		39.413	25315	soluble

Table no : 05 Solubility Analysis Of PVP K15 Solid Dispersion

PEG 4000 Ratio	Solvents	Solubility(mg/ml)	Volume of Solvnet in ml/1gm	Solubility Criteria
1:1	Phosphate buffer 6.8	7.241	13888	Slightly soluble
1:3		10.514	95237	Slightly soluble
1:5		11.503	86938	Sparingly Soluble

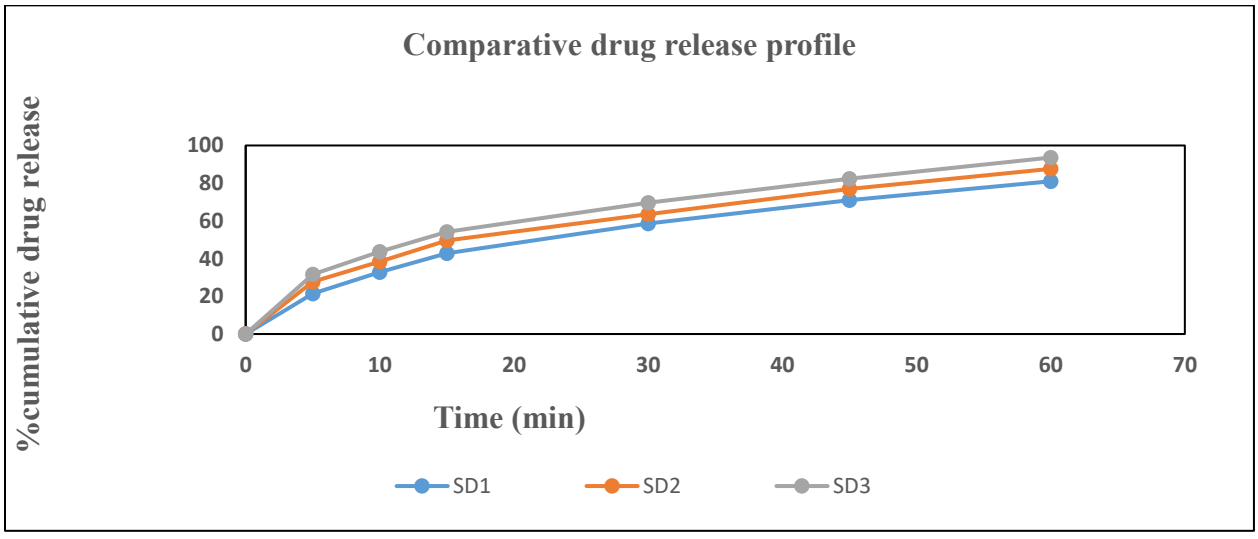

Fig 04: %cumulative Drug release of the Solid Dispersion of Formulation SD1-SD3

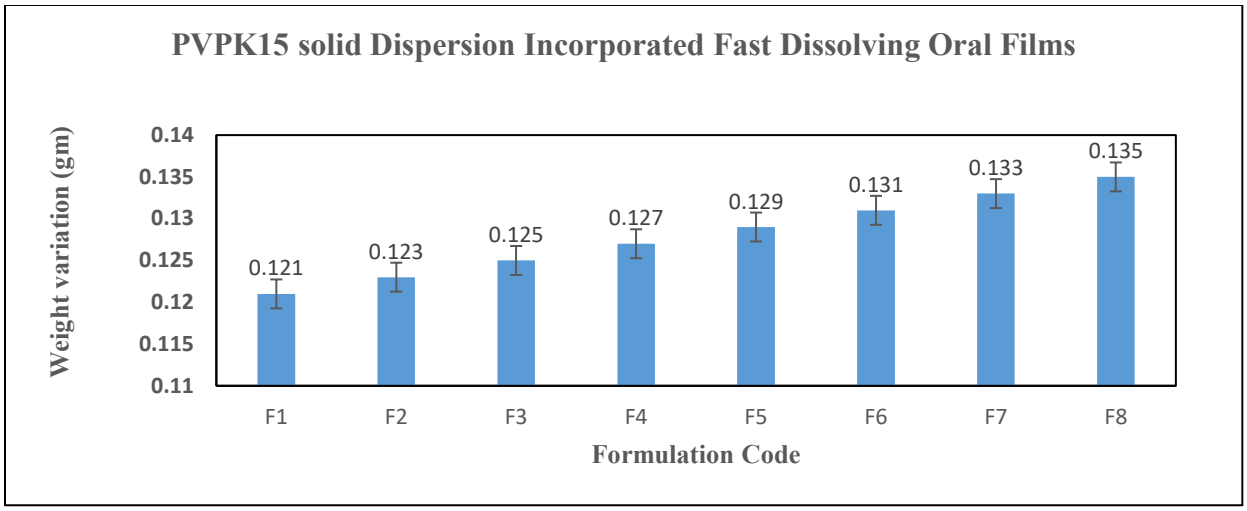

Fig 05:Weight variation PVPK15 solid Dispersion Incorporated Fast Dissolving Oral Films

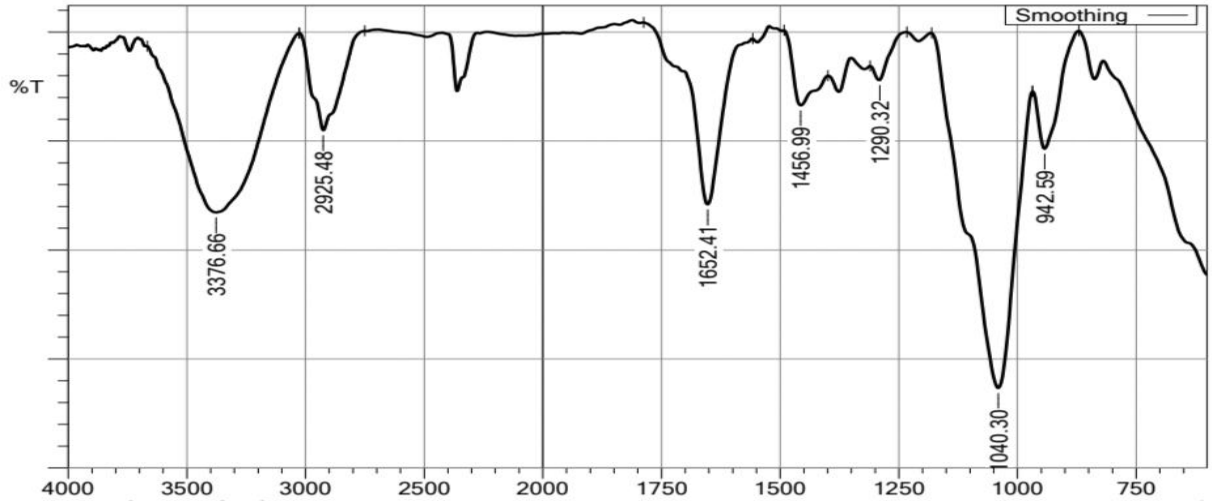

Fig 06: FTIR Spectra of PVP K15 Solid Dispersion Incorporated Fast Dissolving Oral Films

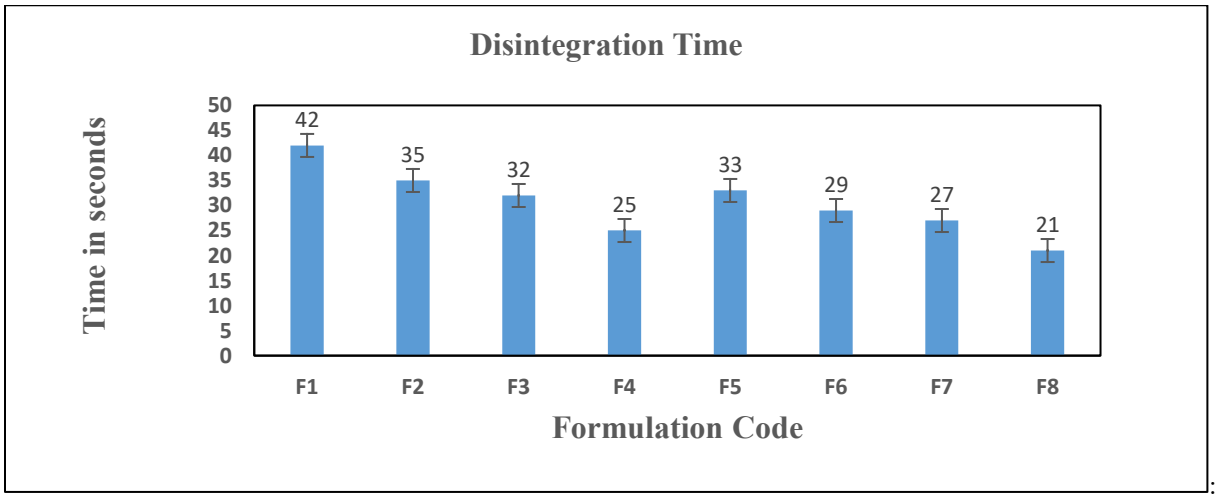

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Fig 07:Disintegration time for Solid Dispersion Incorporated Fast Dissolving Oral Films

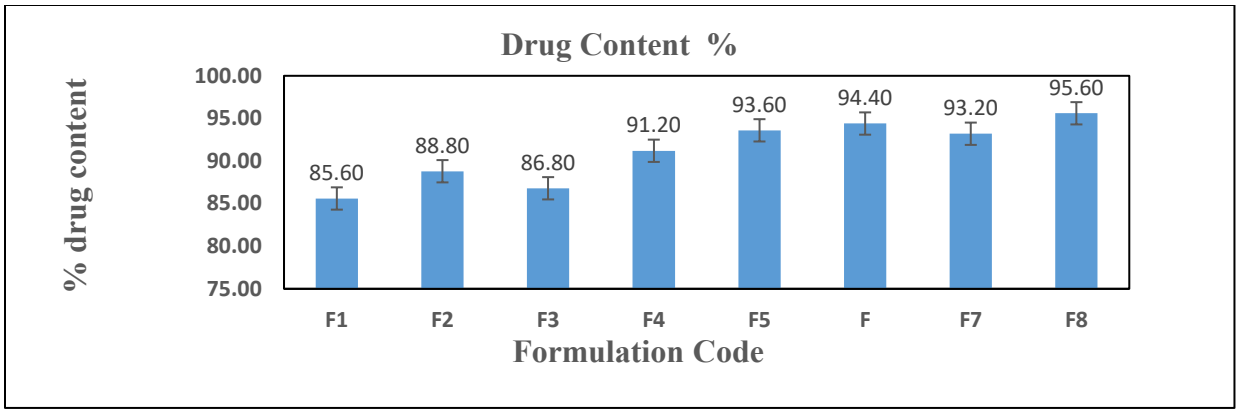

Fig 07:% of Drug content for Solid Dispersion Incorporated Fast Dissolving Oral Films

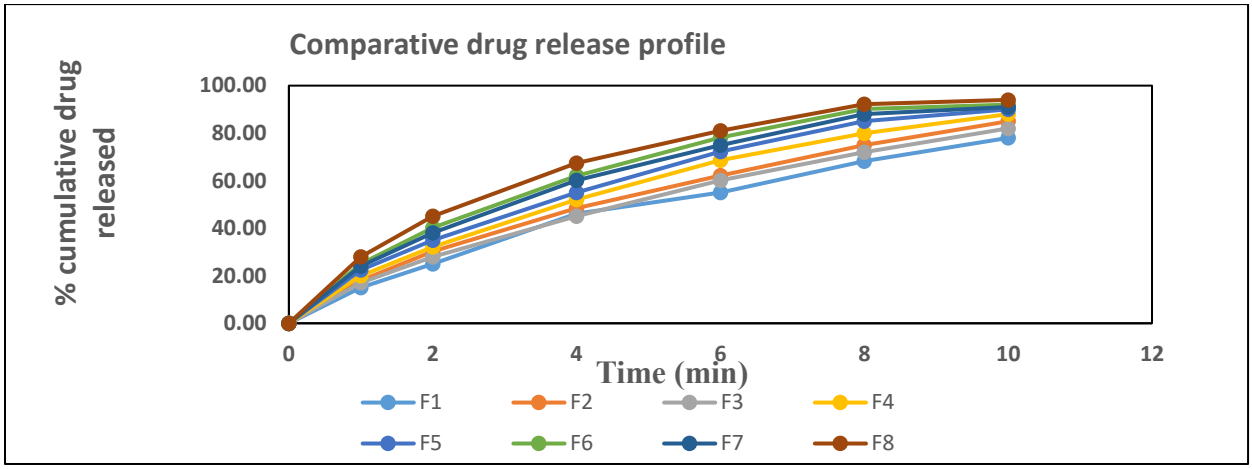

Fig 08 Cumulative %of Drug Release for Solid Dispersion Incorporated Fast Dissolving Oral Films

IV. CONCLUSION

The present study successfully developed Domperidone solid dispersions using PVP and PEG carriers to improve its solubility and dissolution characteristics. Preformulation studies confirmed the purity, identity, and analytical suitability of the drug. Solubility studies demonstrated that PVP was more effective than PEG in enhancing Domperidone solubility, with the PVP 1:5 formulation showing the highest improvement. Drug content analysis confirmed uniform drug distribution and acceptable incorporation in all formulations. Dissolution studies revealed significantly enhanced drug release from solid dispersions compared to the pure drug. Among all formulations, **SD3 (Domperidone:PVP, 1:5)** exhibited the highest drug release and best overall performance. FTIR studies confirmed the absence of drug–polymer incompatibility and indicated successful interaction between the drug and carrier. The enhanced solubility and dissolution were attributed to improved drug dispersion within the polymer matrix. Overall, the solid dispersion technique proved to be an effective approach for enhancing the pharmaceutical performance of Domperidone. SD3 was identified as the optimized formulation for further development and incorporation into fast-dissolving oral films.

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