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FORMULATION AND EVALUATION OF SOLID DISPERSION TABLET CONTAINING TINIDAZOLE

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Keywords:

Tinidazole, Solid dispersions, Fast-release tablet, Carriers, Dissolution kinetics, PEG 4000, Interaction studies

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ABSTRACT: This study focused on the development and evaluation of solid dispersions of Tinidazole, aimed at creating a fast-release tablet formulation. The preparation involved using carriers such as PEG 4000 and HPMC. Solid dispersions were created using both solvent evaporation and fusion methods. The resulting solid dispersions exhibited desirable properties, appearing as fine and free-flowing powders. Interaction studies, including IR spectra analysis, revealed no significant interaction between the drug and the carriers employed. Furthermore, uniform drug content was observed across all prepared solid dispersions. Correlation studies between the percentage of carriers in the dispersions and the dissolution behavior of pure Tinidazole indicated a positive relationship. Dissolution kinetics analysis demonstrated that the release of Tinidazole from all dispersions adhered to first-order kinetics. Notably, PEG 4000 emerged as the most effective carrier, yielding the fastest dissolution rate. The sequence of dissolution rates from various solid dispersions was determined. To extend the evaluation, Tinidazole solid dispersions in a 1:2 drug-to-carrier ratio with PEG 4000 were formulated into capsules. These capsules exhibited significantly enhanced dissolution characteristics compared to the pure drug formulation. The solid dispersion containing a 1:2 ratio of drug to PEG 4000 was identified as a fast-release dosage form of Tinidazole, surpassing the dissolution performance of both the pure drug and other ratios of Tinidazole solid dispersions. Moreover, the successful formulation and evaluation of solid dispersion tablets were achieved, representing a promising advancement in the development of a fast-release tablet formulation for Tinidazole.

INTRODUCTION: Solubility refers to a substance's ability to dissolve in another substance, creating a homogeneous solution. This property depends on factors like the type of solvent used, temperature, and pressure.

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When the solubility limit is reached, further addition of solute does not increase its concentration in the solution. Solubility equilibrium occurs when dissolution and precipitation processes balance. Sometimes, solutions can become supersaturated, which is a metastable state [1-2].

Solubility is not the same as the ability to dissolve, as it can also involve chemical reactions. Solubility is commonly expressed in units of concentration, and its methods of expression vary. Solubility plays a crucial role in drug development, especially for oral delivery.

Poor solubility can lead to low bioavailability and inadequate therapeutic effects. Various methods, like physical and chemical modifications, are employed to enhance solubility. For drugs with low solubility, oral bioavailability can be improved by increasing solubility and dissolution rate in gastrointestinal fluids. The effects of low solubility include poor absorption, challenges in development, and increased costs. Different techniques are used to enhance solubility, including physical and chemical modifications of the drug material [3].

Solid Dispersion: Solid Dispersion is a pharmaceutical technique aimed at enhancing the dissolution, absorption, and therapeutic efficacy of drugs in dosage forms. It involves mixing hydrophilic carriers, like Povidone or polyethylene glycols, with hydrophobic drugs. This method improves drug solubility, with examples like celecoxib and ritonavir utilizing carriers such as Povidone. Two key methods for creating solid dispersions are the Hot-Melt (Fusion) Method and Solvent Evaporation Method [4-5].

Hot-Melt (Fusion) Method: This involves melting and mixing the drug and carrier, then rapidly cooling the mixture to form a solid mass. The composition and thermal stability of the drug-carrier blend are crucial. The final product can be compressed into tablets.

Solvent Evaporation Method: The drug and carrier are dissolved in a common solvent, which is then evaporated under vacuum, forming a solid solution. This method prevents thermal degradation, but challenges include solvent removal and potential effects on drug stability.

Carriers for Solid Dispersions [6-7]:

Poly Ethylene Glycols (PEGs): PEGs are polymers of ethylene oxide with a molecular weight range of 200 to 300,000. PEGs with molecular weights of 1500 to 20,000 are commonly used for solid dispersions. They have good solubility in water and organic solvents, making them versatile for various methods. Higher molecular weight PEGs have greater viscosity and decreased water solubility.

Poly Vinyl Pyrrolidine (PVP): PVP, derived from Vinyl Pyrrolidine, has molecular weights from 2500 to 300,000. It's soluble in organic solvents and water, enhancing wettability. Longer chain lengths reduce aqueous solubility and increase viscosity. Examples include Poly Vinyl Alcohol and Poly Vinyl Pyrrolidine Acetate co-polymer.

Hydroxy Propyl Methyl Cellulose (HPMC): HPMC, or Hypromellose, has molecular weights of 10,000 to 1,500,000. It's soluble in water and organic solvent mixtures like ethanol and chloroform. Like PEGs and PVPs, HPMC improves wettability and is suitable for the solvent method.

MATERIALS AND METHODS: Drug Tinidazole was a gift sample provided by Modern Labs, Indore and other excipients were procured from various sources and details are listed below. All the solvents used in the current project were of UV grade and chemicals used were of analytical grade [8].

Preformulation Studies: It involve investigating the physical and chemical properties of a drug substance, alone and combined with excipients. This initial phase guides formulation approaches, optimizes product quality, and influences performance. It includes assessments such as substance color, solubility, melting point, loss on drying, and IR spectroscopy for identification and fingerprinting. Preformulation provides a rational basis for formulation development and is crucial for designing effective dosage forms.

Drug – Excipient Interaction Study:

Physical Observation: Visual checks were conducted weekly over 4 weeks to monitor any changes in the sample mixture.

Thin Layer Chromatography (TLC): TLC assessed drug-excipients compatibility. Tinidazole (10 mg) mixed with excipients (1:5 ratio) underwent storage at 40°C for 4 weeks. TLC analysis was done using a mobile phase of Ethanol: ammonia (70:30). TLC plates were prepared with silica gel, forming a uniform thin layer as the stationary phase. A dedicated chamber maintained a controlled environment for spot development, preventing solvent evaporation and dust. Filter paper moistened with the mobile phase was placed inside the chamber.

Development of Standard Calibration Curves (UV Spectrophotometry Methodology):

Potassium Dihydrogen Phosphate, 0.2 M Solution: Dissolve 27.318 gm of Potassium dihydrogen Phosphate in 1000 ml distilled water to obtain 0.2 M KH2PO4.

Sodium Hydroxide 0.2 N Solution: Dissolve 8 gm of sodium hydroxide in 1000 ml distilled water to create 0.2 N NaOH solution.

Preparation of pH 7.4 Phosphate Buffer: Combine 50 ml of Potassium dihydrogen Phosphate solution with 39.1 ml of sodium hydroxide solution in a 200 ml volumetric flask. Fill the flask with distilled water.

Standard Graphs Preparation: Dissolve 100 mg of Tinidazole in 100 ml volumetric flask using Methanol and phosphate buffer pH 7.4, creating Stock Solution I (1000 µg/ml). From Stock Solution I, take 10 ml and dilute to 100 ml with phosphate buffer pH 7.4 to form Stock Solution II (100 µg/ml). Pipette 0.5, 1.0, 1.5, 2.0, and 2.5 ml from Stock Solution II into separate 10 ml volumetric flasks. Dilute to the mark with phosphate buffer pH 7.4 to get 5, 10, 15, 20, and 25 µg/ml concentration solutions, using phosphate buffer pH 7.4 as the blank.

Measure absorbance at 279 nm and plot a graph of concentration (µg/ml) against absorbance.

Tinidazole Solid Dispersion Preparation and Evaluation: Solid dispersion enhances dissolution of poorly water-soluble drugs like Tinidazole. HPMC and PEG-4000 were chosen as carriers. Fusion and solvent evaporation methods were employed.

Fusion Method: Polymer placed in a heated China disc melted, then drug added with stirring. Cooled in an ice bath, vacuum-sealed.

Solvent Evaporation Method: Methanol solvent used, varying drug: Carrier ratios (1:1, 1:2, 1:3, 1:4) for Tinidazole solid dispersion. Stirred, evaporated, dried, pulverized.

Physical Mixture: Drug: carrier (1:1) physically mixed via mortar using geometric dilution for uniformity.

TABLE 1: DRUG: CARRIER CONTENT RATIOS AND RESPECTIVE AMOUNT TAKEN

S. no.	Drug: carrierratio	Drug content (mg)	Carrier content (mg)
1	1:1	500	500
2	1:2	333	666
3	1:3	250	750
4	1:4	200	800

Characterization of Tinidazole Solid Dispersion:

IR Spectral Analysis: FTIR spectra (2000-400 cm-1) were acquired using a Jasco - FT-IR 410 PC spectrophotometer (Jasco,). The KBr disc method was employed. Prominent absorption bands were observed at wave numbers: 900, 1032, 1159, 1528, 1650, and 1690.

Evaluation of Solid Dispersion:

Drug Content Uniformity: Tinidazole solid dispersions (in various ratios) underwent analysis for drug content uniformity. 10 mg equivalents were tested from each batch.

Estimation by UV Spectrophotometry: Accurately weighed solid dispersion amounts dissolved in 0.2M pH 7.4 buffer solution within a cleaned, dry 10 ml volumetric flask. Diluted solution measured at 279 nm in a UV/Vis spectrophotometer.

Formulation of Inclusion Complex Tablet: Solid dispersion with drug and PEG4000 (1:2) showed 76.57% W/V maximum release (Solvent evaporation method). This demonstrates a fast-releasing dosage form for poorly water-soluble drugs using solid dispersion technology. Based on *in-vitro* studies, solid dispersion tablets were formulated. Various super disintegrants were tested in different ratios using direct compression method for tablet preparation.

TABLE 2: FORMULATION OF INCLUSION COMPLEX TABLET

Ingredient	F1	F2	F3	F4	F5	F6
Amount of Complex	10	10	10	10	10	10

Sodium Starch Glycolate	5	10	15	-	-	-
Crospovidone	-	-	-	5	10	15
Microcrystalline cellulose	71	66	61	71	66	61
Magnesiumstea rate	6	6	6	6	6	6
Talc	8	8	8	8	8	8
Total weight (mg)	100	100	100	100	100	100

Precompression Parameters:

Flow Properties (Angle of Repose): Angle of repose is the maximum angle between a powder or granule pile's surface and a horizontal plane. Using the fixed funnel method, the angle was determined.

Powder blend was placed in a beaker and allowed to flow through the funnel, forming a cone-shaped pile on paper. Cone diameter (d) and height (h) were measured. Angle of repose (θ) was calculated using the formula.

$$\Theta = \tan -1(h/r)$$

Bulk Density Measurement: Bulk density gauges powder attributes, using mass (M) occupying a known volume (Vo), in g/ml. Granules were weighed, placed in a 50 ml cylinder *via* funnel, and the apparent volume measured. Bulk density calculated with a formula.

$$\rho bulk = m/Vo$$

Tapped Density Measurement: A powder's tapped density is determined by mechanically tapping a cylinder with the powder. Initial and final volume readings are taken after tapping until minimal volume change occurs. Granules in a measuring cylinder (after bulk density measurement) were tapped 500 times using a tapped density tester (Electro Lab USP II).

$$\rho t = m/V_t$$

Compressibility Index and Flowability: Compressibility index gauges arch formation and failure ease. Table illustrates the link between compressibility index and flowability. Calculation employs a specific formula.

$$CI = \rho t - \rho bulk / \rho t \times 100$$

Hausner's Ratio and Flow Prediction: Hausner's ratio (ρt / ρbulk) predicts powder flow based on interparticle friction. Lower ratios (around 1.2) suggest free flow, while higher ratios (above 1.6) indicate less flowable, cohesive powders like flakes. Flow characters and Hausner's ratio relationship are shown in the table. Calculation involves a specific formula.

$$\text{Hausner's Ratio} = \rho t / \rho bulk$$

Solid Dispersion Tablet Formulation: Solid dispersion formulated into tablets using direct compression method. Crosspovidone (5, 10, 15), sodium starch glycolate (5, 10, 15), microcrystalline cellulose, talc, and magnesium stearate added as disintegrants and lubricants. Powder blends mixed in a container and compressed into tablets using a double punch tablet machine.

Post Compression Parameters: The tablets underwent weight variation analysis, hardness testing using a Monsanto hardness tester, and friability assessment using a friabilitor. *In-vitro* disintegration tests measured breakdown time in phosphate buffer.

In-vitro dissolution studies were conducted using USP dissolution apparatus, and stability studies evaluated formulation durability under various conditions. Stability testing provides crucial information on the product's chemical, biological, and physical stability over time, helping determine recommended storage conditions and shelf life. ICH guidelines offer storage recommendations for stability studies.

RESULTS: The present study was carried out to Formulate & Evaluate Solid Dispersion Tablet of Tinidazole. They were evaluated for various parameters and the results are presented in appropriate tables and figures.

Preformulation Studies: The following preformulation studies were performed on Tinidazole.

Evaluation of Tinidazole (API): The color, solubility, melting point and moisture content of the API were evaluated. It was found to be within the range of the monograph.

TABLE 3: PHYSICAL CHARACTERISTICS OF TINIDAZOLE

S. no.	Tests	Specification	Results
1	Physical Description	White or almost white crystalline powder	Conforms
2	Solubility	Tinidazole is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of tinidazole in these solvents is approximately 0.2, 10, and 20 mg/ml, respectively. Tinidazole is sparingly soluble in aqueous buffers.	Positive
3	Melting Point	127-128°C, the range between the beginning and the end of melting point does not exceed 2º C	128ºC
4	Moisture content	NMT 0.6 w/w%	0.23%w/w

IR Spectroscopy of Drug:

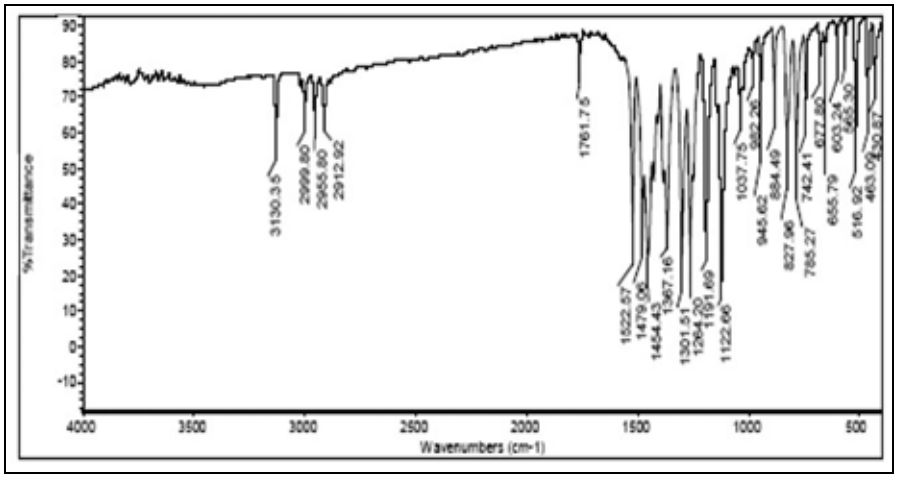

FIG. 1: IR SPECTRA OF TINIDAZOLE

Drug - Excipients Compatibility: From the drug excipients compatibility study, it was observed that there was no characteristic change or interaction between drug and excipients.

TABLE 4: DRUG - EXCIPIENTS COMPATIBILITY (INDIVIDUAL AND WHOLE BLEND)

S. no.	Composition	Initial	After 15 days	After 30 days	Conclusion
1	Tinidazole	White	NCC	NCC	Complies
2	Drugs + All Excipients	Off White	NCC	NCC	Complies

NCC- No Characteristic Change.

TABLE 5: PHYSICAL OBSERVATION OF COMPATIBILITY STUDIES

S. no.	Material	Initial observation	40^0C/75%RH (One month)		40^0C/75%RH (Three month)	
			Open	Close	Open	Close
1	API	White crystalline powder	Complies	Complies	Complies	Complies
2	API + HPMC	White blend	Complies	Complies	Complies	Complies
3	API +PEG	White blend	Complies	Complies	Complies	Complies
4	Drug + Crospovidone	White blend	Complies	Complies	Complies	Complies
5	Drug+Sodium Starch Glycolate	White blend	Complies	Complies	Complies	Complies
6	Drug+Microcrystalline Cellulose	White blend	Complies	Complies	Complies	Complies
7	Drug+Megnessium Stearate	White blend	Complies	Complies	Complies	Complies
8	Drug +Talc	White blend	Complies	Complies	Complies	Complies

As observed in the above studies (physical observation of related substance) there was no any sign of interaction, therefore drug was compatible with excipients.

Thin Layer Chromatography (TLC) Compatibility: Chemical compatibility was assessed using TLC, showing that the drug and excipients remained chemically compatible. No significant change in RF values indicated compatibility, ensuring the suitability of excipients for the formulation.

TABLE 6: THIN LAYER CHROMATOGRAPHY (TLC)

Parameter	Initial	After4weeks	Observation
Pure Drug	Rf=0.180	Rf=0.183	As no changes in RF value was observed hence it shown interaction after 4 weeks
Drug + HPMC	Rf=0.179	Rf=0.172	
Drug +PEG	Rf=0.137	Rf=0.138	
Drug + Crospovidone	Rf=0.070	Rf=0.073	
Drug+Sodium Starch Glycolate	Rf=0.127	Rf=0.129	
Drug + Microcrystalline Cellulose	Rf=0.169	Rf=0.172	
Drug + Megnessium Stearate	Rf=0.054	Rf=0.057	
Drug +Talc	Rf=0.205	Rf=0.209	

UV-spectroscopic Method Analysis of Tinidazole:

Linearity and Range for Calibration Curve of Tinidazole: The straight-line calibration graph was obtained in the concentration of 0-25µg/ml of the Tinidazole in phosphate buffer pH7.4. The linear regression equation was found to be y = 0.0247x + 0.0008 with the correlation co efficient (r^2) of 0.999. The calibration curve was from the linear regression data (r^2 value), it can be concluded that the analyzed concentration of the drug solution followed linearity.

TABLE 7: STANDARD GRAPH OF TINIDAZOLE WITH PHOSPHATE BUFFER pH 7.4

S. no.	Concentration (µg/ml)	Absorbance at 279 nm
1	0	0.0000
2	5	0.1249
3	10	0.2490
4	15	0.3730
5	20	0.4920
6	25	0.6202

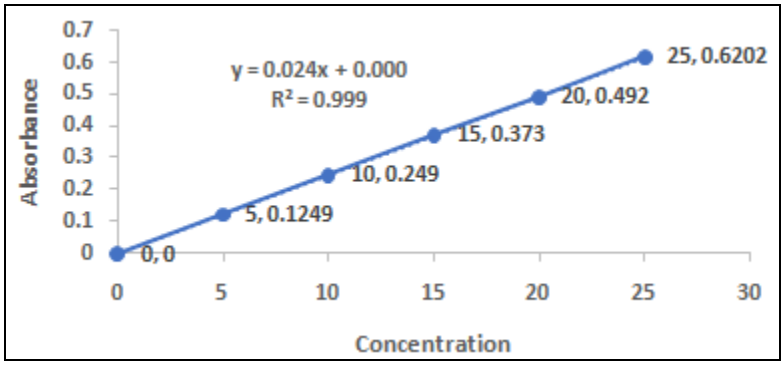

FIG. 2: STANDARD GRAPHS PREPARATION WITH PHOSPHATE BUFFER pH 7.4

Characterization of Tinidazole Solid Dispersion:

IR Spectral Analysis:

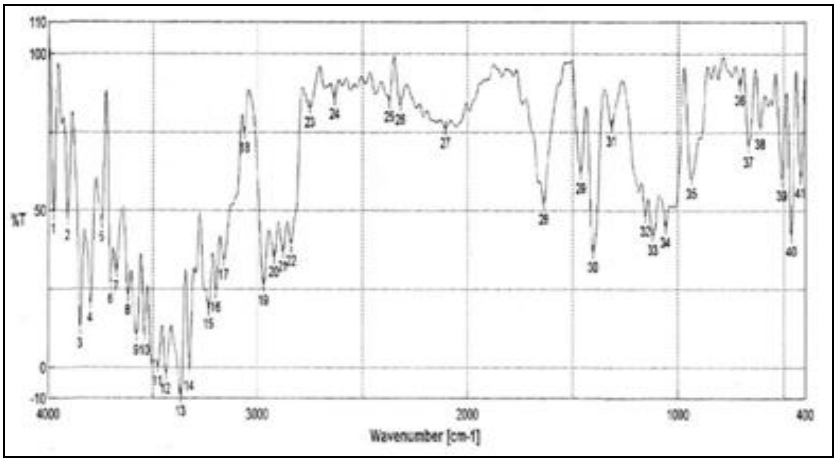

FIG. 3: IR SPECTRA OF PEG4000

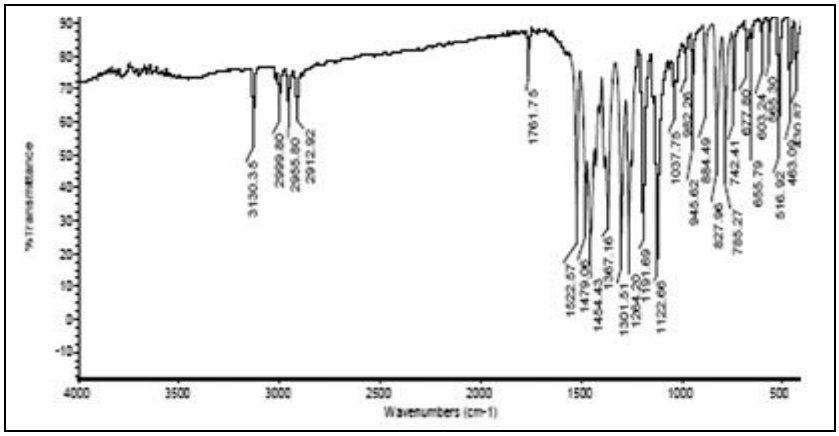

FIG. 4: IR SPECTRA OF HPMC

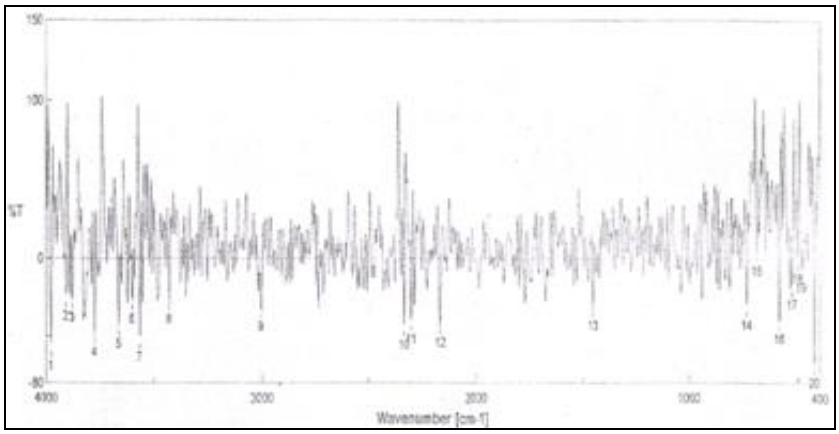

FIG. 5: IR SPECTRA OF TINIDAZOLE

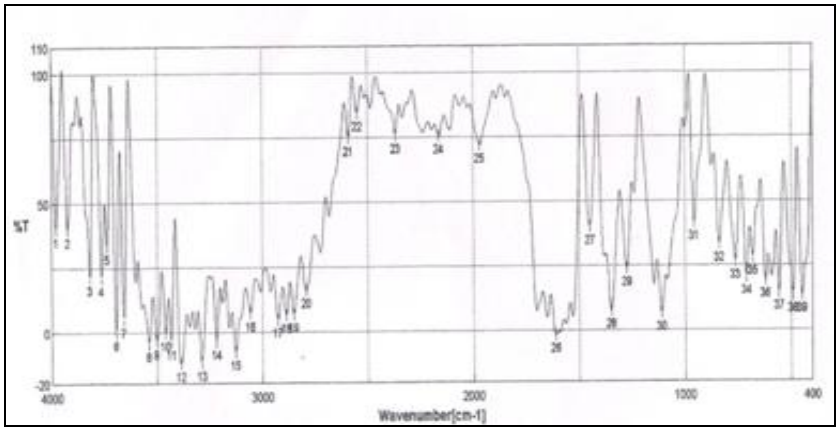

FIG. 6: IR SPECTRA OF TINIDAZOLE AND PEG4000 (BY SOLVENT EVAPORATION METHOD)

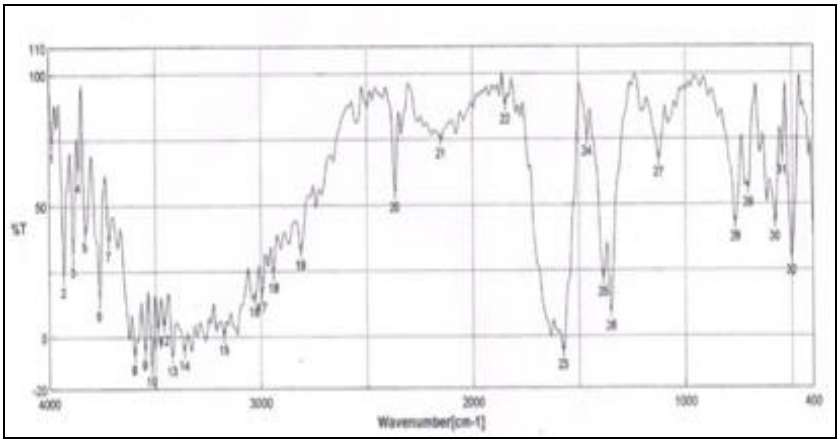

FIG. 7: IR SPECTRA OF TINIDAZOLE AND HPMC (BY SOLVENT EVAPORATION METHOD)

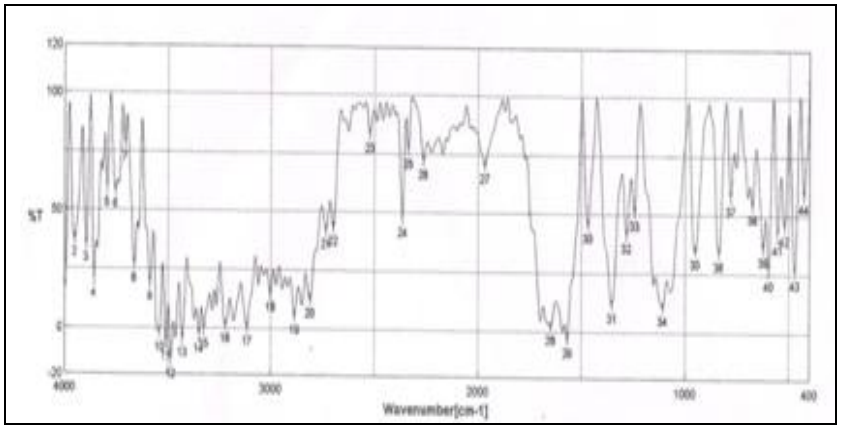

FIG. 8: IR SPECTRA OF TINIDAZOLE AND PEG4000 (FUSION METHOD)

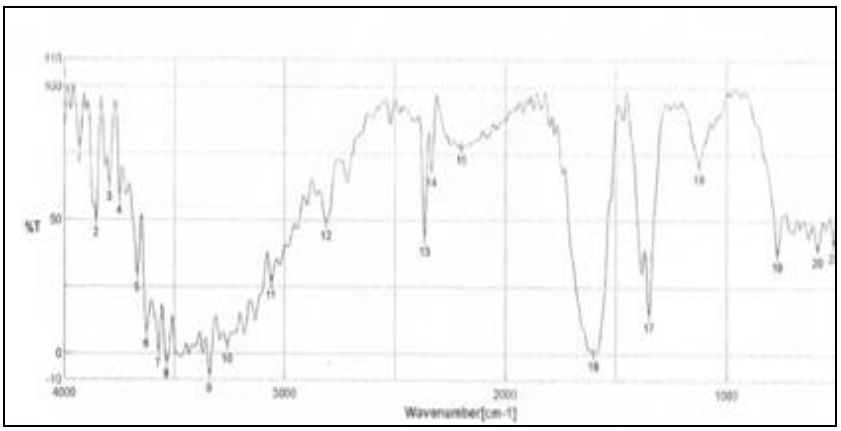

FIG. 9: IR SPECTRA OF TINIDAZOLE AND HPMC (FUSION METHOD)

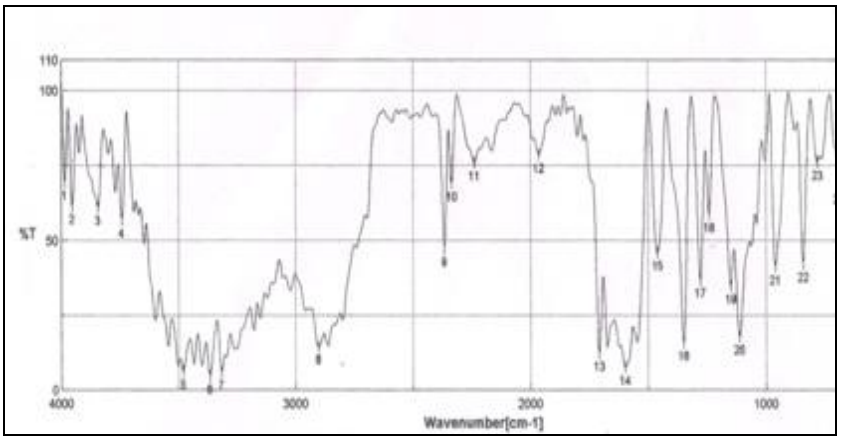

FIG. 10: IR SPECTRA OF TINIDAZOLE AND PEG4000 (PHYSICAL MIXTURE)

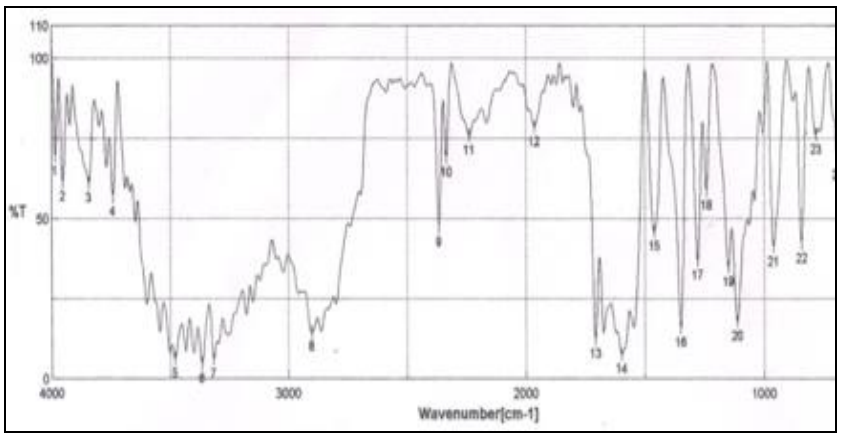

FIG. 11: IR SPECTRA OF TINIDAZOLE AND HPMC (PHYSICAL MIXTURE)

Evaluation of Solid Dispersion:

Drug content Uniformity:

TABLE 8: DRUG CONTENT UNIFORMITY

Solid Dispersion	Drug: Carrier	Amount of SD taken (mg)	Expected Amount of drug in SD (mg)	% of Tinidazole (by solvent evaporation) estimated by UV Spectrophotometer	% of Tinidazole (by fusion) estimated by UV Spectrophotometer
Tinidazole–PEG4000	1:1	10	5	98.4	97.21
	1:2	10	3.3	99.8	96.21
	1:3	10	2.5	97.2	96.12
	1:4	10	2	99.2	92.21
Tinidazole-HPMC	1:1	10	5	99.4	98.91
	1:2	10	3.3	98.21	99.81
	1:3	10	2.5	97.21	94.28
	1:4	10	2	99	94.21

Dissolution Rate Studies: Dissolution rate evaluations of Tinidazole solid dispersions were conducted using a USP XXIV dissolution apparatus in 0.2M, pH 7.4 phosphate buffer. A 40 mg equivalent of Tinidazole in a hard gelatin capsule was used. Stirring was set at 70 rpm, temperature at 37°C, and samples were withdrawn at intervals for analysis. Absorbance at 279 nm was measured using a UV spectrophotometer. Results were obtained in triplicate and plotted over time.

TABLE 9: DISSOLUTION OF TINIDAZOLE SOLID DISPERSION (SOLVENT EVAPORATION) BY PEG4000 AT DIFFERENT DRUG: CARRIER RATIOS

Medium: 0.2M Phosphate Buffer pH 7.4, Temperature: 37ºC±5ºC, RPM: 70						
Time (Min)	Percentage Tinidazoled is solved					
	Pure Drug (4mg)	Physical Mixture (1:1)	1:1	1:2	1:3	1:4
0	0	0	0	0	0	0
5	1.36	1.9	3.2	5.2	3.0	2.4
10	2.03	2.8	5.1	7.5	4.3	4.0
15	4.54	6.1	10.1	15.1	12.3	11.1
30	5.87	9.4	27.9	28.3	26.1	25.2
45	7.13	10.8	38.7	40.5	30.6	30.3
60	10.81	12.3	50.3	52.4	42.7	39.1
90	16.19	18.9	57.3	63.7	50.4	48.2
120	19.99	27.3	65.4	76.57	61.2	58.7

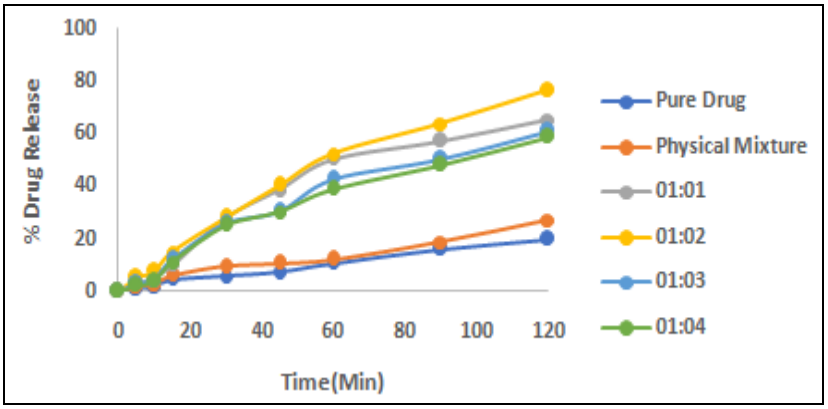

FIG. 12: DISSOLUTION OF TINIDAZOLE SOLID DISPERSION (SOLVENT EVAPORATION) BY PEG 4000 AT DIFFERENT DRUG: CARRIER RATIOS

TABLE 10: DISSOLUTION OF TINIDAZOLE SOLID DISPERSION (SOLVENT EVAPORATION) BY HPMC AT DIFFERENT DRUG: CARRIER RATIOS

Medium: 0.2M Phosphate Buffer pH 7.4, Temperature: 37ºC±5ºC, RPM: 70						
Time(Min)	Percentage Tinidazole dissolved					
	Pure Drug	Physical	1:1	1:2	1:3	1:4

	(4mg)	Mixture (1:1)				
0	0	0	0	0	0	0
5	1.36	2.3	2.0	2.1	1.8	1.5
10	2.03	3.8	3.0	3.20	2.7	2.0
15	4.54	5.3	10.1	10.0	9.8	9.0
30	5.87	6.8	19.2	19.4	17.6	15.6
45	7.13	8.6	28.8	30.2	26.4	22.1
60	10.81	10.1	30.4	39.5	38.1	36.4
90	16.19	15.2	46.3	52.4	49.2	40.8
120	19.99	21.0	61.9	69.3	56.2	54.3

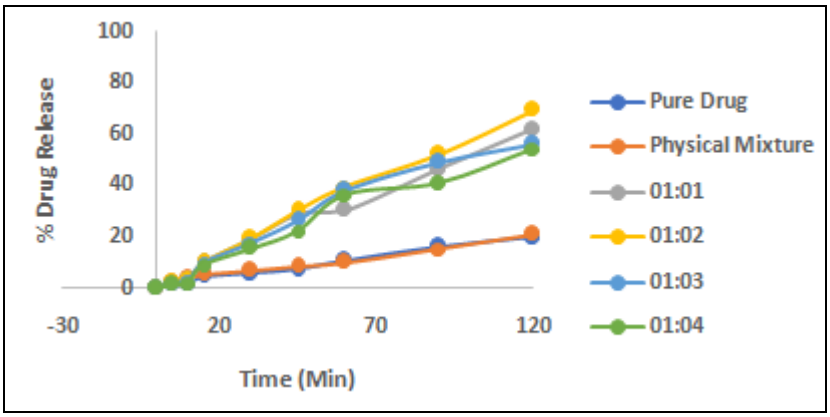

FIG. 13: DISSOLUTION OF TINIDAZOLE SOLID DISPERSION (SOLVENT EVAPORATION) BY HPMC AT DIFFERENT DRUG: CARRIER RATIOS

TABLE 11: DISSOLUTION OF TINIDAZOLE SOLID DISPERSION (FUSION METHOD) BY PEG4000 AT DIFFERENT DRUG: CARRIER RATIOS

Medium: 0.2M Phosphate Buffer pH7.4, Temperature: 37ºC±5ºC, RPM: 70						
Time (Min)	Percentage Tinidazole dissolved					
	Pure Drug (4mg)	Physical Mixture (1:1)	1:1	1:2	1:3	1:4
0	0	0	0	0	0	0
5	1.36	1.9	2.9	3.8	2.0	2.3
10	2.03	2.8	4.0	5.4	3.7	3.2
15	4.54	6.1	9.2	11.0	8.6	7.7
30	5.87	9.4	21.9	23.7	10.7	10.6
45	7.13	10.8	33.3	35.6	28.3	26.4
60	10.81	12.3	41.2	47.8	40.1	30.2
90	16.19	18.9	50.1	55.2	49.5	40.5
120	19.99	27.3	62.6	71.4	58.1	55.4

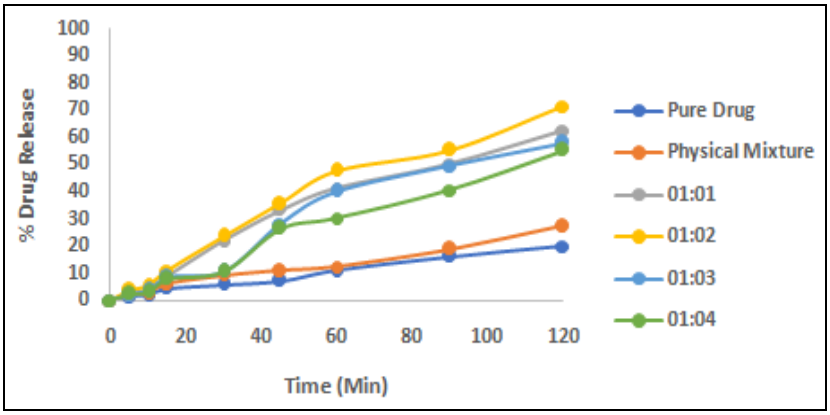

FIG. 14: DISSOLUTION OF TINIDAZOLE SOLID DISPERSION (FUSION METHOD) BY PEG4000 AT DIFFERENT DRUG: CARRIER RATIOS

TABLE 12: DISSOLUTION OF TINIDAZOLE SOLID DISPERSION (FUSION METHOD) BY HPMC AT DIFFERENT DRUG: CARRIER RATIOS

Medium: 0.2M Phosphate Buffer pH7.4, Temperature: 37ºC±5ºC, RPM: 70						
Time (Min)	Percentage Tinidazole dissolved					
	Pure Drug (4mg)	Physical Mixture (1:1)	1:1	1:2	1:3	1:4
0	0	0	0	0	0	0
5	1.36	2.3	1.7	1.8	1.5	1.3
10	2.03	3.8	2.5	2.9	2.6	2.0
15	4.54	5.3	8.6	9.1	8.8	7.9
30	5.87	6.8	14.3	16.4	14.5	12.4
45	7.13	8.6	21.0	28.7	21.4	19.0
60	10.81	10.1	29.4	37.3	32.7	28.7
90	16.19	15.2	45.0	50.4	46.1	39.6
120	19.99	21.0	57.8	66.1	54.8	52.9

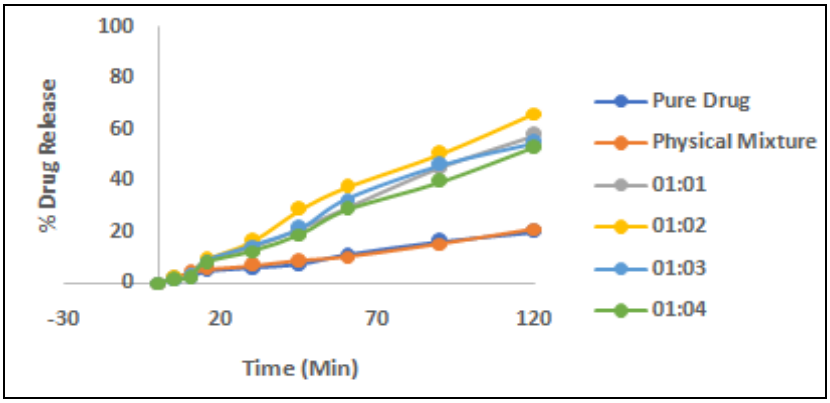

FIG. 15: DISSOLUTION OF TINIDAZOLE SOLID DISPERSION (FUSION METHOD) BY HPMC AT DIFFERENT DRUG: CARRIER RATIOS

TABLE 13: DISSOLUTION OF TINIDAZOLE IN PURE FORM AND FROM SOLID DISPERSION (SOLVENT EVAPORATION) WITH VARIOUS CARRIERS AT DRUG: CARRIER RATIO OF 1:2

Medium: 0.2M Phosphate Buffer pH 7.4,Temperature: 37ºC±5ºCRPM: 70			
Time (Min)	PercentageTinidazole dissolved		
	Pure Drug (4MG)	SE(PEG4000)	SE(HPMC)
0	0	0	0
5	1.36	5.2	2.1
10	2.03	7.5	3.20
15	4.54	15.1	10.0
30	5.87	28.3	19.4
45	7.13	40.5	30.2
60	10.81	52.4	39.5
90	16.19	63.7	52.4
120	19.99	76.57	69.3

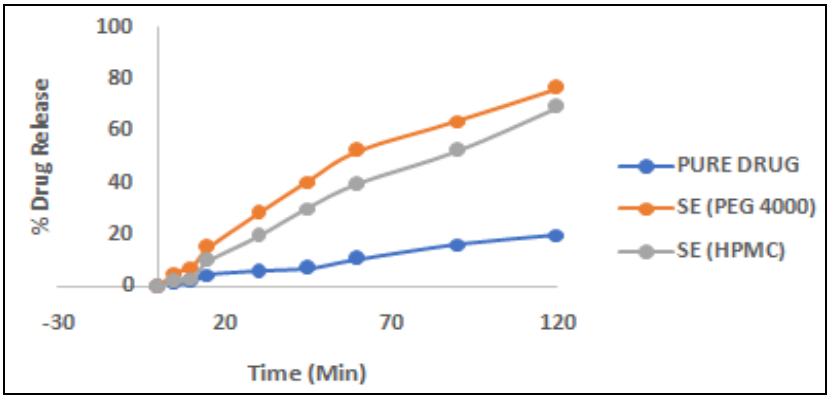

FIG. 16: DISSOLUTION OF TINIDAZOLE IN PURE FORM AND FROM SOLID DISPERSION (SOLVENT EVAPORATION) WITH VARIOUS CARRIERS AT DRUG: CARRIER RATIO OF 1:2

TABLE 14: DISSOLUTION OF TINIDAZOLE IN PURE FORM AND FROM SOLID DISPERSION (FUSION METHOD) WITH VARIOUS CARRIERS AT DRUG: CARRIER RATIO OF 1:2

Medium: 0.2M Phosphate Buffer pH 7.4, Temperature: 37°C±5°C, RPM: 70			
Time (Min)	Percentage Tinidazole dissolved		
	Pure Drug (4MG)	SE(PEG4000)	SE(HPMC)
0	0	0	0
5	1.36	3.8	1.8
10	2.03	5.4	2.9
15	4.54	11.0	9.1
30	5.87	23.7	16.4
45	7.13	35.6	28.7
60	10.81	47.8	37.3
90	16.19	55.2	50.4
120	19.99	71.4	66.1

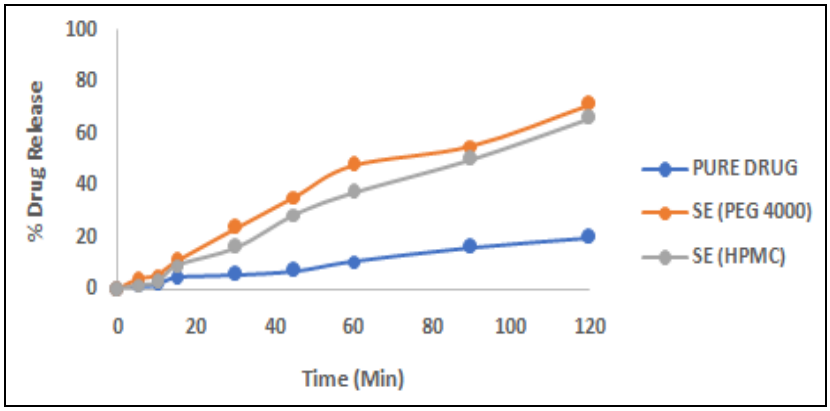

FIG. 17: DISSOLUTION OF TINIDAZOLE IN PURE FORM AND FROM SOLID DISPERSION (FUSION METHOD) WITH VARIOUS CARRIERS AT DRUG: CARRIER RATIO OF 1:2

TABLE 15: DISSOLUTION OF TINIDAZOLE IN PURE FORM, PHYSICAL MIXTURE AND SOLVENT EVAPORATION WITH PEG4000 AT DRUG: CARRIER RATIO OF 1:2

Time (min)	Percentage Tinidazole dissolved		
	Pure drug (4mg)	Physical Mixture (1:1)	SEPEG4000 (1:2)
0	0	0	0
5	1.36	1.9	5.2
10	2.03	2.8	7.5
15	4.54	6.1	15.1
30	5.87	9.4	28.3
45	7.13	10.8	40.5
60	10.81	12.3	52.4
90	16.19	18.9	63.7
120	19.99	27.3	76.57

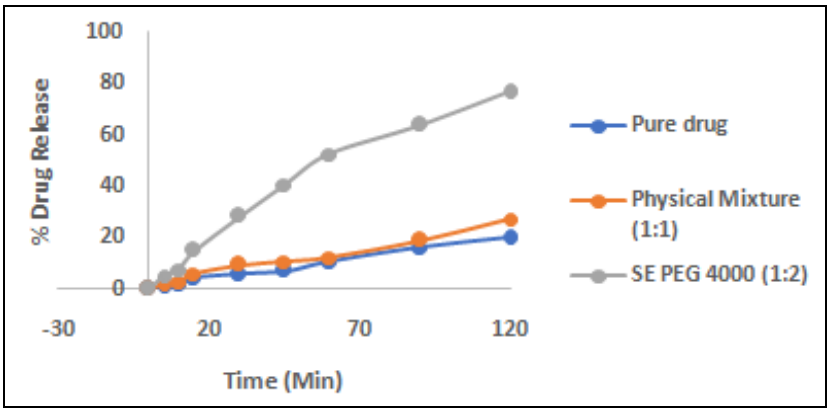

FIG. 18: DISSOLUTION OF TINIDAZOLE IN PURE FORM, PHYSICAL MIXTURE AND SOLVENT EVAPORATION WITH PEG4000 AT DRUG: CARRIER RATIO OF 1:2

TABLE 16: LOG PERCENTAGE TINIDAZOLEUN DISSOLVED FROM PURE FORM AND FROM PEG4000 SOLID DISPERSIONS (SOLVENT EVAPORATION METHOD) OF 1:2 RATIO

Time (min)	Percentage Tinidazole undisclosed from solid dispersions (Log percentage Tinidazole und is solved)		
	Pure drug	Physical mixture	(SE) PEG4000
0	0	0	0
5	98.64 (1.994)	98.10 (1.991)	94.8 (1.976)
10	97.97 (1.991)	97.22 (1.987)	92.5 (1.966)
15	95.46 (1.979)	93.91 (1.972)	84.90 (1.928)
30	94.13 (1.973)	90.63 (1.957)	71.70 (1.855)
45	92.87 (1.967)	89.22 (1.950)	59.5 (1.774)
60	89.19 (1.950)	87.72 (1.942)	47.60 (1.677)
90	83.81 (1.923)	81.12 (1.909)	36.3 (1.559)
120	80.01 (1.903)	72.77 (1.861)	23.43 (1.369)

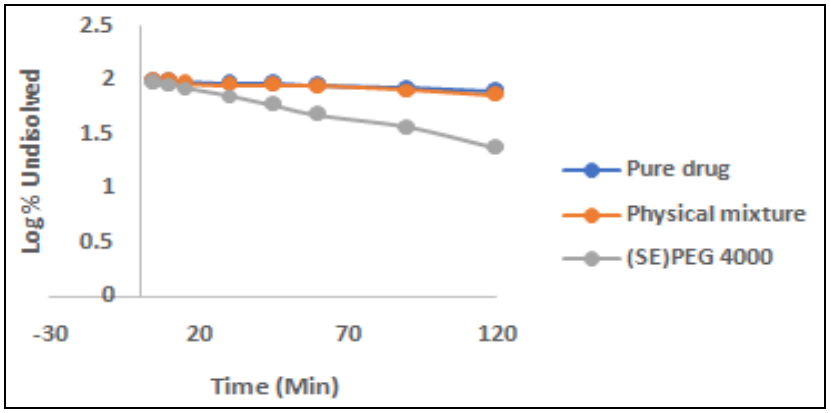

FIG. 19: LOG PERCENTAGE TINIDAZOLEUN DISSOLVED FROM PURE FORM AND FROM PEG 4000 SOLID DISPERSIONS (SOLVENT EVAPORATION METHOD) OF 1:2 RATIO

Discussion: *In-vitro* dissolution studies were performed, and IR spectra confirmed compatibility between the drug and carriers. Solid dispersions with PEG4000 (1:2) showed the highest release (76.57% w/v), while those with HPMC (1:2) exhibited 69.3% (w/v) release. This confirms that solid dispersion technology can yield fast-releasing formulations for poorly water-soluble drugs, as demonstrated in the developed solid dispersion tablet.

Pre-compression Parameters: The complex tablets exhibited favorable flow properties with Hausner's ratio of 1.14 to 1.19 and angle of repose ranging from 28.36±0.26 to 30.46±0.32. This suggests efficient flow, potentially requiring less glidant in manufacturing. A Carr's index of 12.22 to 16.30 indicates good compressibility. Based on these parameters, the direct compression technique was chosen for solid dispersion tablet development.

TABLE 17: PRE COMPRESSION PARAMETERS

Batch code	Bulk Density (gm/ ml)	Tapped Density (gm /ml)	Car'sindex (%)	Hausner's Ratio	Angle of Repose (o)
F1	0.55±0.12	0.64±0.18	14.44±0.38	1.16±0.23	28.36±0.26
F2	0.56±0.14	0.65±0.29	14.78±0.48	1.17±0.25	29.74±0.10
F3	0.54±0.22	0.64±0.37	16.30±0.59	1.19±0.29	30.46±0.32
F4	0.53±0.29	0.63±0.39	15.17±0.30	1.1±8±0.32	29.39±0.24
F5	0.55±0.26	0.63±0.27	14.60±0.29	1.14±0.16	29.03±0.36
F6	0.56±0.18	0.65±0.51	12.22±0.58	1.14±0.18	28.53±0.40

Values are Expressed as Mean ± SEM; (n=3).

Post – compression Parameter: Hardness of three tablets per batch was tested with Monsanto hardness tester, yielding results within the standard range of 2.0 to 2.4 kg/cm². Weight variation test showed tablets within the average weight range of 100 to 105 mg, meeting pharmacopeia limits. Tablets from various batches exhibited low friability (0.68 to 0.83%), indicating strong mechanical integrity.

TABLE 18: POST – COMPRESSION PARAMETER

Batch code	Hardness (kg/ cm2)	Friability (%)	Thickness (mm)	Avg. Weight (mg)
F1	2.3±0.32	0.692±0.35	2.58±0.34	102±2.46
F2	2.3±0.53	0.722±0.31	2.49±0.26	105.6±3.7
F3	2.1±0.31	0.685±0.42	2.64±0.28	103±1.16
F4	2.2±0.29	0.757±0.14	1.73±0.19	101.6±3.92
F5	2.0±0.54	0.832±0.20	2.98±0.31	100.23±3.16
F6	2.4±0.25	0.773±0.16	2.86±0.17	102.01±1.28

Disintegration Time: Key optimization parameter for inclusion complex tablet is disintegration time (<60 seconds). Observed disintegration times ranged from 20 to 50 seconds, with Crospovidone< Sodium starch Glycolate. Increased super disintegrant concentration led to faster disintegration. Wetting time in buccal cavity indicated Crospovidone's superior performance. Batch F5 (10% Crospovidone) exhibited the shortest disintegration time, making it the optimized formulation.

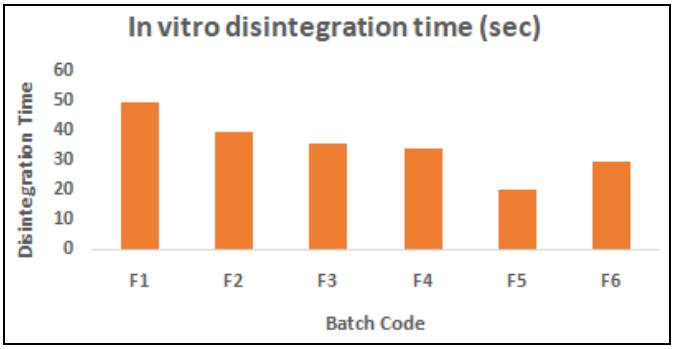

FIG. 20: *IN-VITRO* DISINTEGRATION TIME OF BATCH F1 TO F6

TABLE 19: DISINTEGRATION TIME

Batch code	*In-vitro* disintegration time (sec)
F1	50±1.02
F2	40±1.28
F3	36±2.02
F4	34±1.75
F5	20±0.97
F6	30±1.28

***In-vitro* Dissolution profile:** Disintegration profiles of 6 complex tablet formulations with different ratios of Crospovidone (5, 10, 15) and Sodium starch Glycolate (5, 10, 15) were compared. Among them, Crospovidone 10 showed the best disintegration time in formulation F5.

TABLE 20: *IN-VITRO* DISSOLUTION PROFILE

Time (min)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
10	43.63±0.12	41.25±0.40	55.65±0.22	53.11±0.05	62.37±0.45	58.52±0.10
20	58.38±0.18	53.15±0.43	63.31±0.25	67.42±0.10	75.43±0.42	66.56±0.08
30	66.58±0.15	63.73±0.41	71.50±0.28	80.48±0.08	88.58±0.44	74.68±0.05
40	74.52±0.16	75.70±0.45	80.64±0.24	86.65±0.02	90.29±0.48	85.66±0.03
50	78.54±0.13	83.22±0.46	86.65±0.23	91.50±0.04	92.91±0.46	89.73±0.06
60	89.31±0.14	91.32±0.47	90.55±0.21	92.18±0.06	96.21±0.47	92.62±0.04

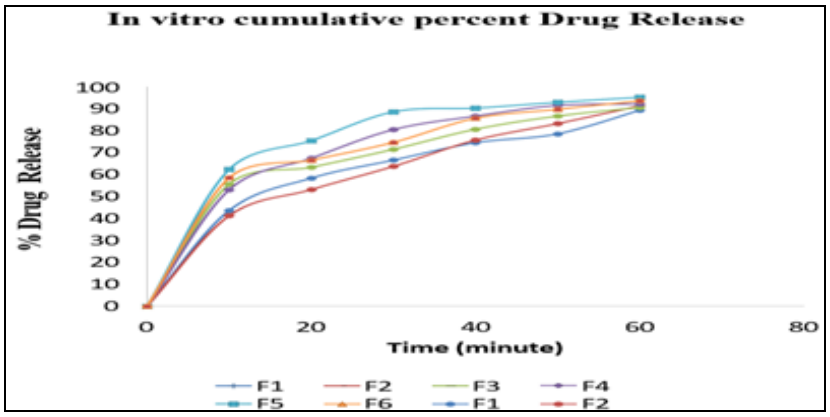

FIG. 21: DISSOLUTION PROFILE OF BATCHES F1 TO F6

Stability Studies: Tablets underwent a 3-month short-term stability study at 40°C / 75% RH. The results indicated no significant changes in physical attributes, drug content, or *in-vitro* drug release rate, ensuring formulation stability.

TABLE 21: STABILITY DATA

Stability period	40 °C / 75% RH			
	Hardness Mean ± SD	% Friability Mean ± SD	% Drug content Mean ± SD	Drug release
Initial	2.05±0.67	0.36±0.01	99.23±0.532	99.413
1 month	2.08±0.49	0.43±0.03	99.35±0.751	99.581
2 months	2.41±0.49	0.56±0.06	98.96±0.792	99.142
3 months	2.33±0.60	0.73±0.03	96.94±0.921	98.728

CONCLUSION: A study focused on creating fast-release Tinidazole tablets using solid dispersions was conducted. Polyethylene glycol 4000 (PEG 4000) and hydroxypropyl methylcellulose (HPMC) were used as carriers. Both solvent evaporation and fusion methods were employed to prepare the solid dispersions. The resulting solid dispersions were fine, free-flowing powders with no observed interaction between the drug and carriers. Uniform drug content was achieved in all dispersions. PEG 4000 showed the highest dissolution rate among the carriers, following first-order kinetics. Capsules containing Tinidazole solid dispersions in PEG 4000 (at a ratio of 1:2) exhibited rapid dissolution compared to pure drug capsules. The study successfully formulated and evaluated solid dispersion tablets, indicating PEG 4000-based solid dispersion (1:2 ratio) as a fast-release Tinidazole dosage form compared to pure drug and other solid dispersion ratios.

ACKNOWLEDGEMENT: Nil

CONFLICTS OF INTEREST: Nil

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