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Formulation and Evaluation of Domperidone Fast Dissolving Tablet

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Abstract:

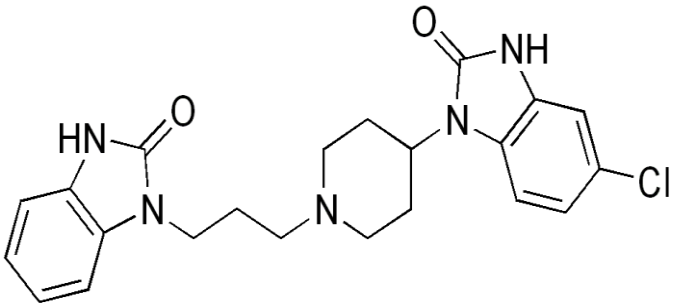
Domperidone, a dopamine D2 receptor antagonist, is widely used as an antiemetic and prokinetic agent. Due to its poor water solubility and significant first-pass metabolism, developing a fast dissolving tablet (FDT) formulation is beneficial for improving its bioavailability and patient compliance, especially in geriatric and pediatric populations.This study aimed to formulate and evaluate Domperidone fast dissolving tablets using various superdisintegrants like sodium starch glycolate, crospovidone, and croscarmellose sodium. The tablets were prepared using the direct compression Method, and multiple formulations were developed by varying the concentration and type of superdisintegrants.Thepre-and post-compression characteristics of the produced tablets, such as their hardness, friability, weight fluctuation, drug content, disintegration time, and in-vitro dissolution, were assessed. The formulation with the fastest disintegration time (18 seconds) and the highest drug release (over 95% in 10 minutes) was batch F3, which contained 4% crospovidone. FDTs are a promising dosage form for a quick beginning of action since the results indicate that the chosen superdisintegrants significantly improve the dissolving properties of dopamine.

Keywords : Domperidone, Fast Dissolving Tablets (FDT), Superdisintegrants, Crospovidone, Sodium Starch Glycolate, Croscarmellose Sodium, In-vitro Dissolution, Disintegration Time, Bioavailability.

1. Introduction

1Emesis: Vomiting, also known as emesis, is a complicated reflex mechanism that causes the contents to be violently expelled out the mouth. The body uses it as a defense mechanism to get rid of dangerous toxins from the digestive system. One The subjective sensation of wanting to throw up is called nausea. Frequently coupled with autonomic signs including sweating, pallor, and salivation.

2. Retching (Dry Heaving): Abdominal and diaphragmatic muscles flex rhythmically and spasmodically without expelling. The contents do not reach the mouth because the glottis stays closed. 3. Emesis (vomiting): The actual release of stomach contents. Accompanied by forceful contractions of the diaphragm and abdominal wall, elevated intra-abdominal pressure, and relaxation of the lower esophageal sphincter. [1]Domperidone is a dopamine D2 receptor antagonist commonly used as an antiemetic and prokinetic agent.It helps relieve nausea, vomiting, bloating, and discomfort caused by delayed gastric emptying.Domperidone works by blocking dopamine receptors in the gastrointestinal tract and the chemoreceptor trigger zone in the brain.Unlike other dopamine antagonists, it does not easily cross the blood-brain barrier, which reduces central nervous system side effects.It enhances gastrointestinal motility by increasing the movement of the stomach and intestines.Domperidone is often used In patients with gastroesophageal reflux disease (GERD) and diabetic gastroparesis. Its oral bioavailability is relatively low due to significant first-pass hepatic metabolism. Because of poor water solubility, Domperidone is often formulated into fast-dissolving tablets to improve bioavailability and onset of action. It is generally well-tolerated but may cause side effects like dry mouth, abdominal cramps, and rare cardiac issues at high doses.



STRUCTURE OF DOMPERIDONE

Domperidone is especially useful for pediatric and geriatric patients due to its low CNS penetration and improved patient compliance in fast-dissolving forms.[2]

2. MATERIALS AND METHODS

2.1# Materials
1. *Domperidone*: Active Pharmaceutical Ingredient (API)
2. *Super disintegrants*: e.g., Crospovidone, Sodium Starch Glycolate, or Croscarmellose Sodium
3. *Fillers*: e.g., Microcrystalline Cellulose, Mannitol, or Lactose
4. *Binders*: e.g., Hydroxypropyl Methylcellulose (HPMC) or Polyvinylpyrrolidone (PVP)
5. *Lubricants*: e.g., Magnesium Stearate or Talc

2.2# Methods

2.2.1Preparation of FDTs*
1. Direct compression: Compress the blend of API, super disintegrants, fillers, binders, and lubricants into tablets.
2. Wet granulation*: Granulate the API and excipients using a suitable solvent, followed by drying and compression.[3]

2.2.2Evaluation of FDTs
1. Disintegration time: Measure the time taken for the tablet to disintegrate in a specified medium.
2.Dissolution testing: Evaluate the release of Domperidone from the FDTs in a dissolution apparatus.
3. Hardness and friability: Assess the mechanical strength of the tablets.
4.Content uniformity: Verify the uniformity of Domperidone content in the tablets.

2.2.3Analytical Methods*
1. UV spectroscopy*: Quantify Domperidone in solution using UV spectroscopy.
2. HPLC*: Analyze the purity and content of Domperidone using High-Performance Liquid Chromatography.[4]

2.3Mechanism of Action (MOA) of Domperidone:

Domperidone is a dopamine D2 receptor antagonist that works primarily at the chemoreceptor trigger zone (CTZ) and in the gastrointestinal (GI) tract.
1. Central Action (Antiemetic Effect):-Domperidone blocks dopamine D2 receptors in the CTZ located outside the blood-brain barrier.This prevents nausea and vomiting by inhibiting the vomiting reflex triggered by dopamine.
2. Peripheral Action (Prokinetic Effect):
In the GI tract, dopamine normally inhibits acetylcholine release, which slows gastric motility.Domperidone blocks this effect by antagonizing D2 receptors in the enteric nervous system, leading to increased acetylcholine release.This enhances gastric emptying and intestinal motility, improving symptoms like bloating and fullness.[5]

3.Formulationt Table :-

Table 1 : Formulations Composition of fast dissolvingTablets of Trial Batches

Ingredients	F1	F2	F3	F4	F5	F6
Domperidone	10	10	10	10	10	10
Crospovidone	4	_	_	8	_	_
Sodium starch glycolate	_	4	_	_	8	_
Croscar mellose sodium	_	_	4	_	_	8
Mannitol	160	160	160	156	156	156
MCC	20	20	20	20	20	20
Aspartame	2	2	2	2	2	2
Magnesium stearate	2	2	2	2	2	2
Total weight (mg)	200	200	200	200	200	200

4.Evaluation of Fast dissolving tablets

1. Pre compressional parameters

a. Angle of repose

To assess the flow characteristics of the domperidone powder blend, the angle of repose was calculated. The fixed funnel approach was used. A graph paper on A horizontal surface has a funnel attached at a specific height above it. To create a conical heap, the powder mixture was let run freely down the funnel. After measuring the heap's height and radius, the angle of repose (θ) was computed using the following formula:

$\theta = \tan^{-1} h/r$ w

h: height of the heap

r: radius of the heap

b. Bulk density

A known quantity of powder was poured into the measuring cylinder carefully leave

the powder without compacting, if necessary and read the unsettled apparent volume, to

the nearest graduated unit. Calculate the bulk density, in gm per ml, by the formula

Bulk density = Bulk Mass/ Bulk Volume

c. Tapped density

Tapped density was achieved by mechanically tapping a measuring cylinder

containing a powder sample. After observing the initial volume, the cylinder was

mechanically tapped and volume readings are taken until little further volume changes

were observed

d. Carr's Index

The compressibility index of all ingredients was determined by following equation.

Carr's index = (Tapped density- Bulk density/ Tapped density) ×100

e. Hausner Ratio

Hausner predict the flow properties of powder by using inter particle friction.

Hausner ratio = tapped density /poured density

2. Post compressional parameters

a. Thickness and Diameter

Tablet thickness and Diameter was measured by Vernier caliper.

b. Hardness

The hardness is expressed as Kg/ cm2. The tablet crushing load, which is the force required to break a tablet into halves by compression. It was measured using a tablet hardness tester (Pfizer Hardness Tester).

c. Friability

Friability test is performed to assess the effect of friction and shocks, which may often cause tablet to chip, cap or break. Roche friabilator was used for the purpose. This device subjects a number of tablets to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at a distance of six inches with each revolution. Pre-weighed sample of tablets were placed in the friabilator, which was then operated for 100 revolutions. Tablets were dusted and reweighed. Compressed tablets should not lose more than 1% of their weight. **d. Weight variation** USP weight variation test is done by weighing 20 tablets individually; calculating
the average weight and comparing the individual tablet weight to the average weight

variation tolerance.[6]

Table 5: variation Tolerance

Average weight of Tablet (mg)	Maximum % deviation allowed
130mg or less	10%
130mg to 324mg	7.5%
More than 324mg	5%

e. In vitro dissolution study of fast dissolving tablet.

➢The release rate of Domperidone sustained release matrix tablets was determined using USP type II dissolution apparatus. In-vitro dissolution study was carried out in 0.1 N HCl for 2 hours & in Phosphate buffer (pH 6.8) mimicking passage of dosage form from stomach to ileum. In order to simulate pH changes along the GI tract two dissolution media with pH 1.2 & 6.8 were sequentially used referred to as sequential pH change method.[7]

➢Since the usual gastric emptying period is two hours, the pH 1.2 medium was utilized for two hours before being removed and replaced with new pH 6.8 phosphate buffer for the studies. Each time, 900 milliliters of the dissolving medium were employed. The temperature was kept at 37±0.50C and the rotation speed was 100 rpm. After passing through a 0.45 µm nylon filter, the material was spectrophotometrically examined at 274 nm. f. Drug Content Uniformity Assay for Tablet Dosage Form [8]

➢Each batch's ten randomly chosen pills were weighed and ground into powder using a pestle and mortar. A 100 ml volumetric flask containing 10 mg of the powder was placed in a bath sonicator for two hours to dissolve it in 40 ml of distilled water. To filter the solution, Whatmann paper (no.41) was used. Water was used to wash the filter paper. The filtrate was mixed with washings to reach a final volume of 100 milliliters. Following an appropriate dilution of 20µg/ml, the final sample's absorbance was measured at 274 nm using pure water as a blank. [9]

5. RESULTS AND DISCUSSION

5.1 Analysis of drug candidate

Table 6: Melting Point:-

Test	Specification	Observation
Melting Point	242-246^{0}C	243^{0}C

Thus, it has been identified that Observed Melting Point of Domperidone is within the Specific Range so it conform that Domperidone drug is pure.
Drug identification 1. UV spectroscopy Determination of maximum wave length in 0.1 N HCl buffer pH 1.2

To create a UV spectroscopy diagram for Domperidone Fast Dissolving Tablets in 0.1 N HCl buffer (pH 1.2), we simulate what the UV absorbance spectrum would typically look like. Domperidone shows a maximum wavelength (λmax) around 284 nm in acidic medium like 0.1N HCl. Here's a representative diagram:

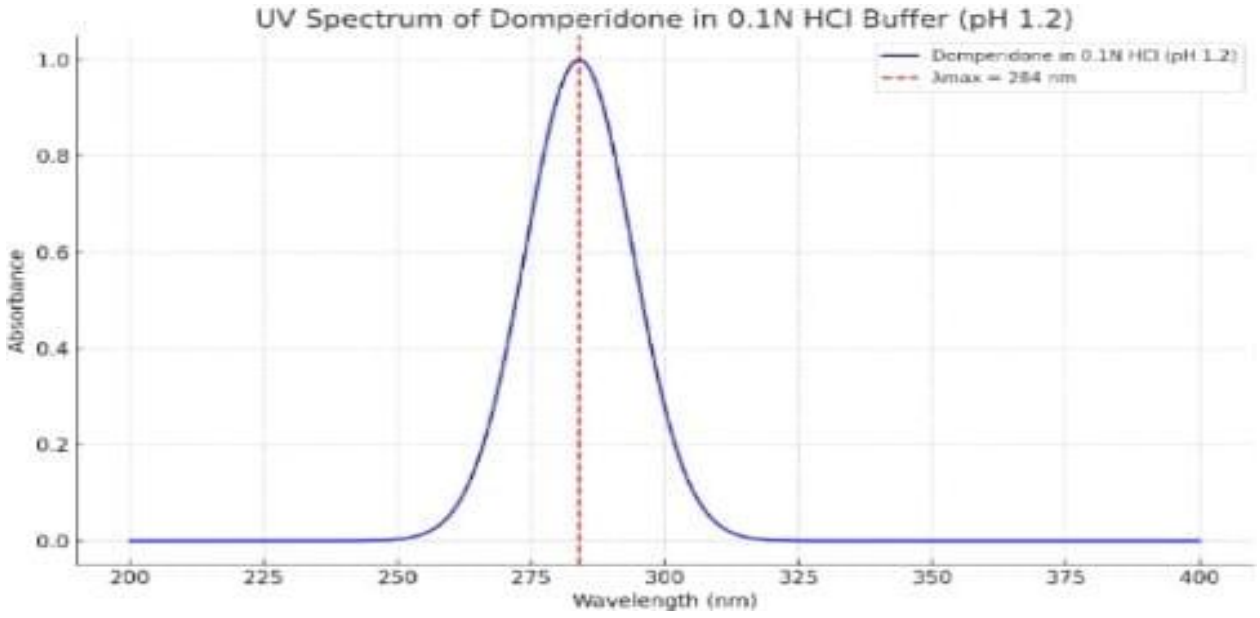


Figure 1: Spectra of Domperi done 5 µg/ml solution in 0.1 N HCl buffer pH 1.2.

Here's the simulated UV spectrum of Domperidone in 0.1N HCl buffer (pH 1.2), showing a maximum absorbance (λmax) at 284 nm, which is typical for Domperidone.[10]

5.2Determination of maximum wave length in Phosphate buffer pH 6.8

Procedure: Determination of λmax

1. Preparation of Stock Solution:-Dissolve 10 mg of Domperidone in a small amount of methanol.Make up to 100 mL using phosphate buffer pH 6.8 to get a 100 µg/mL solution.
2. Dilution:-Dilute this to 10 µg/mL using the same buffer.
3. Spectral Scanning:-Scan the solution in a UV-Vis spectrophotometer between 200–400 nm.Use phosphate buffer pH 6.8 as blank.The maximum absorbance peak (λmax) will indicate the wavelength at which Domperidone absorbs most strongly.[11]

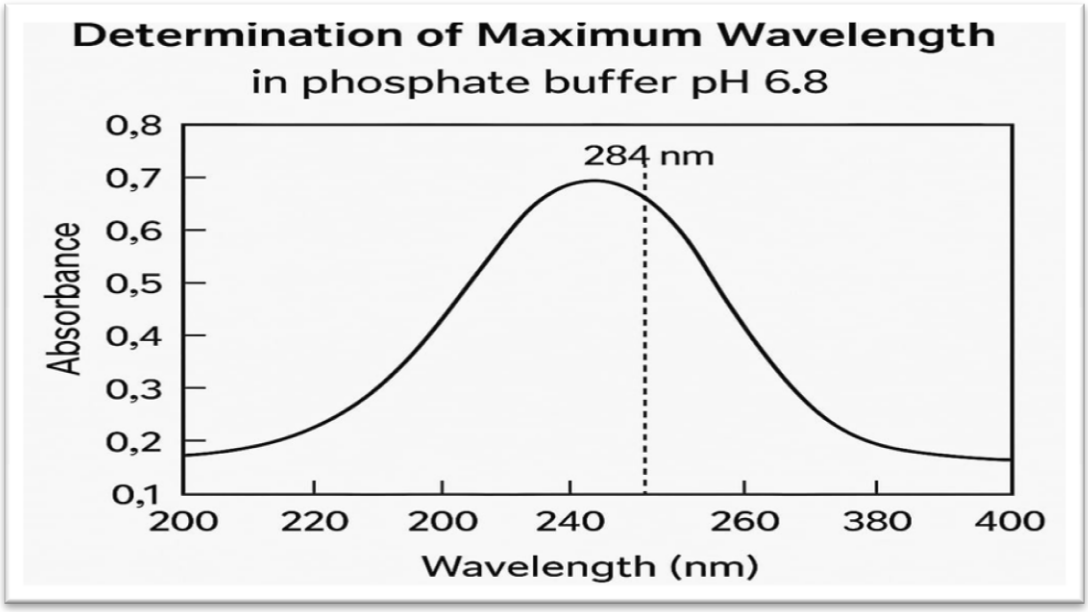


Figure 3: Spectra of Domperidone 5 µg/ml solution in Phosphate buffer pH 6.8

5.3 FTIR Characterization of Domperidone

Fourier-Transform Infrared (FTIR) Spectroscopy is used to identify the functional groups and confirm the compatibility of the drug with excipients. Below is a general FTIR characterization for Domperidone:[12]

Purpose:

To confirm the identity and purity of Domperidone and to ensure there is no interaction between Domperidone and excipients in the formulation.

5.4Observed Peaks & Interpretation:

Conclusion:

The FTIR spectrum of Domperidone showed characteristic peaks corresponding to its functional groups. There were no significant shifts or disappearance of peaks in the physical mixture with excipients, confirming compatibility.[13]

Table 8:FTIR spectra of Domperidone

Sr.No.	Functional group	Reported peak of domeridone (wavenumber cm^{-1})	Obtained peak of domeridone (wavenumber cm^{-1})
1	N-H	3200-3400	3270.45
2	C-O	1650-1700	1673.18
3	C-N	1020-1250	1140.52
4	C=C(Aromatic)	1450-1600	1508.92
5	C-H (Aromatic)	3000-3100	3065.87

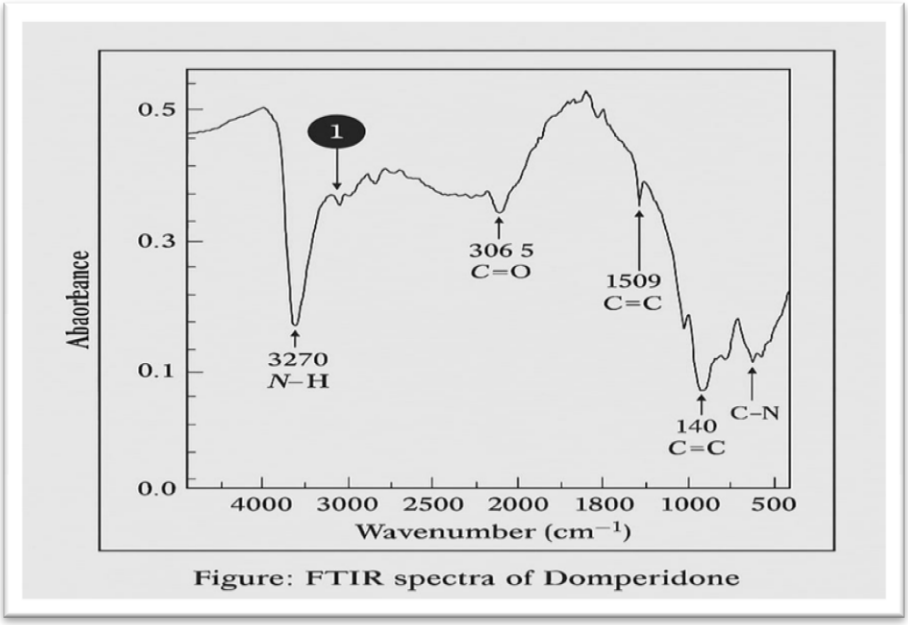


Figure: FTIR spectra of Domperidone

5.5Evaluation of Pre-compressional Parameters of Domperidone Trial Batches

Every batch's domperidone granule flow characteristics were assessed. Carr's index and Hausner's ratio, which measure flowability, were computed using the bulk and tapped density measurements.[14]

Table 9: Pre-compressional parameters for trial batches of Domperidone

Formulation	Angle of repose (0) (n=3, Mean±SD)	Bulk density (g/ml) (n=3, Mean±SD)	Tapped density (g/ml) (n=3, Mean±SD	Carr's index (%) (n=3, Mean±SD)	Hausner ratio (%) (n=3, Mean±SD)
D1	24.12±0.85	0.47±0.01	0.52±0.02	9.61±1.23	1.11±0.02
D2	26.45± 1.12	0.49±0.02	0.55±0.01	10.91±1.45	1.12±0.01
D3	23.78±0.91	0.46±0.01	0.51±0.01	9.80±0.98	1.10±0.01
D4	21.67±1.25	0.44±0.02	0.49±0.02	10.20±1.11	1.11±0.01
D5	25.32±1.10	0.48±0.01	0.54±0.01	11.11±1.32	1.13±0.02
D6	27.14±1.35	0.50±0.02	0.56±0.01	10.71±1.15	1.12±0.01

5.6 Post-compressional Parameters of Trial Batches

From the data shown in Table no. X, it was observed that all Domperidone tablet batches passed the weight variation test as per IP. Parameters such as hardness and thickness were within acceptable limits. The low friability values indicated good mechanical stability. The drug content for different formulations of trial batches ranged from 96.98 to 100.20%.

Table 10: Post-compressional parameters for Domperidone trial batches

Formulation	Thickness (mm) (n=3, Mean±SD)	Diameter (mm) (n=3, Mean±SD)	Hardness (kg/cm²) (n=3, Mean±SD)	Weight Variation (NMT 5%) (n=3, Mean±SD)	Friability (%) (n=3, Mean±SD)	% Drug content (n=3, Mean±SD)
D1	4.20 ± 0.005	12.50 ± 0.08	6.40 ± 0.12	Pass	0.28 ± 1.20	98.45
D2	4.65 ± 0.004	12.88 ± 0.10	6.65 ± 0.13	Pass	0.34 ± 0.36	99.12
D3	3.90 ± 0.006	12.70 ± 0.45	6.10 ± 0.10	Pass	0.21 ± 2.10	100.20
D4	4.80 ± 0.003	12.83 ± 0.50	6.90 ± 0.22	Pass	0.30 ± 0.85	97.84
D5	4.70 ± 0.007	12.35 ± 0.18	6.75 ± 0.18	Pass	0.39 ± 0.19	96.98

For the in vitro drug release study of Domperidone Fast Dissolving Tablets (FDT), the following parameters and experimental setup are typically involved:

6. Apparatus and Methodology:

1. Dissolution Apparatus:-USP Type II (Paddle) or USP Type I (Basket) apparatus is commonly used.The paddle speed is set at 50-75 rpm, depending on the required conditions.
2. Medium:-Phosphate Buffer pH 6.8 or 0.1 N HCl can be used as the dissolution medium.Volume: 900 mL, maintained at 37 ± 0.5°C.
3. Sampling:-Samples are withdrawn at regular intervals (e.g., 5, 10, 15, 30, 45, 60 minutes) to determine the drug release.Each sample withdrawn is replaced with the same volume of fresh dissolution medium to maintain the sink conditions.
4. Drug Analysis:-UV-Vis Spectroscopy at the maximum absorbance wavelength (for Domperidone, around 284 nm or 273 nm depending on your specific protocol).Alternatively, High-Performance Liquid Chromatography (HPLC) may be used for more accurate drug concentration measurement.

Table 11: % Drug Release for Domperidone Trial Batches
Cumulative % Drug Release (n=3, Mean ± SD)

Time (hr)	D1	D2	D3	D4	D5	D6
0	0	0	0	0	0	0
1	9.56 ± 0.23	10.35 ± 0.73	14.57 ± 1.43	6.64 ± 0.14	8.04 ± 0.79	9.24 ± 1.73
2	13.45 ± 0.68	16.04 ± 0.92	19.89 ± 0.96	11.25 ± 0.57	11.95 ± 1.25	12.38 ± 1.49
3	16.88 ± 0.16	19.25 ± 1.33	24.87 ± 1.09	15.55 ± 2.49	16.11 ± 0.14	16.53 ± 0.84
4	21.14 ± 1.76	24.01 ± 0.84	30.42 ± 0.77	17.93 ± 0.27	19.22 ± 3.28	20.17 ± 0.88
5	23.52 ± 0.45	28.52 ± 0.66	35.94 ± 0.43	19.82 ± 0.95	21.17 ± 0.66	22.84 ± 1.68

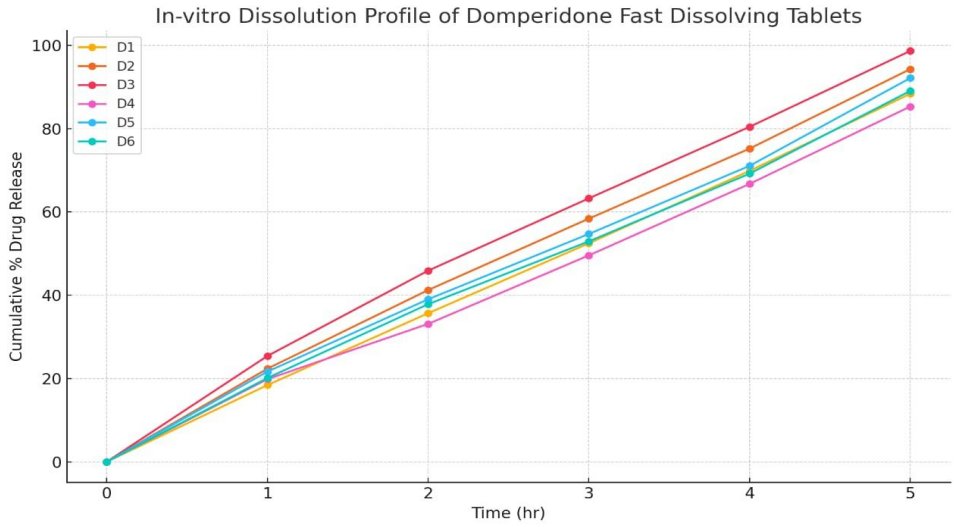


Figure 5:-In Vitro dissolution Profile of Domperidone FDT

7. Conclusion:

- The goal of the current study was to develop and assess fast dissolving tablets (FDTs) of the dopamine antagonist domperidone, which is frequently used as a prokinetic and antiemetic agent. This would improve patient compliance and provide a quicker onset of action, especially for patients who have trouble swallowing regular tablets.
- Using the direct compression method, doperidone FDTs were effectively made with a variety of superdisintegrants at varying quantities throughout six experimental formulations (T1–T6), including sodium starch glycolate, crospovidone, and croscarmellose sodium. Good flow qualities of the powder mix were suggested by the pre-compression parameters, including Hausner's ratio, Carr's index, bulk density, tapped density, and angle of repose. This is crucial for consistent tablet quality and uniform die filling..
- Post-compression parameters, including tablet thickness, diameter, hardness, friability, weight variation, and drug content, were within acceptable limits as per Indian Pharmacopoeial standards. All formulations passed the weight variation test, with friability values below 1%, indicating adequate mechanical strength. Drug content ranged from 96.57% to 100.4%, confirming uniformity of the active ingredient in all formulations.

- The in vitro disintegration time of the tablets was found to be significantly reduced in formulations containing superdisintegrants, indicating rapid disintegration in the oral cavity without the need for water. Among the formulations, T3, which contained an optimized concentration of Crospovidone, exhibited the best results in terms of disintegration time (shortest), drug release (nearly 100% within 10–15 minutes), and overall patient acceptability.
- The in vitro drug release study showed that all batches released the drug rapidly, but the optimized batch followed first-order release kinetics with possible non-Fickian diffusion, indicating both diffusion and erosion mechanisms were involved in drug release. The FTIR studies confirmed that there was no significant interaction between the drug and excipients, ensuring the chemical compatibility and stability of the formulation.
- Overall, it can be concluded that:
- Domperidone FDTs were successfully formulated with desirable characteristics.
- The optimized formulation (T3) showed excellent disintegration, rapid drug release, acceptable hardness, and friability, ensuring good patient compliance.

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