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Fabrication and evaluation of fast dissolving dosage form of Domperidone

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ABSTRACT

Fast dissolving dosage form (FDDF) is designed to allow administration of an oral solid dose form in the absence of water or fluid intake. Such formulation readily dissolve or disintegrate in the saliva generally within <60seconds. Fast dissolving System are useful for pediatric, geriatric, and bedridden patients and for patients who are suffered with Dysphagia. This fast dissolving drug delivery system (FDDS) is suited for the drugs which undergo high first pass metabolism and is used for improving bioavailability with reducing dosing frequency to mouth plasma peak levels, which in turn minimize adverse/side effects. Some drugs are absorbed well from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablet dosage form. Most fast-dissolving delivery system films must include substances to mask the taste of the active ingredient. This masked active ingredient is then swallowed by the patient's saliva along with the soluble and insoluble excipients. The sublingual and buccal delivery of a drug via oral film has the potential to improve the onset of action, lower the dosing, and enhance the efficacy and safety profile of the medicament. In this paper we have compared fast dissolving tablet and fast dissolving oral film.

Keywords: FDDF, FDDS, Fast dissolving tablet, Bioavailability, Fast dissolving oral film etc.

INTRODUCTION

Despite the tremendous advancement in the drug delivery system, oral route is the most preferred route of administration and tablet and capsules are the most preferred dosage form [1-3] but now they experienced several limitations like chocking and swelling discomforts in the geriatric and paediatric patients [4-5]. Among the plethora of avenues explored oral strips gain more attention as it emerging new platform for geriatric and paediatric patients [6-8]. Fast dissolving dosage forms can be disintegrated, dissolved, or suspended by saliva in the mouth. This fast dissolving tablet disintegrates instantaneously when placed on tongue and releases the drug dissolves or disperses in the saliva. Fast dissolving tablets are useful in patients, like pediatric, geriatric, bedridden, or mentally disabled, who may face difficulty in swallowing conventional tablets or capsules leading to ineffective therapy, with persistent nausea, sudden episodes of allergic attacks, or coughing for those who have an active life style. Fast dissolving tablets are also applicable when local action in the mouth is desirable such as local anesthetic for toothaches, oral ulcers, cold sores, or teething, and to those who cannot swallow intact sustained action tablets/capsules.[9] Fast dissolving drug delivery system (FDDS) was introduced in late 1970 as the alternative to conventional tablet, capsule and syrups especially for the geriatric and paediatric patients suffering from the dysphasia problem [10]. Fast dissolving tablets are the solid dosage form which disintegrates rapidly in the oral cavity without the need of water [11-12]. Some problems are associated with the OFDF like they are sometime difficult to carry, storing and handling (friability and fragility), these are prepared using the expensive lyophilisation method [13-14]. To overcome these problems oral films were developed, which are very popular now a days. The concept of oral film

was come from confectionary industry [15-16]. Oral films are the recent ultra thin novel formulation of postage stamp size which contains active pharmaceutical ingredients and excipients. Domperidone is a specific blocker of dopamine receptors. It speeds gastrointestinal peristalsis, causes prolactin release, and is used as antiemetic and tool in the study of dopaminergic mechanisms. Domperidone acts as a gastrointestinal emptying (delayed) adjunct and peristaltic stimulant. The gastroprokinetic properties of Domperidone are related to its peripheral dopamine receptor blocking properties. Domperidone facilitates gastric emptying and decreases small bowel transit time by increasing esophageal and gastric peristalsis and by lowering esophageal sphincter pressure. Antiemetic: The antiemetic properties of Domperidone are related to its dopamine receptor blocking activity at both the chemoreceptor trigger zone and at the gastric level. It has strong affinities for the D2 and D3 dopamine receptors, which are found in the chemoreceptor trigger zone, located just outside the blood brain barrier, which - among others - regulates nausea and vomiting.

MATERIALS AND METHODS

DRUG AND CHEMICALS

Domperidone (Centurion pharmacy, Vadodara), Sodium starch glycolate (SDFCL), Corn starch (SDFCL), Sodium CMC (Ranken F.C.L), Crosspovidone (ACROS ORGANICS), Mg stereate (CDH pvt Ltd), Mannitol (SDFCL), Polyvinyl alcohol (HI-MEDIA), Glycerin (SDFCL), DMSO (SDFCL)

INSTRUMENTS

Electronic weighing machine (Sartorious), UV-VIS spectrophotometer (SHIMADZU), Friability test apparatus EF-2 (NISCO), Dissolution apparatus (VEEGO), Disintegration apparatus (NISCO), Hardness tester (Pfizer type tester).

METHOD

FORMULATION DEVELOPMENT OF FAST DISSOLVING DOSAGE FORM:

Formulation of Fast dissolving tablet by Direct compression method

Each tablet containing 10 mg Domperidone were prepared as per composition given in Table no 12. The drug and excipients passed through sieve no '20' to ensure the better mixing. Mannitol, Crosspovidone, SSG and other excipients were used in different ratio. The powder was compressed by Direct compression machine. 50 tablets were prepared for each batch and the weight of each tablet was 350 mg.

Table no 1: List of ingredients used in the direct compression method

INGRADIENTS	QUANTITY	FUNCTION
Domperidone	10 mg	API
Mannitol	44 - 66 %	Diluent
Sod- CMC	5 – 15 %	Binder
Mg stearate	1%	Lubricant
Talc	3%	Glident
Crosspovidone	1 – 3 %	Superdisintegrant
Sodium starch glycolate	2 – 8 %	Superdisintegrant
Corn starch	3 – 10 %	Antiadherent

OPTIMIZATION OF EXCIPIENTS:

Optimization was carried out for the best results. In the formulation of Fast dissolving tablet the excipients were optimized. The optimized excipients were CMC as binder, Crosspovidone and Sodium starch glycolate was used as superdisintegrating agent and mannitol as a Diluent.

Table no 2: List of excipients which were optimized :

S. NO	EXCIPIENTS	CONCENTRATION
1	CMC	5 %, 10 %, 15 %
2	SSG	2 %, 4 %, 8 %
3	Crosspovidone	1 %, 2 %, 3 %
4	Mannitol	47 %, 56 %, 66 %

FORMULATION TABLE FOR FAST DISSOLVING TABLET:

Table no 3: Composition of fast dissolving tablet of Domperidone

INGREDIENTS (Mg/tablet)	F_1	F_2	F_3	F_4	F_5	F_6
Domperidone	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg
Mannitol	164.5 mg	164.5 mg	197.75 mg	197.75 mg	231 mg	231 mg
CMC	17.5 mg	17.5 mg	35 mg	35 mg	52.5 mg	52.5 mg
Crosspovidone	3.5 mg	-	7 mg	-	10.5 mg	-
SSG	-	7 mg	-	17.5	-	28 mg
Mg stereate	3.5 mg	3.5 mg	3.5 mg	3.5 mg	3.5 mg	3.5 mg
Corn starch	10.5 mg	10.5 mg	10.5 mg	10.5 mg	10.5 mg	10.5 mg
Talc	28 mg	28 mg	28 mg	28 mg	28 mg	28 mg

Formulation of Fast dissolving oral film by Solvent casting method

The oral fast dissolving film of Domperidone was prepared by solvent-casting method. Film forming polymer PVA (polyvinyl alcohol) was dissolved in 10 ml of distilled water by continuous stirring with the help of magnetic stirrer for 2 hrs in 100 ml beaker. After 2 hrs, 1.5 gram of glycerin and dissolved drug (Domperidone in DMSO) was incorporated into the beaker. It was further stirrer for 2 to 3 hrs. Finally the entire mixture was casted into the petri dish and allowed to dry at room temperature. The film was carefully removed from the petri dish, and cut into size of 2 cm^2.

Table no 4: List of ingredients used in the Fast dissolving oral film

INGRADIENTS	QUANTITY	FUNCTION
Domperidone	10 mg	API
PVA	1 – 5 % w/v	Film former
Glycerin	11 – 20 % w/v	Plasticizer
DMSO	1 ml	Drug solubilizing agent
Distilled water	10 ml	Dissolution medium for PVA

OPTIMIZATION OF POLYMER:

In the formulation of Fast dissolving oral film the polymer was optimized. The optimized polymer was PVA which was used as a film forming agent. The concentration of polymer was optimized from 1% - 5 % (w/v).

FORMULATION TABLE FOR FAST DISSOLVING ORAL FILM:

Table no 5: Composition of Fast Dissolving Oral Film of Domperidone

INGREDIENTS	N_1	N_2	N_3	N_4	N_5	N_6	N_7	N_8	N_9
Domperidone	10 mg	10 mg	10 mg	10mg	10 mg	10 mg	10mg	10 mg	10 mg
PVA	0.10gm	0.15gm	0.20gm	0.25gm	0.30gm	0.35gm	0.40gm	0.45gm	0.5gm
Glycerin	1.5 gm	1.5 gm	1.5 gm	1.5 gm	1.5 gm	1.5 gm	1.5 gm	1.5 gm	1.5 gm
DMSO	1 ml	1 ml	1 ml	1 ml	1 ml	1 ml	1 ml	1 ml	1 ml
Distilled water	10 ml	10 ml	10 ml	10 ml	10 ml	10 ml	10 ml	10 ml	10 ml

EVALUATION

PRE-COMPRESSION PARAMETERS OF MOUTH DISSOLVING TABLET:

Bulk density- It was defined as the ratio of total mass of powder to the bulk volume of powder. It was determined by pouring preseived (20 mesh) bulk drug in a graduated cylinder via a large funnel and measured the volume. Bulk density was calculated by the formula.

Bulk density = Weight of powder / Bulk volume

Tapped density- It was defined as the ratio of total mass of powder to the tapped volume of the powder. Weighed 1 gm of drug which was passed through 20 mesh sieve, was transferred in 50 ml graduated cylinder. The cylinder was tapped several times primarily and the tapped volume (V1) was measured to the adjoining graduated units, the tapping was repeated an extra several times and the tapped volume (V2), was measured to the adjacent graduated units. The tapped bulk density in gm/ml was calculated by the following formula.

Tapped density = Weight of powder / Tapped volume

Angle of repose: It was related to the flow property. The friction force can be calculated by this method. It was defined as the maximum angle made between the surface of pile of powder and the horizontal plane.

$\tan \theta = h/r$

The powder mixture was allowed to flow through the funnel fixed to a stand at definite height. The angle of repose was calculated by measuring the height at the radius of heap of the powder form.

Table no 6: Effect of Angle of repose (ϕ) on flow property

S. No.	Angle of repose	Type of slope
1	<20	Excellent
2	20-30	Good
3	30-34	Passable
4	>34	Very poor

Carr's Index or Compressibility- It was related with the flow property. The Carr's index or Compressibility was calculated by the formula.

Carr's index (percentage) = [(TD – BD) × 100] / TD

Table no 7: Effect of Carr's index on flow property

S. No.	Carr's index or compressibility (%)	Type of Flow
1	5-12	Excellent
2	12-16	Good
3	18-21	Fair passable
4	23-35	Poor
5	33-38	Very poor
6	<40	Very very poor

Hausner's ratio: It was defined as the indirect index of ease of powder flow. It is measured by the formula
Hausner's Ratio = TD / BD

Table no 8: Hausner's ratio-

Hausner's ratio	Properties
0 – 1.2	Free flow
1.2 – 1.6	Cohesive powder

EVALUATION OF FAST DISSOLVING DOSAGE FORM

Evaluation of Mouth dissolving tablet

Weight variation: The cause of weight variation can be divided into granules and mechanical problem. If the granule size is large, the dies will not be uniformly filled. Similarly mechanical problem can be traced of lower punches of non-uniform length [16].

Method Uncoated tablets complies this test. The average weight was determined by weighing 20 tablets. Not more than 2 tablets deviate from the average weight by a percentage greater than that given in Table no 16 and no tablet deviate by more than double that percentage. Weight variation tolerance for uncoated tablet is given in Table no 9.

Table no:9 Weight variation specification as per IP

Average Weight of Tablet	% Deviation
80 mg or less	±10
More than 80 mg but less than 250 mg	±7.5
250 mg or more	±5

Tablet Hardness: The strength of tablet was expressed as tensile strength (Kg/cm2). The tablet crushing load, which was the force required to break a tablet into halves by compression .It was measured using a tablet hardness tester (Pfizer Hardness Tester) [16].

Friability testing: The friability were determined using Roche Friabilator. It was expressed in percentage (%). Ten tablets were initially weighted ($W_{Initial}$) and transferred into Friabilator. The Friabilator was operator at 25 rpm for 4 minutes or run up to 100 revolutions. The tablets were weight again (W_{final}). The % friability was then calculated by,

$$F=100\ (W_{Initial} - W_{Final}) / W_{Initial}$$

Wetting time: A piece of tissue paper folded twice and placed in a small petridish containing 10 ml of water. A tablet was placed on the paper and the time for complete wetting was measured.
Water absorption ratio: A piece of tissue paper folded twice and placed in a small petridish containing 10 ml of water. A tablet was placed on the paper and the time for complete wetting was measured. The wetted tablet was again weighted. Water absorption ratio, R, was calculated using the formula;

$$R=100\ (W_{after} - W_{before}) / W_{before}$$

In vitro Disintegration studies: The disintegration time was performed using USP disintegration test apparatus with 6.8 phosphate buffer solution at 37 $\pm 0.5^0$C. Disintegration time was recorded when all the fragments of the disintegrated tablet (6 tablet) passed through the screen of the basket. The time and mean value were reported.

Drug content: For the drug content 10 tablets were powdered and the blend was equivalent to 100 mg of Domperidone was weighted and dissolved in 100 ml of pH 6.8 phosphate buffer solution, stirred for 15 minutes and filtered. 1 ml of filtrate was diluted upto 100 ml with 6.8 pH phosphate buffer. Absorbance of this solution was measured at 287 nm using 6.8 pH phosphate buffer as blank and content of drug was estimated.

In vitro Dissolution studies: It was carried out in 100 ml of pH 6.8 phosphate buffer in dissolution apparatus at 50 rpm. A measured 5 ml amount of dissolution medium was withdrawn at regular interval and diluted up to 10 ml with 6.8 PBS. An equal volume of phosphate buffer was added to maintain the sink condition. Absorbance was measured at 287 nm [17].

Evaluation of fast dissolving oral film:
Visual Inspection: The fast dissolving films were inspected manually for their transparency and air bubble.

Weight variation: The four individual batches of fast dissolving film of size (2x2 cm^2) was weighted on an electronic balance and the average weight was determined.

Thickness: The thickness of film (2x2 cm^2) was measured by using a micrometer screw gauge. The thickness of each film at three different places determined [18,19,20].

Folding Endurance: The folding endurance of patches was determined by repeatedly folding one patch at the same place till it break or up to 300 times without broken. The experiments were performed in triplicate, and average values were reported [21].

Surface pH: For the determination of surface pH combined glass electrode was used. The patches were kept in contact with 5 ml of distilled water for 1 hr. The pH was noted by bringing the electrode near the surface of formulations and allowed it to equilibrate for 1 min.

Weight of film: The fast dissolving oral film were weighted on analytical balance (Shimadzu).

In vitro Disintegration studies: The disintegration time was performed using USP disintegration test apparatus with 6.8 phosphate buffer solution at 37 $\pm 0.5^0$C. Disintegration time was recorded when all the patches (2 x 2 $cm^{2)}$ of the disintegrated film (6 tablet) dissolved or passed through the screen of the basket. The time and mean value were reported

Drug content: A film of 2 x 2 cm^2 was cut and placed in a beaker containing 10 ml of 6.8 pH phosphate buffer solution. The content was stirred in magnetic stirrer to dissolve the film. The content was transferred to a volumetric flask of 10 ml. The absorbance of the solution was measured against 6.8 pH phosphate buffer as a blank solution at 287 nm [17].

In-vitro dissolution studies: The dissolution study was carried out in 100 ml of 6.8 pH phosphate buffer solution. The dissolution study was used to study the drug release from the bilayered and multilayered patches. The dissolution medium consisted of phosphate buffer pH 6.8. The drug release study was performed at $37^{0\pm}$ 0.5°C, with a rotation speed of 50 rpm. Samples (3 ml) were withdrawn at predetermined time intervals of 2 min and replaced with fresh medium. The samples filtered through whatman filter paper and absorbance was taken at 287 nm [22].

RESULTS AND DISCUSSION

PREFORMULATION STUDIES:

Drug Identification-

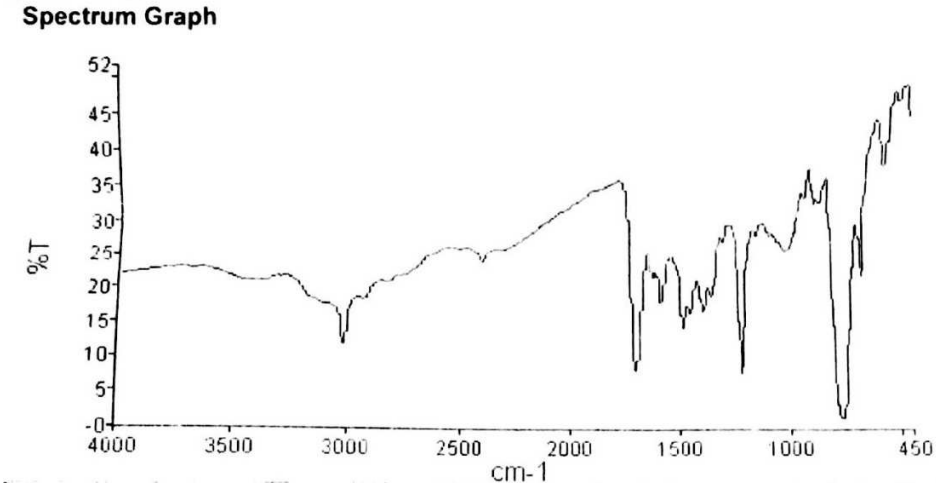

Fig no 1: FT IR spectra of Domperidone

COMPATIBILITY STUDY-

The compatibility studies were performed using IR spectrophotometer.

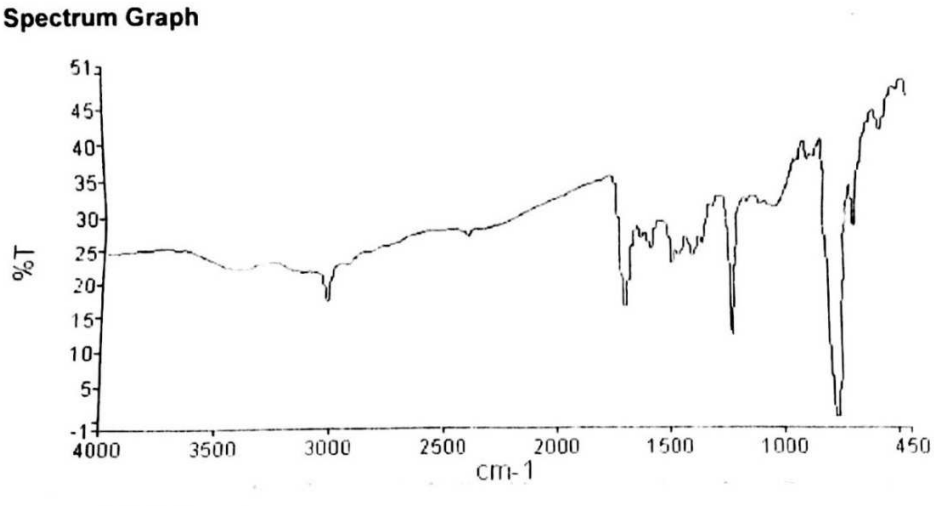

Fig no 2: FT IR spectra of Domperidone + Crosspovidone

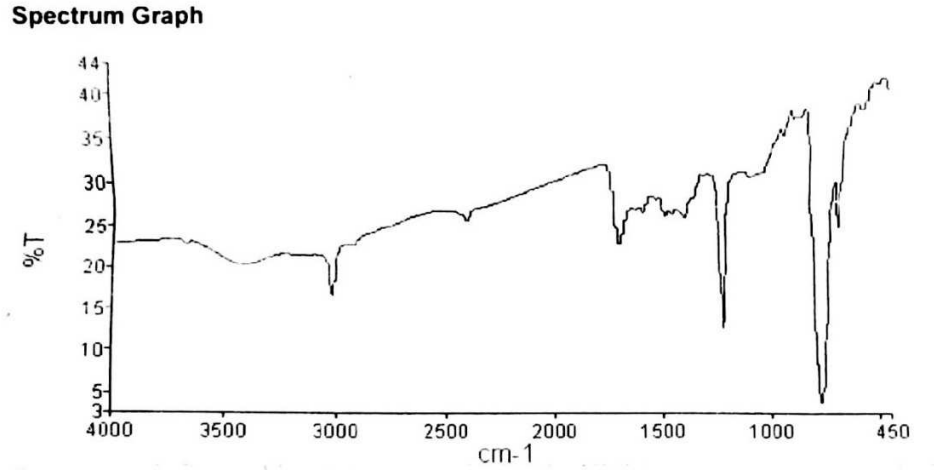

Fig no 3: FT IR spectra of Domperidone + PVA

All the significant peaks of Domperidone were present in the entire spectrum obtained between the drug and excipients. It shows that there was no significant change in integrity of the drug.

CALIBRATION CURVE

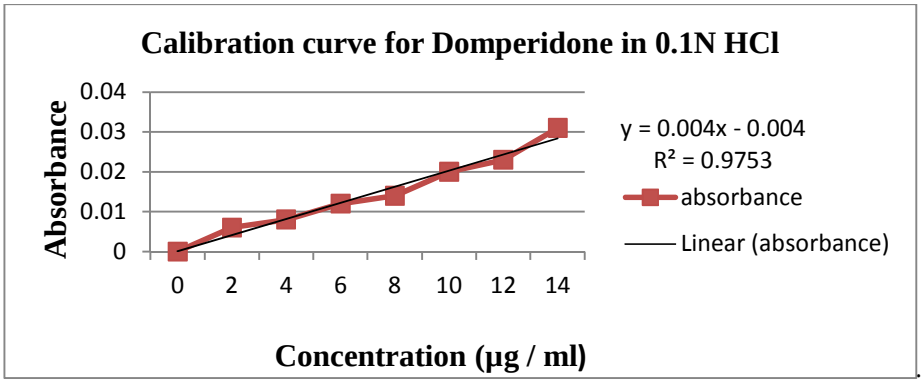

Fig no 4: Calibration curve for Domperidone in 0.1 N HCl at 287 nm

EVALUATION OF PRE-COMPRESSION PARAMETERS OF MOUTH DISSOLVING TABLET:
Bulk density: The bulk density was shown in Table no 10. The bulk density ranged from (0.303 – 0.433) which indicated the good properties of powder blend.

Tapped density: The tapped density was shown in Table no 10 ranged from (0.28 – 0.52). The results of tapped density indicated good flow properties of powder blend.

Angle of repose: The values obtained for angle of repose for all (F_1- F_2) batches was shown in Table no 10. The values were found to be in range from 22.4 – 32.8. This indicated good flow properties of blend.

Carr's Index: The values obtained for Carr's index for all batches was shown in Table no 10. Compressibility value ranged from 13.6 – 20.7 indicated good flow properties of batches F_2 ,F_3 and F_5 and passable flow properties of batches F_1 and F_6.

Hausner's ratio: The values obtained from for Hausner's ratio for all batches was shown in Table no 10, ranged from 0.62 – 1.93 indicated that all batches having good flow properties.

Table no 10: Pre-compression evaluation parameters for Mouth dissolving tablet:

FORMULATION	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Angle of Repose (θ)	Carr's index (%)	Hausner's Ratio (%)
F_1	0.303	0.40	27.9	19.2	0.86
F_2	0.321	0.32	28.3	13.1	0.62
F_3	0.418	0.28	22.4	13.6	1.14
F_4	0.402	0.46	30.2	19.4	1.93
F_5	0.428	0.52	32.8	15.7	1.87
F_6	0.378	0.37	25.6	20.7	1.12

EVALUATION OF POST COMPRESSION STUDIES OF DOMPERIDONE MOUTH DISSOLVING TABLET-
Shape of the tablet: Microscopic examination of all batches of formulation showed circular shape without any cracks.

Hardness test: The measured hardness of tablets of each batch was shown in Table no 11 and the range between 2.9 kg/cm^2 to 4.1 kg/cm^2. The hardness was increased with the compression force. This ensures good handling characteristics of all batches.

Friability test: The values of friability test were shown in Table no 11. The friability range was between 0.61 % to 0.95 %.The friability values was not more than 1% in all the formulation which ensuring that the tablets were mechanically stable.

Wetting time: The wetting time of the tablets was given in Table no 11. The wetting time obtained from the direct compression method was in range of 24 – 32 sec. These result shows that the disintegration time was good.

Water absorption ratio: The water absorption ration was given in Table no 11. The water absorption ration from the direct compression method was between 9.1 – 12.3 %. This method shows that the water absorption ratio was within limit.

Weight variation: The percentage weight variation for all formulation was within Pharmacopoeia limits. The limit was ±5%. All the formulations passed weight variation test as per I.P limits. The weights of all the tablets were found to be uniform.

Disintegration time: The in-vitro disintegration time of the tablet was given in the Table no-21. The in-vitro disintegration time obtained from direct compression method was between 32 – 37sec. The formulation showed that the disintegration time was within the limit particular in Pharmacopoeia.

Drug content: The percentage of drug content was found to be in range of 88.3 – 98.4 of Domperidone, which was within acceptable limits. Table no 21 showed the results of drug content uniformity in each batch.

In-vitro drug release: The in-vitro dissolution time was 25 minutes in which 98.5 % drug was released for formulation F_5. Therefore formulation no F_5 showed better in-vitro drug release within 25 minutes.

Table no 11: Physical properties of all formulation of Mouth dissolving tablet (F_1 - F_6):

Formulation	Hardness (Kg/cm^2)	Friability (%)	Disintegration Time (sec)	Water absorption ratio (%)	Wetting Time(sec)	Drug Content (%)
F_1	3.8	0.77	35	11.2	25	93.6
F_2	3.2	0.75	38	12.3	29	96.8
F_3	3.6	0.95	33	12.1	24	95.1
F_4	2.9	0.74	37	11.3	32	92.7
F_5	4.1	0.61	32	9.1	22	98.4
F_6	3.3	0.76	41	10.7	30	88.3

DISSOLUTION PROFILE FOR MOUTH DISSOLVING TABLET:

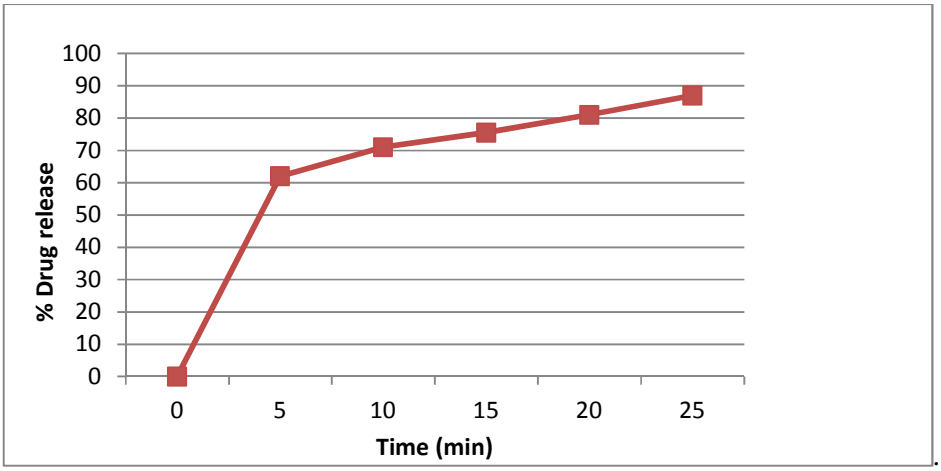

Fig no- 5: Drug release profile of formulation F_1

Dissolution profile of Formulation F_2

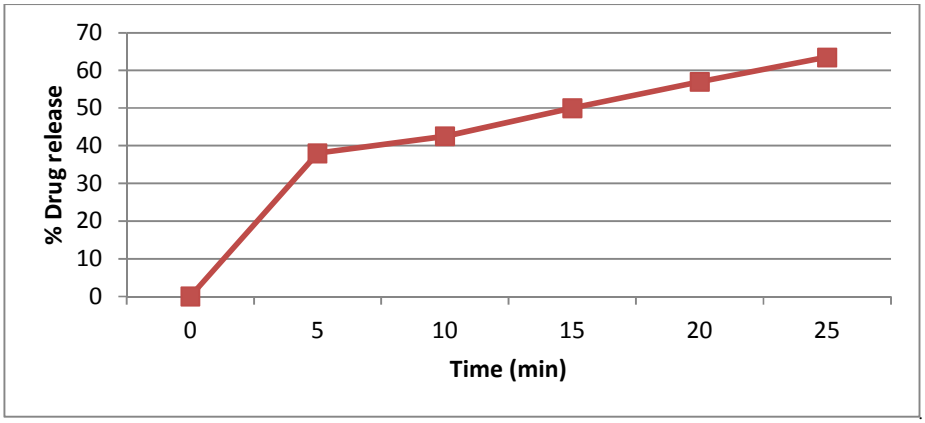

Fig no 6: Drug release profile of formulation F_2

Dissolution profile of Formulation F_3

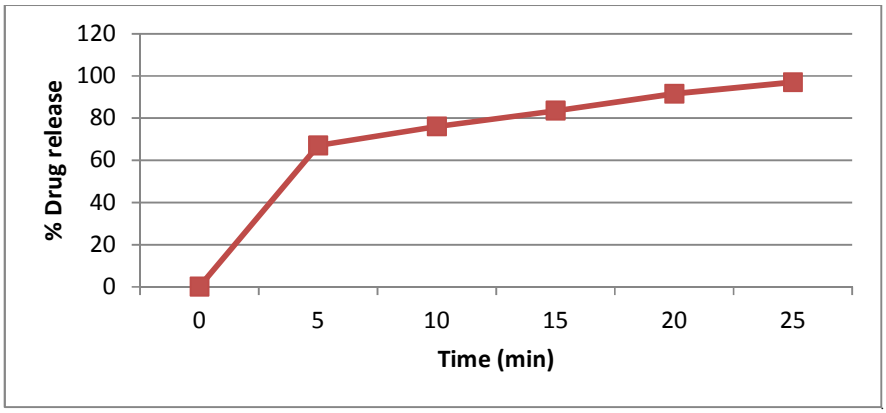

Fig no 7: Drug release profile of formulation F_3

Dissolution profile of Formulation F_4

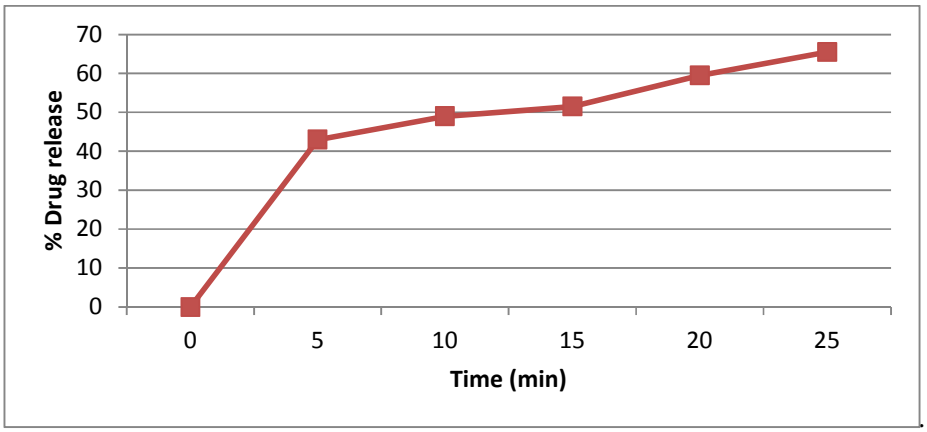

Fig no 8: Drug release profile of formulation F_4

Dissolution profile of Formulation F_5

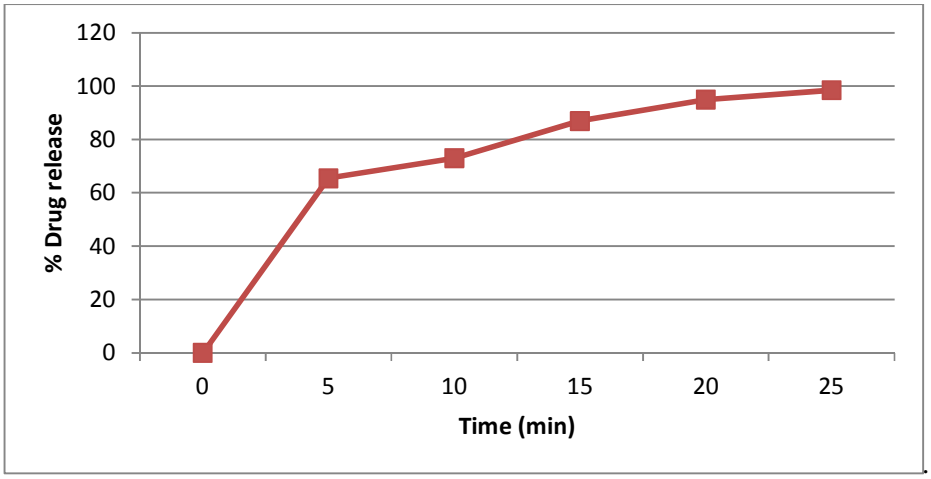

Fig no 9: Drug release profile of formulation F_5

Dissolution profile of Formulation F_6

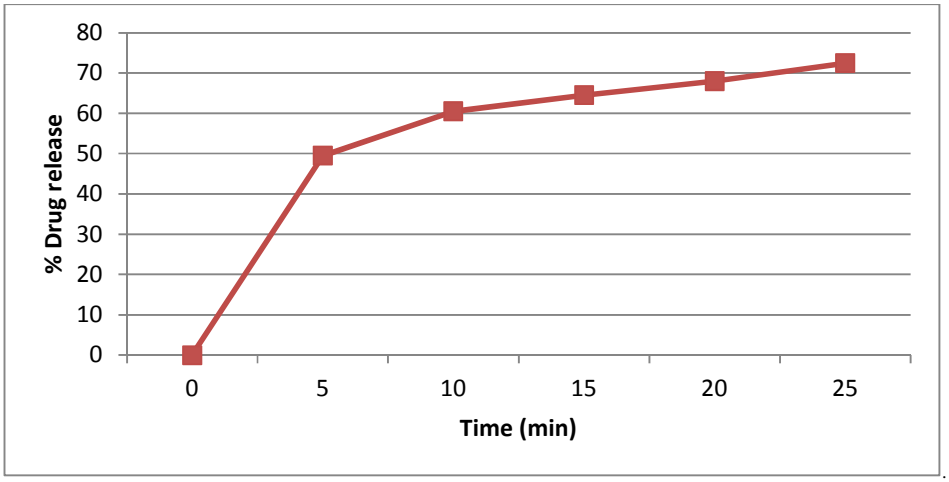

Fig no 10: Drug release profile of formulation F_6

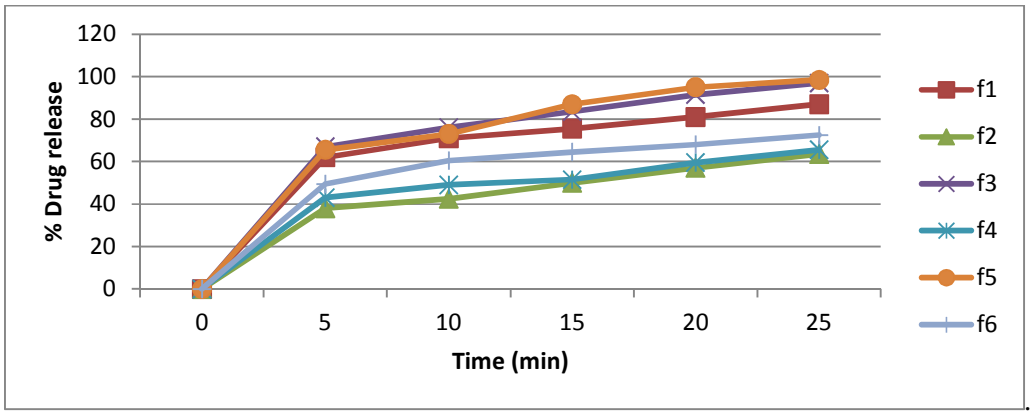

Fig no 11: Comparative percentage Drug release vs. Time for all batches of MDT

The comparative percentage Drug release was shown in Fig no 11. Among all the formulation, F_5 formulation achieved maximum percentage drug release at the end of 25 minutes. Therefore formulation F_5 was the best formulation for Mouth dissolving tablet of Domperidone.

EVALUATION PARAMETERS OF FAST DISSOLVING ORAL FILM:

Visual Inspection: The visual Inspection was carried out manually which showed in Table no 12. Formulation N_3 and N_4 were transparent but formulation N_1 and N_6 were semi transparent.

Weight of film: As the weight of polymer increased, the weight of film was also increased. Weight of the film of N_2 - N_6 was found in range of 83 mg – 125 mg. Minimum weight of the film was found of the N_2 formulation which was 83 mg and the maximum weight of the film was 125 mg of N_6 formulation shown in Table no 12.

Folding endurance: The folding endurance of the film formulation by solvent casting method was found to be in range of 104 – 150. The result was shown in Table no 12.

Thickness: Thickness of the film was found in increasing order. As polymer concentration increased the thickness of the film also increased as shown in Table no 12. Film thickness of formulation N_2 – N_6 was found to be in range of 137 - 194µm.

Disintegration time: Disintegration time was found in range of 28 second to 37 seconds shown in Table no 12. Disintegration time for formulation N_4 was found 28 seconds as fastest and for N_6 was 37 seconds as slowest.

Surface pH : The pH of the film was found in the range of 6.3– 7.5 for all formulation. The result was showed in Table no 12.

Drug content: The percentage of drug content was found to be in range of 89.7 – 98.6 of Domperidone, which was within acceptable limits. Table no 12 showed the results of drug content in each batch.

Dissolution studies: The dissolution studies of the formulation batches from N_2 – N_6 were carried out to know the in-vitro drug release. The drug release at different time intervals was determined and calculated to know the release at variable concentration of polymer used. The results were converted in form of % drug release. For formulation N_4 the dissolution time was 10 min in which 98.7% drug was release.

Table no 12: Evaluation tests for Fast dissolving film

Batch	Visual appearance	Thickness of film (µm)	Disintegration Time (sec)	Folding endurance	Weight of Film (mg)	pH	Drug Content (%)
N_2	Semi Transparent	137	30	104	83.0	7.2	89.7
N_3	Transparent	156	32	127	98.3	6.3	95.2
N_4	Transparent	175	28	148	107.6	6.1	98.6
N_6	Semi Transparent	194	37	150	125.0	7.5	97.3

DISSOLUTION PROFILE FOR FAST DISSOLVING ORAL FILM OF DOMPERIDONE.

Dissolution profile of Formulation N_2

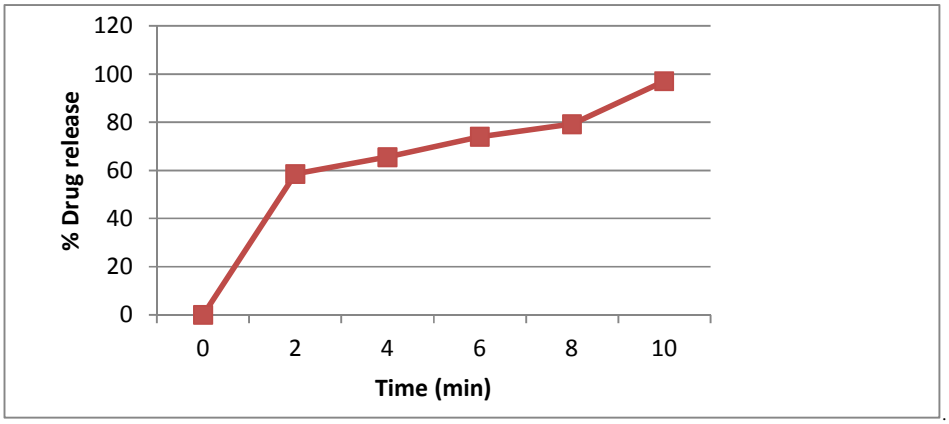

Fig no 12: Drug release profile of formulation N_2

Dissolution profile of Formulation N_3

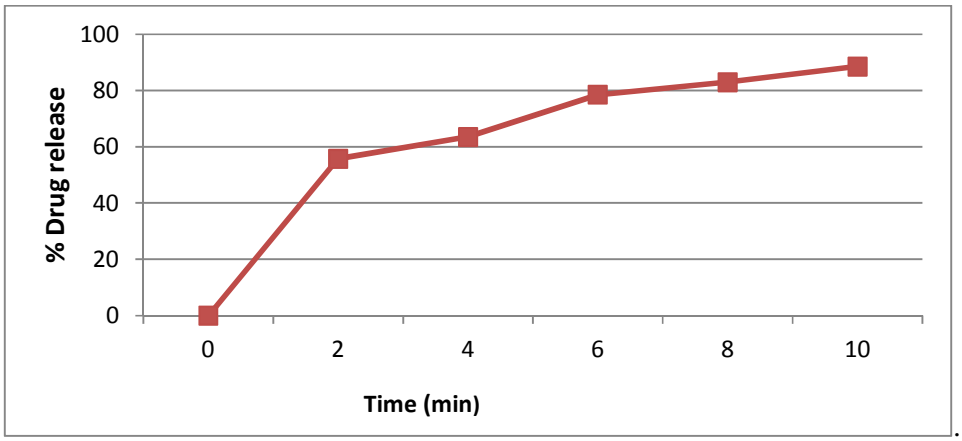

Fig no 13: Drug release profile of formulation N_3

Dissolution profile of Formulation N_4

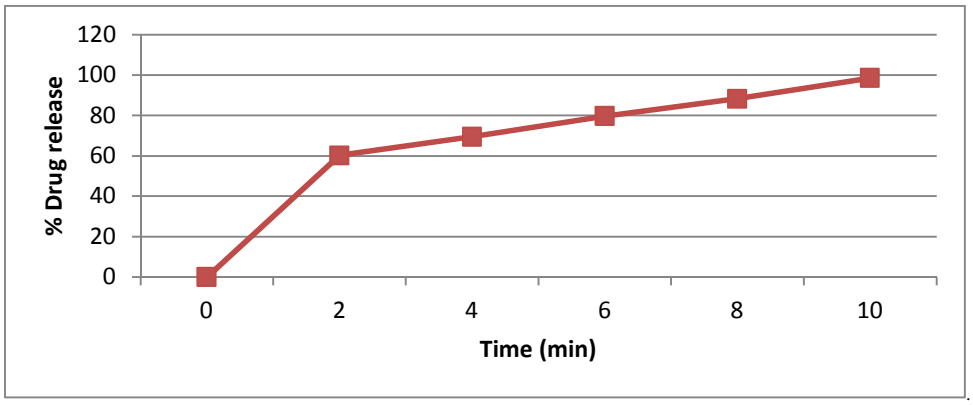

Fig no 14: Drug release profile of formulation N_4

Dissolution profile of Formulation N_6

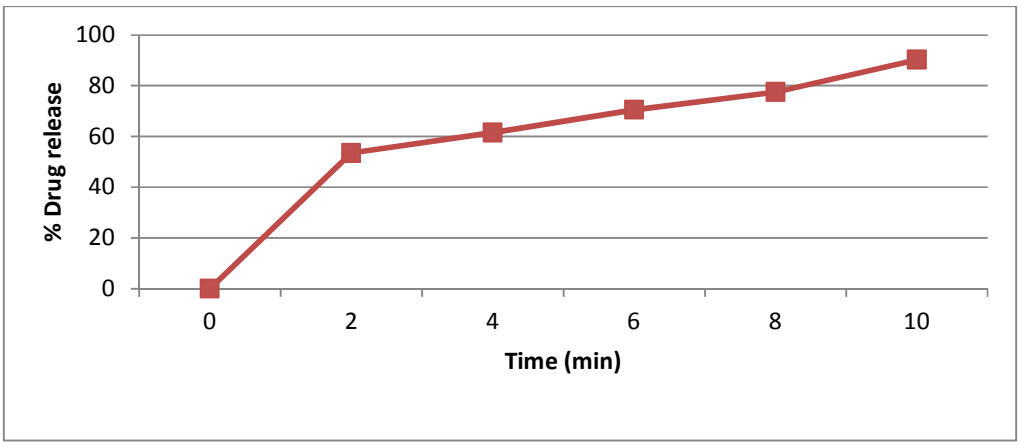

Fig no 15: Drug release profile of formulation N_6

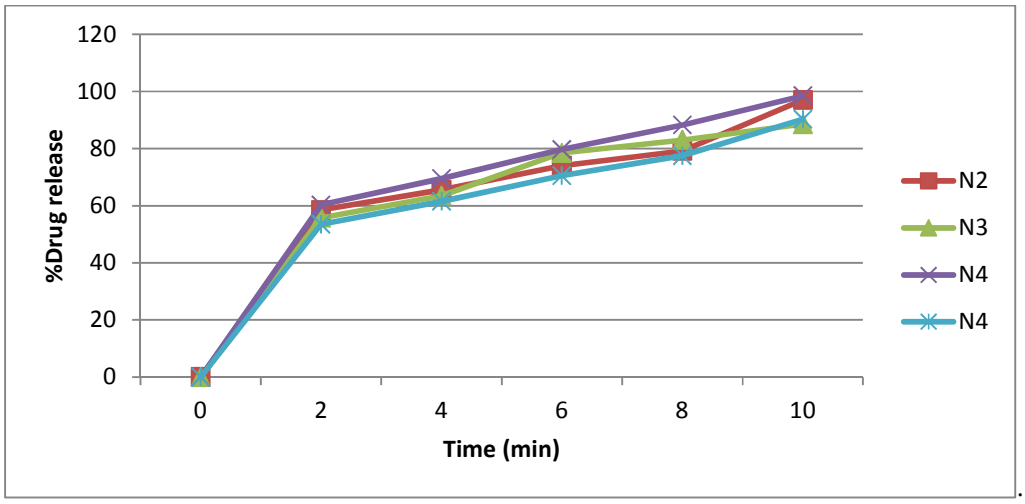

Fig no 16: Comparative percentage Drug release vs. Time for all batches of Fast dissolving film

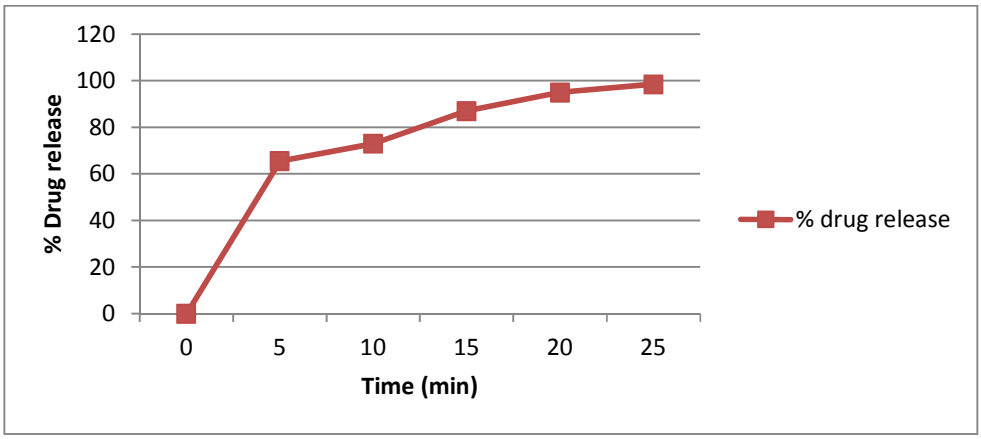

Fig no 17: Drug release profile of batch F_5

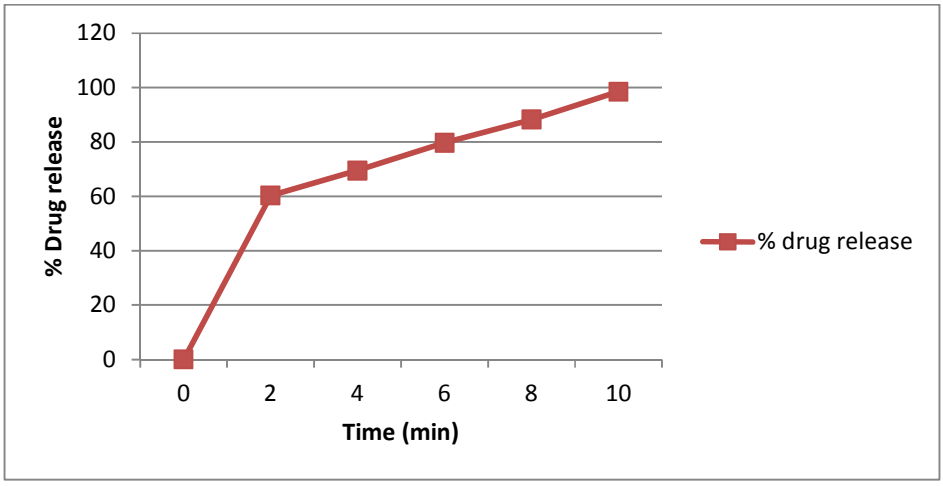

Fig no 18: Drug release profile of batch N_4

The comparative percentage Drug release was shown in Fig no 16. Among all the batches, N_4 batch achieved maximum percentage drug release at the end of 10 minutes. Therefore formulation N_4 was the best formulation for Fast dissolving oral film of Domperidone

The drug release for the batch F_5 (MDT) was 98.5 % at the end of 25 minutes, where the drug release for the batch N_4 (MDF) was 98.7 % at the end of 10 minutes. Hence Fast dissolving film is producing rapid action in comparison to Mouth dissolving tablet and provide fast relief in case of nausea and vomiting.

DISCUSSION

The Mouth dissolving tablets of Domperidone were prepared by Direct compression method. Formulation of tablets was carried out using different types of superdisintegrating agents and excipients. The optimization of concentration of excipients and superdisintegrants was carried out for hardness of the tablet to give the least disintegration time and get greatest drug release. The taste and odour was acceptable for the geriatric and pediatric patients. Domperidone drug was used as an anti-emetic drug because of best relief in the nausea and vomiting.

The Fast dissolving oral film of Domperidone was prepared by Solvent casting method. Formulation of film was carried out using film forming polymer (PVA), plasticizer, DMSO and distilled water. The optimization of concentration of polymer was performed for least disintegration time and good drug release as well. Taste and odour was acceptable for both types of patient like geriatric and pediatric. The obtained calibration curve was straight line. The curve was obtained in 0.1N HCl at the maximum wavelength of 287 nm. The slope, intercept and regression coefficient were obtained from the graph. The calculation of in-vitro drug release study was based on the calibration curve.

Compatibility studies of Domperidone with different excipients and polymer were carried out prior to the preparation. All the significant peaks of Domperidone were present in the entire spectrum obtained between the drug and excipients. It shows that there was no significant change in integrity of the drug.

CONCLUSION

The aim of this study was to Fabricate and Evaluate the Fast dissolving dosage form of Domperidone drug as an anti-emetic drug. The direct compression method was used for the formulation of Mouth dissolving tablet and Solvent casting method was used for the formulation of Fast dissolving oral film of Domperidone. The Mouth dissolving tablet and Fast dissolving oral film both are beneficial for geriatric and pediatric patients. The Crosspovidone as Superdisintegrant shows better results in compare to Sodium starch glycolate for Mouth dissolving tablet. Therefore F_5 formulation is the best formulation of Mouth dissolving tablet among all formulations. The disintegration time and in-vitro drug release is good. About 98.5% drug was released within 25

minutes by direct compression method. For the Fast dissolving oral film formulation N_4 is the best formulation among all formulation. The disintegration time and in-vitro drug release is good. About 98.7% drug was released within 10 minutes by Solvent casting method. The percent drug release of Mouth dissolving tablet (F_5) was 98.5 % at the end of 25 minutes and disintegration time was 32 seconds where the percent drug release of Fast dissolving film (N_4) was 98.7 % at the end of 10 minutes and the disintegration time was 28 seconds. Therefore on the basis of percentage drug release and disintegration times the Fast dissolving film of Domperidone was produce rapid action and provide relief in case of nausea and vomiting.

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