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FORMULATION AND EVALUATION OF DOMPERIDONE MOUTH DISSOLVING TABLETS

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ABSTRACT

Key Words

Crospovidone; Croscarmellose sodium; Domperidone; Oro dispersible tablets.



Oral medication conveyance is the most prominent defeat. It is outstanding since quite a while for its generally utilized course of organization among all the failure that has been investigated for the precise conveyance of medication arranged different measurements from the pharmaceutical items. Dysphagia is a typical issue which needs to look in all times of gatherings in worry to strong dose shapes. The patient needs to improve consistency to take care of the problem of Dysphagia. The mouth dissolving tablets have risen as an option in contrast to regular oral medication use. Based on present work, Orodispersible tablets of domperidone were structured to expand technique, crospovidone (2-6% w/w) croscarmellose sodium (2-6% w/w). And in the blend as super deteriorates were utilized alongside straightforwardly miniaturized scale crystalline cellulose to improve mouthfeel. The tablets for clumps arranged were assessed for hardness, friability, sedate substance, consistency, wetting time and water assimilation proportion and in vitro diissolution time. In light of in vipro scattering time (Approximately 7-30 s), All detailing were tried for in vitro medication discharge design (in phosphate cradle). Check the momentary security (for three months at 40 degree centigrade/75% RH), and medication excipient connection contemplate. Among all the definition, the definition arranged by 4% croscarmellose was found to have the least scattering time 7.36 s. Momentary dependability examines the best detailing showed that there were no significant changes in medication content and in vitro scattering time.

INTRODUCTION

Mouth dissolving tablets (MDT): These are the tablets which dissolve or disintegrate rapidly within the spit to produce their activities within a few seconds without the help of water. A mouth dissolving tablet mainly dissolves in the mouth over 15seconds-3minutes.

Primarily the MDT's (mouth dissolving tablets) have superb disintegrates and flavour masking agents. To solve this difficulty mouth dissolving tablets are formulated. For mouth dissolving tablet formulation, the principal criteria are to get rid of the bitterness of this tablet by

incorporating the sweetening agent or from sugar coating on the tablets. To overcome this problem and to create the dental route is more suitable for patients that a new drug delivery method is evolved known as oral dissolving drug delivery method or dispersible or mouth-melt etc. These mouth dissolving tablets should dissolve or disintegrate rapidly in the mouth within a few seconds without needing water, chewing with the help of saliva within the mouth. Time to get MDT disintegration dissolving tablets) generally assumed to be less than 1 min. The patients can feel that the standard disintegration time of MDT dissolving tablets) from 5-30sec. MDT's (mouth dissolving tablets) are mainly prepared by various techniques like direct compression, wet granulation, solid dispersion, and tablet molding, etc... The direct compression method is the most frequently used and simplest or costeffective way of MDT (mouth dissolving tablets) compared to other methods. Domperidone is used anti-emetic drug. It dopaminergic inhibit receptor. Domperidone does not cross blood brain barrier. Domperidone is also effective in gastroparesis, paediatric gastroesophageal reflux (infant vomiting). Domperidone after oral dosing It have bioavaibality (15%) which therefore, may not minimize the rate of vomiting. The formulated domperidone tablets of will characterized for various parameters like hardness, friability, disintegration, wetting and in vitro dissolution

Materials and Method: Domperidone was a gift from ambark life science (roorkee, U.K.), Other ingredients like mannitol, crospovidone, croscarmellos, aspartame, and MCC was gift from GS Pharmaceutical Paonta himachal pradesh, india as a sampils. All other reagents and chemicals used were of analytical grade.

Preparation of domperidone fast dissolving tablets: Accurately weighed the quantity of domperidone,

crospovidone, croscarmellose sodium, and microcrystalline sodium other ingredient and passed in 44 mesh sieve. The drug and microcrystalline cellulose were taken in a mortar and mixed and blending it to get a uniform mixture and kept aside. After this procedure, the other ingredient was mixed in geometrical odour passed through 44 mesh sieve. The tablets were compressed using a hydraulic press. And the adjusted the compression force of machine to obtain the hardness in the range 3—4 kg/cm2 for all batches. The weight of tablets of the formulation was 150 mg mention in (table no. 3).

Evaluation of domperidone fast dissolving tablets:

Pre formulation studies:

Angle of Repose: Its significant parts of the tablet definitions are the point of rest of granules was controlled by the pipe technique. The precisely gauged granules were taken in a pipe. The stature of the channel was balanced so that the tip of the pipe contacts the zenith of the pile of the granules. The granules were allowed to flow through funnel freely onto the surface. The diameter of the powder cone was measured, and the angle of repose was calculated using the following equation101, 102.

Tan q = h / r

Hence, q = tan-1 h/r

Where, q = angle of repose

h = height of the cone

r = radius of the cone base

The results are shown in Table 14 and 15

Bulk Density and tapped density: Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. A quantity of 2 g of powder from each formula, previously lightly shaken to break any agglomerates formed, was introduced

into a 10 ml measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its weight onto a hard surface from the height of 2.5 cm at 2-second intervals. The tapping was continued was until no further change in volume was noted102. LBD and TBD were calculated using the following formulas:

LBD = Weight of the powder/ Volume of the

Packing

TBD = Weight of the powder/ Tapped volume of the packing

Compressibility Index: The compressibility of the granules was determined by Carr's Compressibility Index102, 103.

Carr's compressibility index (%) = [(TBD-LBD) X 100]/TBD

Or it can be expressed as Carr's Index relates the poured density of the material to the tapped density and was calculated by using the following relationship:

Carr's Index=Tapped density-Poured density/ Tapped density X 100

Carr's Index values for pure drug, guar gum, and granules were determined by measuring the initial volume (Vp) and final volume (Vt) of known weight (W) of material after subjecting to 100 tapings in a graduated measuring cylinder. From these volumes, the poured density (W/Vp) and the tapped density (W/Vt) values were calculated and were substituted in the above equation to determine Carr's Index.

EVALUATION OF PHYSICOCHEMICAL PROPERTIES OF TABLETS

Thickness: The thickness of tablets was determined using Venire calliper. Five tablets from each batch were used, and

average values were calculated10, 104. The result is shown in Table 15.

Weight variation Test: To study weight variation, 20 tablets of each formulation were weighed using an electronic balance (AW-220, Shimadzu), and the test was performed according to the official method 10, 105 (Table 15).

Drug content: Four tablets were finely powdered; quantity equivalent to 50 mg of Domperidone was accurately weighed and transferred to 100 mol volumetric flask containing 50 mol of methanol. This was allowed to stand for six h to ensure complete solubility of the drug. Solutions were made up to volume, filtered, suitably diluted, and estimated for Domperidone contents at 284 nm, using a UV-visible spectrophotometer using methanol as blank106,107.

Hardness: For each formulation, the hardness of 6 tablets was determined using the Monsanto hardness tester (Cad match). The tablet was held along its oblong axis in between the two jaws of the tester. At this point, reading should be zero kg/cm2. Then constant force was applied by rotating the knob until the tablet fractured101 (Table 15).

Friability: It is a measure of tablet strength. It is related to tablet ability to withstand both shock and abrasion without crumbling during the handling manufacture, packing, shipment consumer use108 (Table 15). Method: 6 matrix tablets were weighed and placed in Roche's Friabilator where the tablets were exposed to rolling, and repeated shocks are resulting from free falls within the apparatus. After 25 revolutions, the tablets were de-dusted and weighed again. The friability was determined as the percentage loss in the weight of the tablets. A loss of less than 1 % in weight is generally considered acceptable.

In-Vitro Release Studies (Dissolution study)

In-vitro drug release study for the prepared matrix tablets was conducted for 10-12 hours using a six-station USP XXVI type II (paddle) apparatus at $37^{\circ}C \pm 0.5^{\circ}C$ and 50 rpm speed. The dissolution studies were carried out in triplicate for 8 hours in phosphate buffer of pH 6.8 under sink condition107. At first half, an hour and then every 1- hour interval samples of 5 ml were withdrawn from dissolution medium and replaced with fresh medium to maintain the volume constant. After filtration and appropriate dilution, the sample solution was analyzed at 284 nm Domperidone by a spectrophotometer for determining its cumulative % drug release or amount present in the sample.

Disintegration test: USP was used to perform the disintegration test is taken water at 27+ 050C in disintegration apparatus. The take six tablets, the tablets completely disintegration time noted.

Data Analysis (Curve fitting analysis):

To determine the mechanism of drug release rate kinetics of tablets and the data obtained was plotted as: The Vs of time and Cumulative percentage of drug release (In vitro drug released plots). The Vs of Square root of time and Log Cumulative percentage drug release (Higuchi, splots). The Vs of time of the log Cumulative percentage drug remained (First-order plots). The Vs of time of the loge percentage drug release (Peppas plots).

Higuchi released model:

It represents the equation as, F = K .t1/2

Where,

F =The amount of drug release

K =the release rate constant

T = Release time

When the data are plots between cumulative drug release and the square root of time. The straight line produces. It is indicated that the drug was released by diffusion mechanism. The slope is equal to 'k'90.

Kasmeyer and Peppas release model

The following equation was fitted to the release rate data, Mt $/M\infty$. = K. in

Where,

Mt $/M\infty$ = Fraction of drug release, K = Release constant, 't' = Release time

When the data plots between the log of drug release and a long time, a straight line are obtained with a slope equal to 'n' and 'k' can be obtained from Y-intercept.

Zero-order release rate kinetics: The study the release rate dada was fitted to zero-order release kinetics in the following equation,

$$F = K.t$$

Where, F = Release fraction, K = Release rate constant, t = Release time

When data are plotted between cumulative per cent drug release and time. If the plot is liner than the data obeys zero-order release kinetics, with a slope equal to K0.

In vitro dispersion time: Take 10 ml of distilled water, Tablets are added in distilled water at 37 + 0.50C. Determined the tablets for completes dispersion at time require.

Wetting time and water absorption ratio: It is determined by; take 5 cm culture dish with solvent. Two-piece of tissue paper is placed in the dish. The tablets are put on the surface of tissue paper. After some time, the red colour is produced on the surface of tablets, the time is noted. It is a wetting time. The same procedure is followed for the water absorption ratio.

Stability The studies: selected formulation (HC2 & HC3) was tested for 3 Months at the storage conditions. At room temperature and 40°C at 75% RH, were analyzed for their drug content105. The residual drug contents of formulations were found to be within the permissible limits, as shown in the Table. The tablets showed satisfactory physical stability at room temperature and 40°C at 75% RH. No appreciable changes were found in any of the formulations. The tablets were also subjected to IR studies to determine compatible the drug with the recipients used in the tablets. The IR studies showed that there are no interactions between the drug and polymers 109.

RESULT AND DISCUSSION

Evaluation of pre-compression parameter of all formulation:

- **A) Bulk density:** The Ascertain worth of bulk density of formulation was Cite in the table 3. The obtained values are 0.478 -- 0.538 gm/cm2.
- **B) Tapped density:** The ascertain values of exploited density of formation were cited in the table3. The obtained values are 0.543 -- 626 gm/cm2.
- C) The angle of all Repose: The ascertain values of angle of repose has been 260-290, which mention in the table 3.
- **D)** Compressibility indicator: The ascertain values of compressibility of the formulation are mention in the table 3.The ascertain values are 9.33percent 15.86%.
- **E) Hausner ratio:** The acquired Hauser's ratio values are 1.10 -- 1.17, which Mention in the table3.

Assessment of post-compression parameters of formulation:

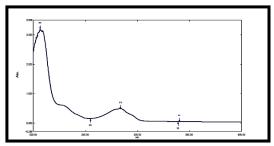
- **A)** Form of tablets: The invented tablets of batches are circular, and it's no cracks at microscopic evaluation.
- **B)** Thickness: The thicknesses of invented tablets were uniform in character. The depth values of the formulation are 3.78mm -- 3.81 mm. The values cited in the table 4.
- **C) Diameter:** The obtained values of Formula were cited over table 4. The values are 8.0 mm -- 8.04 mm. This is mentioned in the table 4.
- **D)** Hardness: The every formula of formulated ablates possess the hardness together with the Array of 3 kg/cm2 -- 4 kg/cm2. Which mention in the table 4.
- **E) Friability**: The obtained values of friability evaluation of formulation were cited in the table4. The values are 0.198 -- 0.635. The friability of pills of the formulation isn't greater than 1 percent.
- f) Weight Variant: The decide of weight variant all batches were cited in the table 4. The all formulated tablets are passed in weight variant test. The values have been 149.8±1.13 milligrams 150.5±2.17 mg.
- **G)** Medication content uniformity: The Obtained values drug content uniformity of formulation was mention in the table 4. The found values of per cent of medication are 96.88 -- 100.5.
- h) Dispersion time: The Formulated tablets of formulation have dispersion time in < 30 minutes and fulfilling necessity within < 3 minutes. The obtained values of in vitro dispersion period cited in the Mouth dissolving tablets of table 5. domperidone was devised by direct compression procedure with the help of super disintegrates such as crospovidone. croscarmellose sodium. The in vitro dispersion period was 7.36 -- 11.29 seconds, 17.66 -- 26.34 minutes and 9.68 -12.77 minutes respectively. The management formula in vitro dispersion

period was discovered 73.69 minutes. The dispersion time additionally effected by immersion of super disintegrates. But in this instance, croscarmellose sodium and crospovidone independently and also mix the concentration increases 4 per cent w/w. Therefore dispersion time has been raised. All batches of formula have less than 30 seconds of dispersion time.

- I) Wetting time: that the obtained wetting of tablets of formulation cites in the table 5. Tablets were formulated using domperidon+crospovidone+croscamellous sodium. The Wetting time was 69.34 --88.44 seconds, 50.02 -- 65.03 minutes and 33.6 49 Seconds. The control formula needed wetting time 164.4 minutes.
- J) Water Absorption ratio: The water absorption of the formulation ratio is mention in the table 5. The tablets are formulated with the help of super disintegrates such as crospovidone and croscarmellose sodium alone and together with a mix. So, the water absorption ratio is 61 66 Seconds, 57.97 -- 59.85 minutes and 60.54 -- 62.60 minutes respectively. The controller formula wetting period is 56.6 minutes.
- K) In vitro dissolution research: The accessed in vitro dissolution period is mention in the above table. Phosphate buffer 6.8 (aroused fluid) was utilized to determine the in vitro dissolution period of The chart plotted between tablets. accumulative drug discharge and time The at Vitro dissolution figure 13-18. statistics, medication release of formula (F0-F3) with croscarmellose sodium was 90.93 per cent, 99.37 percent, and 96.56 The medication release of per cent. formula (F4-F6) with crospovidone has been 90.93%, 97.5%, and 95.62 per cent. The medication release of formula (F7-F9) using crospovidone and croscarmellose sodium was 92.81 per cent, 99.37percent and 98.43% respectively. The without super disintegrates the formula (F1) has

medication release 60%. According to the outcomes, we see that the formula with croscarmellose sodium has the highest drug release rate of 99.3% over half an hour. With a mix of crospovidone and croscarmellose sodium, the drug release rate over 99.3% over half an hour. The formulations with crospovidone possess the medication release over 97.5%. So, based on preceding research, it was apparent that super disintegrates raising the in vitro dissolution rate

- L) **Curve fitting evaluation:** The acquired kinetic values cited in table 5. The curve fitting information of medication release kinetic equation the arrangement of discharge flow the first-order equation.
- M) Stability research: Stability studies have been conducted on the chosen formulations of Domperidone of formula (F4) to evaluate their stability related to their bodily appearance, drug material and In-vitro dispersion time following storage in 40° C/75 ±5 per cent RH for three weeks to evaluate their long-term stability. When the tablets of Domperidone were saved at 40°C/surrounding RH for 3Weeks there was no considerable change in bodily appearance or medication content revealed in Table 28. The insignificant change in the natural look, drug material of those chosen formulations (F4) following storage at 40° C/ / 75 ± 5 per cent RH for three weeks indicate the formations could



offer a minimal shelf life of two decades.

Fig. 1 - Absorption maxima of Domperidone

Table1: Standard calibration curve of Domperidone in Phosphate Buffer.

S.No.	Concentration (µg/ml)	Absorbance
1	0	0.00
2	2	0.090
3	4	0.191
4	6	0.272
5	8	0.354
6	10	0.461

Fig. 2 Standard calibration curve of domperidone in Phosphate Buffer (6.8 p^H) at 284nm

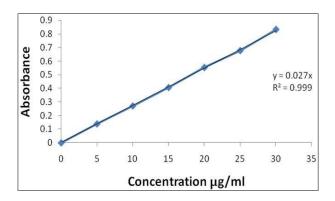


Fig. no. 3: FT-IR spectra of domperidone

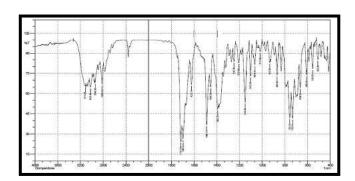


Figure 4: Infrared spectral assignments for Domperidone and croscarmellose sodium

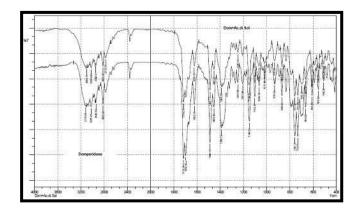


Figure 5: Infrared spectrum of Combination of domperidone and crospovidone

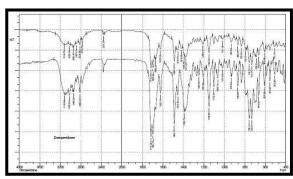


Figure 6: Infrared spectrum of Combination of domperidone and mannitol

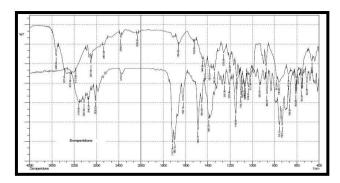


Table 2: Composition of different batch of oro-dispersible tablets of domperidone.

Ingrediants(mg/tab)	F0	F ₁	F2	F3	F4	F5	F6	F ₇	F8	F9
Domperidone	10	10	10	10	10	10	10	10	10	10
Croscarmellose	10	20			10	20		-	20	10
Crospovidone	ı	-	10	20			10	20		
Mannitol	35	35	35	35	35	35	35	35	35	35
Aspartame	4	4	4	4	4	4	4	4	4	4
Magnesium Stearate	3	3	3	3	3	3	3	3	3	3
Orange flaver	3	3	3	3	3	3	3	3	3	3
Talc	2	2	2	2	2	2	2	2	2	2
M.C.C(Avicel)	83	83	83	83	83	83	83	83	83	83
Total weight	150	150	150	150	150	150	150	150	150	150

Table 3: Pre- compression parameters of mouth dissolving tablets of all formulations.

Formulations	Bulk density*	Tapped density*	Angle of repose*	Compressibility	Hausner's ratio
	(g/cc)	(g/cc)	(θ)	Index (%)	
F_0	0.520	0.615	27°.33′	15.86	1.17
F_1	0.538	0.626	$26^{\circ}.70'$	13.2	1.16
F_2	0.478	0.543	$26^{\circ}.14'$	10.99	1.12
F ₃	0.497	0.550	26°.01′	9.25	1.13
F ₄	0.529	0.587	$28^{0}.95'$	10.2	1.11
F ₅	0.522	0.597	27°.65′	12.7	1.14
F_6	0.493	0.543	$28^{0}.75'$	9.33	1.10
F ₇	0.508	0.594	27°.49′	15.3	1.17
F ₈	0.522	0.596	$26^{\circ}.28'$	12.5	1.15
F ₉	0.521	0.595	26°.27′	12.4	1.14

Table no. 4: Physical properties mouth dissolving tablets of all formulation

Formulations	Diameter* (mm)	Thickness*(mm)	Weight variation* (mg)	Hardness* (kg/cm ²)	Friability (%)
F_0	8.04±0.050	3.81±0.007	149.9±1.48	3.21±0.6	0.398
F_1	8.02±0.044	3.80±0.058	149.8±1.13	3.00±0.2	0.396
F_2	8.03±0.043	3.80±0.007	149.8±1.83	3.32±0.2	0.337
F ₃	8.01±0.036	3.80±0.012	150.1±1.48	3.19±0.4	0.333
F ₄	8.02±0.043	3.78±0.011	149.8±1.23	3.22±0.6	0.266
F ₅	8.00±0.024	3.79±0.009	149.7±1.26	3.24±0.4	0.635
F_6	8.01±0.041	3.79±0.008	150.5±2.17	3.34±0.3	0.198
F ₇	8.00±0.033	3.80±0.008	149.4±3.46	3.25±0.2	0.266
F ₈	8.02±0.049	3.79±0.009	149.8±1.47	3.31±0.3	0.296
F ₉	8.01±0.048	3.79±0.008	149.7±1.46	3.30±0.2	0.295

Table no 5: Post Compression parameters of mouth dissolving tablets of all formulation.

	Wetting time*	Water absorption ratio* (in	<i>In vitro</i> dispersion time*	
Formulations	(in sec)	sec)	(in sec)	Drug content* (%)
F_0	88.4±1.528	61.25±1.002	9.8.0±1	96.88±0.523
F_1	72.7±1.546	66.4±0.557	7.36±0.578	99.55±0.666
F_2	69.34±7.766	65.77±1.096	11.29±1.1548	99.3±0.262
F ₃	65.3±2.082	60±0.080	17.9±1.733	99.9±0.398
F ₄	53.0±3	57.97±0.2	17.67±0.578	98.7±0.546
F ₅	50.2±3.055	59.85±0.057	26.34±0.576	99.45±0.152
F ₆	49.0±1	60.07±1.95	11.9±2	100.05±0.407
F ₇	37.0±2	60.54±0.55	9.68±0.578	100.05±0.525
F ₈	33±3.05	62.6±2.108	12.77±0.576	99.3±0.152
F ₉	32±3.04	62.5±2.107	12.76±0.575	99.2±0.151

Table 6: Stability data of F₄ formulation

	Formulation F ₄ stored at 40 ⁰ c/75% RH						
Time in months	Physical appearance	In vitro Dispersion time	% Drug content				
1	+++	7.44	98.11				
2	+++	7.90	97.43				
3	++	8.83	96.98				

+++ = Same as on zero day, ++ = Slight change in color

Table no7: *In vitro*% drug release of mouth dissolving tablets for all formulation.

Time										
(mins)	F_0	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F ₉
5	74.08	75.96	79.69	70.32	78.76	75.1	68.44	78.76	77.82	77.82
10	78.81	79.78	85.32	77.82	84.38	80.63	76.88	84.38	83.44	83.44
15	83.44	89.15	91.88	86.26	88.13	88.13	84.37	90.94	89.07	89.07
20	88.22	94.78	93.76	89.07	93.76	91.88	89.08	95.63	94.69	94.69
25	90.2	96.65	95.63	90.1	95.63	94.69	90.94	97.6	96.57	96.57
30	90.94	99.4	96.57	90.94	97.6	95.63	92.82	99.4	98.44	98.44

Figure no. 7: In vitro drug released profile of domperidone with formulation (F₀-F₃)

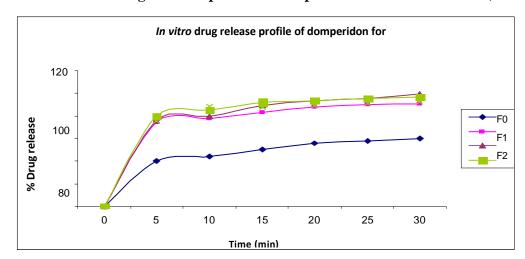
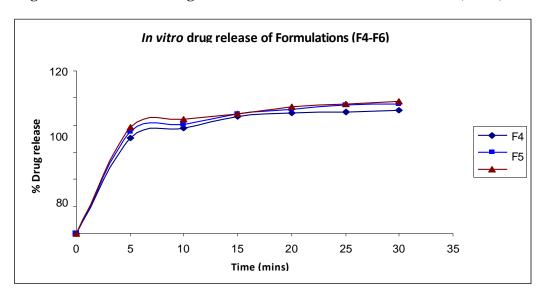


Figure No. 8: *In vitro* drug release of tablets with the formulation (F₄-F₆)



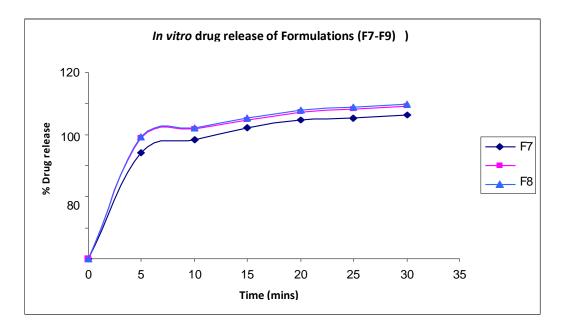


Figure No. 9: In vitro drug release profile of tablets of domperidone with the Formulation (F₇-F₉)

CONCLUSION:

of Mouth dissolving tablets domperidone was prepared by direct method compression with superdisintegrants like crospovidon, mnnitol. croscarmellose sodium. magnasium stearate, and MCC. On the basis of above work was concluded that post compression and pre compression obtain values are in the limits. Formulation F4 has the maximam 98.6% within 25 minutes drug release. The drug release profile depends on the concentration of superdisintegrants. All formulation has good dissolution rate and good wetting time.

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