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Formulation and In-Vitro Evaluation of Antiemetic Orodispersible Combination Tablets of Domperidone and Cinnerizine by using various Superdisintegrants

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ABSTRACT

The purpose of this investigation was to enhancement of solubility of cinnarizine by using solid dispersion technique solvent evaporation method using polymer PEG 6000 & develop combination ODT of cinnarizine with domperidone by using direct compression technique using crospovidone, croscarmellose sodium and sodium starch glycolate as a superdisintegrants. The preformulation study includes the compatability of drugs with the polymers by using FTIR,UV,TLC. The batches were evaluated for weight variation, hardness, friability, drug content, wetting time, IN In-vitro dispersion, in-vitro dissolution. The formulation F2 which contain 8% crospovidone and 10 % sodium starch glycolate showed best results and rapid in-vitro dissolution. The results revealed that the tablets containing superdisintegrants combination had a good dissolution profile. The drug content of all the batches was within the acceptable limits of the United States Pharmacopoeia with maximum drug being released at all time intervals. The present study demonstrated potentials for rapid absorption, improved bioavailability, effective therapy and patient compliance. The results conclusively demonstrate successful enhancement of solubility, disintegration and dissolution of the formulated tablets.

Keywords: Ebola haemorrhagic fever, EBOV, WHO, NHP, EVD

INTRODUCTION

Many orodispersible tablets available in pharma market are single drug tablets & no combination form of orodispersible tablets is available in the market. Hence it is new drug delivery system that is alternative to conventional tablets. Domperidone and cinnarizine combination is rational combination and this combination is available in the market in conventional dosage form. But this combination not available in orodispersible tablet form which has fast dissolution, disintegration & better result than conventional tablets. Oro-dispersible tablet (ODT) is "A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue". The aim of this study is to formulate directly compressible rapidly disintegrating tablets of Domperidone and Cinnerizine and investigate different factors affecting the formula like the effect of diluents, the type and concentration of superdisintegrant (SD) on the characteristics of the resulted ODTs, and performs physical and chemical evaluation of the prepared formulas. Also to prepare ODTs that contains combination of Domperidone and Cinnerizine for the use in diseases that need antiemetic effect [1].

MATERIAL AND METHODS

Domperidone (Gift sample from Vasudha PharmaChem LTD. Andhra Pradesh.), cinnarizine (ZCL Chemicals LTD. Mumbai), crospovidone, croscarmellose sodium, sodium starch glycolate

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(Maple Biotech PVT LTD, Pune), microcrystalline cellulose, magnesium stearate (Loba chemicals. Mumbai), sodium saccharine, colour and flavour (Symbiosis Pharmaceuticals, Sangli).

METHODS:-

Formulation and optimization of solid dispersion:-

Solvent evaporation systems were prepared by dissolving the quantities of cinnarizine as indicated in table no. 6, 7(equivalent to 20 tablets) in dichloro-methane to produce a clear solution, and then the solution was added in the various quantities of Polyethylene glycol 4000 and polyethylene glycol 6000 as per Table No.1,2. This was evaporated to form solid mass at 40^0C with constant stirring with the help of magnetic stirrer. Then dry mass was collected, triturated. Dried power was passed through sieve no.60 and stored in desiccators until further evaluation. The binary system was optimized after studying its solubility study and entrapment[2].

Table No 1:- Formulation of binary system with PEG 4000

Formulation	Micro particle system	Ratio of Drug: Surfactant
T1	CIN: Polyethylene Glycol 4000	1:1
T2	CIN: Polyethylene Glycol 4000	1:2
T3	CIN: Polyethylene Glycol 4000	1:3
T4	CIN: Polyethylene Glycol 4000	1:4
T5	CIN: Polyethylene Glycol 4000	1:5
T6	CIN: Polyethylene Glycol 4000	1:6
T7	CIN: Polyethylene Glycol 4000	1:7
T8	CIN: Polyethylene Glycol 4000	1:8
T9	CIN: Polyethylene Glycol 4000	1:9

Table No 2:- Formulation of binary system with PEG 6000

Formulation	Micro particle system	Ratio of Drug: Surfactant
S1	CIN: Polyethylene Glycol 6000	1:1
S2	CIN: Polyethylene Glycol 6000	1:2
S3	CIN: Polyethylene Glycol 6000	1:3
S4	CIN: Polyethylene Glycol 6000	1:4
S5	CIN: Polyethylene Glycol 6000	1:5
S6	CIN: Polyethylene Glycol 6000	1:6
S7	CIN: Polyethylene Glycol 6000	1:7
S8	CIN: Polyethylene Glycol 6000	1:8
S9	CIN: Polyethylene Glycol 6000	1:9

PHYSICOCHEMICAL EVALUATION OF THE COMPRESSED TABLETS:-[2].

PREFORMULATION STUDY:

FTIR spectroscopy:- IR spectrum showed dominant characteristic peaks of cinnarizine

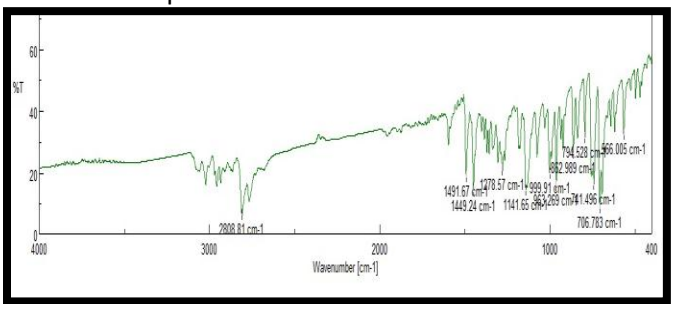

Fig. No 1: IR spectrum of cinnarizine

IR spectrum of domperidone:-IR spectrum showed dominant characteristic peaks of domperidone.

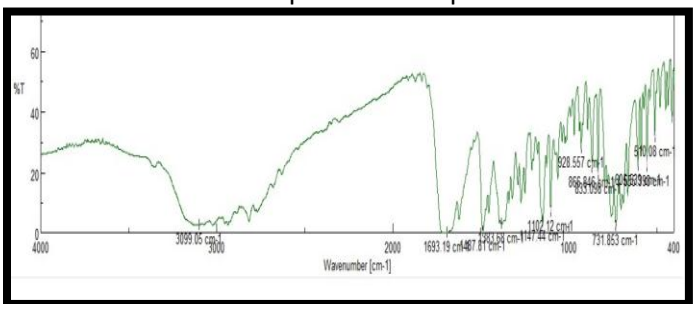

Fig. No 2: IR Spectrum of domperidone.

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UV Spectrum:- Maximum absorption of cinnarizine was found to be 253 nm. This is characteristic property of cinnarizine in its pure form. Hence, it can be conformed that received sample is authentic[3].

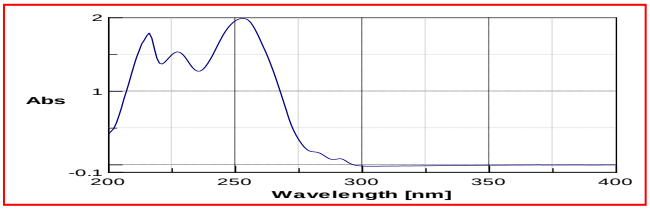

Fig. No 3: UV spectrum of cinnarizine

Maximum absorption of domperidone was found to be 284 nm. This is characteristic property of domperidone in its pure form. Hence, it can be conformed that received sample is authentic.

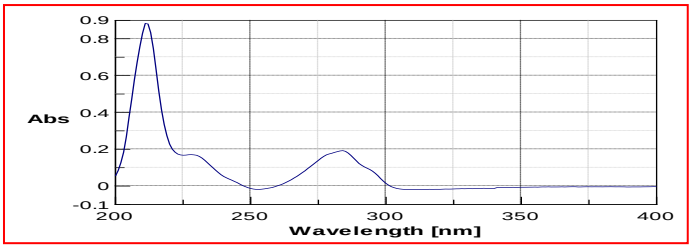

Fig. No 4: UV spectrum of domperidone.

Compatibility study:-

The proper design and formulation of a dosage form requires consideration of physical, chemical and biological characteristics of all the drug substance and excipients that used in fabricating the product. The drug and the excipients must be compatible with one another to produce a products that is stable, effective, attractive, easy to administer and safe.

IR compatibility study:-

Drug and all the polymers showed characteristic spectrum of their functional groups. All the physical mixture showed characteristics peaks of drug corresponding to N-H functional group. It indicated that the drug and polymer does not have any major interaction. Therefore it is enough to consider that the drug is compatible with given excipients [4].

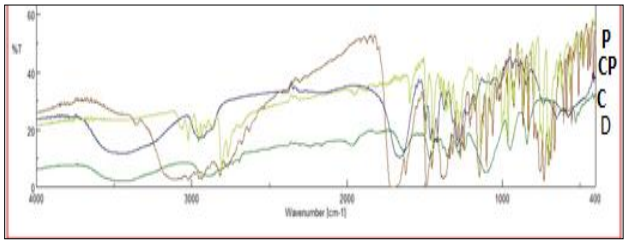

Fig. No 5: IR Spectra study of pure drug (Dom+Cinn+ PEG 6000)

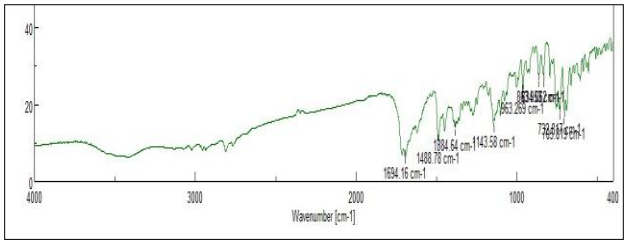

Fig. No 6: Initial IR Spectra study of physical mixture. (Dom+Cinn+ PEG 6000)

CALIBRATION CURVE:-

Calibration curve of cinnarizine (In pH 6.8):- observed values are listed below: The scanning of drug solution was done in the UV region 200-400nm to find out the wavelength of maximum absorption (λ_{max}) in the pH 6.8. The λ_{max} was found to be 284nm and 253 nm for domperidone and cinnarizine respectively. The calibration curve was linear between 3 to 15 µg/ml concentration ranges, the standard calibration curve was obtained by plotting absorbance vs concentration, and it follows Beer's law [5, 6].

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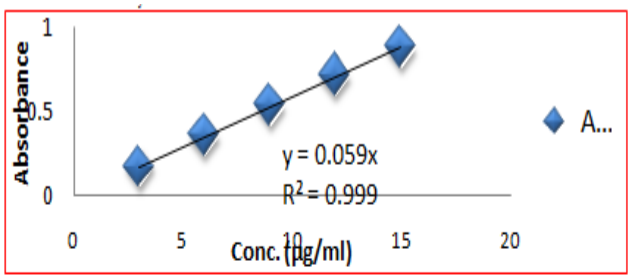

Fig. No 7: Calibration curve of cinnarizine

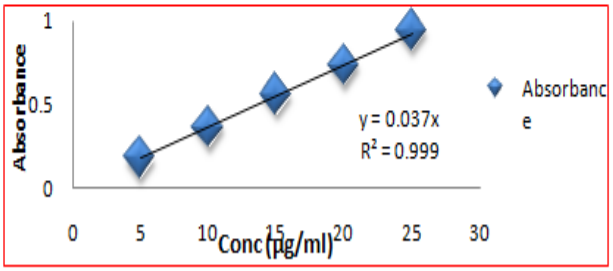

Fig. No 8: Calibration curve of domperidone

Phase solubility study:-

Solubility of cinnarizine in SSF was found to be 0.039 mg/ml this indicated that cinnarizine is practically insoluble in SSF. Graph and various parameters computed from the phase solubility studies (Table No. 3) showed a non linear increase in drug solubility with increased in carrier levels. Hydrophilic carriers are known to interact with drug molecule mainly by electrostatic forces and occasionally by other type of forces, like hydrogen bonding [7].

Table No.3:- Phase solubility study with PEG 6000

Conc. of solubilizer (mg/ml)	Conc. of drug (mg/ml)
0	0.03932±0.002
1	0.05277±0.007
2.5	0.06211±0.002
5.0	0.07991±0.003
7.5	0.08618±0.002
10	0.1028±0.0001

All value are mean ±S.D (n=3)

EVALUATION AND CHARACTERIZATION OF SOLID DISPERSIONS

Drug entrapment:-

The percentage of drug entrapment of various binary solid dispersions of cinnarizine prepared by solvent evaporation method is given in Table No.4 & 5 respectively. Polyethylene glycol 6000 showed higher percentage of drug entrapment. The values are ranging between 88.67±0.256 % to 96.22±0.354% and for PEG 4000 the drug entrapment was found to be in the ranging of 82.45±0.236 % to 91.97±0.342 %. Batch F4 showed higher percentage of drug entrapment with PEG 6000, while batch T7 showed higher drug entrapment with PEG 4000 [8].

Table No. 4:- Drug entrapment of binary solid dispersion by using PEG 6000

Batch NO	Ratio	% drug entrapment
S1	1:1	88.67±0.256
S2	1:2	89.75±0.132
S3	1:3	92.43±0.453
S4	1:4	97.87±0.243
S5	1:5	96.22±0.354
S6	1:6	95.61±0.123
S7	1:7	95.27±0.165
S8	1:8	94.90±0.154
S9	1:9	94.06±0.178

All value are mean ±SD. (n=3)

Table No. 5:- Drug entrapment of binary solid dispersion by using PEG 4000

Batch NO	Ratio	% drug entrapment
T1	1:1	82.45±0.236
T2	1:2	84.20±0.182
T3	1:3	85.98±0275
T4	1:4	86.63±0.176
T5	1:5	89.78±0.245
T6	1:6	91.39±0.635
T7	1:7	91.97±0.342
T8	1:8	90.24±0.173
T9	1:9	89.39±0.342

All value are mean ±SD. (n=3)

Solubility studies:-

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Improved dissolution behavior of solid dispersion of drug can be attributed to increase the solubility of drug as per Noyes Whitney equation. Solid dispersion system leads to reduction in particle size; increase in hydrophilicity or due to micellar solubalization of drug because of which there is an enhancement of solubility. This effect was confirmed by conducting similar saturation solubility studies on untreated drug as control.There are various reports that withstand the increased solubility of cinnarizine with polyethylene glycol especially PEG 6000 that facilitates solubalization of poorly water soluble drugs [9, 10].

Table No. 6:-Solubility study of binary solid dispersion

Type of formulation	Ratio	Solubility (µg/ml)
Pure Cinnarizine		30.32±0.52
S1	1:1	332.4±0.05
S2	1:2	522.5±0.72
S3	1:3	711.2±0.54
S4	1:4	1198.1±0.17
S5	1:5	1120.4±0.27
S6	1:6	1110.5±0.84
S7	1:7	1098.9±0.64
S8	1:8	1071.5±0.47
S9	1:9	1054.7±0.38

All value are mean ±SD. (n=3)

The binary solid dispersion values were found to be 332.4±0.05 to 1198.1±0.17 µg/ml for PEG 6000.

IR Spectroscopy:-

Drug and excipients interaction play a crucial role with respect to the stability and potency of the drug. FTIR techniques a have been used here to study the physical and chemical interaction between drug and excipients used. Compatibility studies were performed using FTIR spectrophotometer, the IR spectrum of pure drug cinnarizine and physical mixture of drug and polymer were studied. The FTIR scan shows characteristic absorption peak of cinnarizine 2808 & 3067 cm^{-1} respectively. The peak obtained spectra of drug have correlation with the peak obtained when the drug and excipients were scanned together, thus indicating that drug was compatible with formulation, excipients. Based on this study it was concluded that there is no chemical interaction between drug and excipients used and thus it can be safely used in formulation [11].

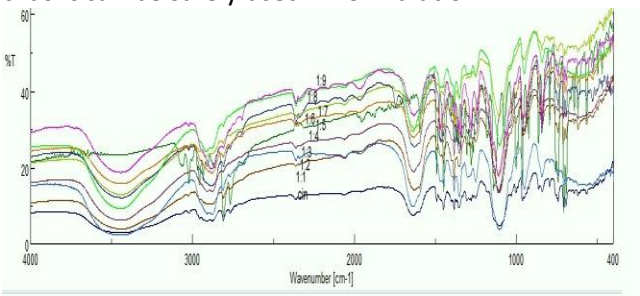

Fig. No 9: IR spectra of drug and binary solid dispersion with PEG 6000

Drug release study:

Dissolution profile of pure cinnarizine& solid dispersion were indicated differences between dissolution rates. Solid dispersion showed enhancement in dissolution as compared to pure cinnarizine, which indicated the effect of PEG 6000 on cinnarizine. The system prepared with PEG 6000 resulted in dissolution enhancement. Extremely high concentration of cinnarizine in the state was maintained for the entire dissolution span in the case of PEG 6000 system. Solid dispersion of PEG 6000 showed more than 50 % drug released within 20 min [12, 13].

Table No 7:- Drug release study for formulation S1,S2,S3

Time (min)	Cumulative % drug released				
	CINN	PM1	S1	S2	S3
0	0	0	0	0	0
10	7.309±0.023	9.530±0.370	51.80±0.365	53.07±0.257	77.72±0.186

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20	9.811±0.779	16.21±0.292	55.53±0.341	56.25±0.211	79.35±0.147
30	12.95±0.195	21.48±0.320	60.49±0.427	71.49±0.530	80.64±0.241
40	18.00±0.205	25.43±0.358	70.16±0.277	76.17±0.290	81.97±0.282
50	22.06±0.115	32.49±0.482	73.30±0.186	79.40±0.426	83.90±0.425
60	25.16±0.305	41.63±-.516	79.24±0.227	80.68±0.297	85.91±0.231
70	28.09±0.115	43.71±0.411	79.35±0.306	84.97±0.457	87.02±0.515
80	33.04±0.202	52.02±0.387	80.05±0.436	88.74±0.231	88.54±0.205
90	36.54±0.176	59.95±0.345	82.59±0.302	89.91±0.227	89.71±0.198
100	41.64±0.214	68.38±0.283	85.69±0.366	91.55±0.476	91.39±0.253
110	43.82±0.196	74.31±0.273	89.56±0.424	93.14±0.352	95.79±0.342
120	48.54±0.169	79.35±0.365	93.96±0.283	95.02±0.345	98.85±0.157

All value are mean ±SD. (n=3)

Table No. 8:- Drug release study for formulation S4, S5,S6

Time (min)	Cumulative % drug released				
	CINN	PM1	S4	S5	S6
0	0	0	0	0	0
10	7.309±0.023	9.530±0.370	80.57±0.224	80.48±0.302	54.98±0.126
20	9.811±0.779	16.21±0.292	82.47±0.256	81.90±0.387	60.10±0.287
30	12.95±0.195	21.48±0.320	85.34±0.259	84.86±0.362	63.54±0.181
40	18.00±0.205	25.43±0.358	88.68±0.176	87.05±0.210	69.28±0.247
50	22.06±0.115	32.49±0.482	89.85±0.241	91.25±0.250	72.71±0.156
60	25.16±0.305	41.63±-.516	91.19±0.257	93.25±0.268	75.86±0.281
70	28.09±0.115	43.71±0.411	92.59±0.156	94.07±0.169	77.63±0.219
80	33.04±0.202	52.02±0.387	94.27±0.280	96.97±0.302	81.31±0.198
90	36.54±0.176	59.95±0.345	97.50±0.276	97.80±0.265	85.81±0.145
100	41.64±0.214	68.38±0.283	97.63±0.215	98.28±0.246	87.24±0.231
110	43.82±0.196	74.31±0.273	98.84±0.196	98.43±0.243	89.53±0.261
120	48.54±0.169	79.35±0.365	99.46±0.245	99.28±0.241	92.55±0.179

All value are mean ±SD. (n=3)

Table No. 9:- Drug release study for formulation S7, S8,S9

Time (min)	Cumulative % drug released				
	CINN	PM1	S7	S8	S9
0	0	0	0	0	0
10	7.309±0.023	9.530±0.370	56.34±0.224	61.02±0.226	61.63±0.202
20	9.811±0.779	16.21±0.292	60.71±0.290	69.19±0.210	67.63±0.515
30	12.95±0.195	21.48±0.320	67.21±0.255	70.72±0.266	68.63±0.305
40	18.00±0.205	25.43±0.358	71.51±0.209	74.72±0.176	73.06±0.115
50	22.06±0.115	32.49±0.482	73.98±0.176	76.05±0.175	76.13±0.205
60	25.16±0.305	41.63±-.516	77.06±0.172	79.14±0.200	77.65±0.185
70	28.09±0.115	43.71±0.411	80.15±0.234	80.43±0.270	81.84±0.196
80	33.04±0.202	52.02±0.387	82.36±0.256	83.84±0.205	85.52±0.167

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90	36.54±0.176	59.95±0.345	84.73±0.197	87.21±0.220	89.24±0.657
100	41.64±0.214	68.38±0.283	89.54±0.223	88.28±0.196	91.13±0.231
110	43.82±0.196	74.31±0.273	91.36±0.269	91.87±0.184	93.13±0.235
120	48.54±0.169	79.35±0.365	95.78±0.257	95.33±0.155	96.40±0.215

All value are mean ±SD. (n=3)

Formulation design:-

The orodispersible powder blend ware prepared by using formula tabulated in Table No. 10.

The actual values of the ingredients for the designed formulation of orodispersible tablets by direct compression method.[14, 15]

Table No. 10:- Formulation (direct compression)

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Domperidone	20	20	20	20	20	20	20	20	20
SD (CIN)	100	100	100	100	100	100	100	100	100
Crosspovidone	7.2	9.6	12	7.2	9.6	12	-	-	-
Croscarmellose Na	-	-	-	9.6	12	19.2	7.2	9.6	12
Na starch glycolate	9.6	12	19.2	-	-	-	9.6	12	19.2
Magnesium stearate	2	2	2	2	2	2	2	2	2
MCC	95.2	90.4	80.8	95.2	90.4	80.8	95.2	90.4	80.8
Mannitol	24	24	24	24	24	24	24	24	24
Sodium saccharine	2	2	2	2	2	2	2	2	2
TOTAL	260	260	260	260	260	260	260	260	260

PRE-COMPRESSION PARAMETERS [16]

Angle of repose (Ø):- The data obtained for angle of repose for all the formulation were tabulated in Table No. 11. The values were found to be in the range of 24^0 c and 28^0 c. All the formulation prepared by the methods direct compression showed the angle of repose less than 30^0 c which reveals good flow property.

Bulk Density:- Loose bulk density (LBD) and tapped bulk density (TBD) for the blends are shown in Table No. 11. The loose bulk density and tapped density for the entire formulation blend varied from 0.51 gm/cm^3 to 0.62 gm/cm^3.

Tapped Density:-

Tapped densities for the blends are showed in Table No. 11.

Carr's Index (Carr's Consolidation Index):-

The results of Carr's consolidation index (%) for the entire formulation blend were ranged from 14.29 to 19.67. The directly compressible blend had shown excellent compressibility index values up to 20 % resulted in good to excellent flow properties. The results for all the formulation were shown in Table No. 11.

Hausner Ratio:- It is an indirect index of ease of powder flow. It is calculated by the following formula**.**

Hausner ratio= Tapped density/ Bulk density.

Lower Hausner ratio (<1.25) indicated better flow properties than higher ones (>1.25). The results in Table No. 11 showed that the ratio are ranges between 1.16 - 1.24 & hence better flow property.

Table No. 11:- Precompression parameters

Formulation	Angle of Repose	Bulk Density	Tapped density	Carr's Index	Hausner's Ratio
F1	25.67±0.02	0.47±0.01	0.56±0.01	16.07	1.192

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F2	26.43±0.02	0.49±0.01	0.59±0.03	16.95	1.204
F3	27.35±0.02	0.51±0.03	0.63±0.01	19.05	1.235
F4	28.75±0.01	0.51±0.02	0.62±0.02	17.75	1.126
F5	26.98±0.01	0.49±0.01	0.61±0.01	19.67	1.245
F6	25.12±0.03	0.54±0.01	0.63±0.01	14.29	1.167
F7	24.12±0.04	0.54±0.02	0.64±0.03	15.63	1.185
F8	24.63±0.03	0.48±0.03	0.60±0.01	18.33	1.225
F9	24.23±0.04	0.51±0.03	0.60±0.01	17.75	1.216

All value are mean ±SD. (n=3)

POST COMPRESSION PARAMETERS [17]

General appearance:- The general appearance of a tablet, its visual identity and overall elegance is essential for consumer acceptance.

Size and shape:- Formulations prepared were randomly picked from each batch & examined under lens for shape and in presence of light for colour. All tablets showed flat and circular shape with white colour.

Thickness:- Thickness of tablets was measured by vernier caliper by picking tablets randomly from all the batches. The result of thickness of tablets is shown in Table No. 12. The mean thickness was (n=5) almost uniform in all the formulation and values ranged from 4.7±0.2 mm to 5.1±0.2 mm. The standard deviation values indicated that all the formulation ware within the range.

Table No 12: Thickness:-

Formulation code	Uniformity of Thickness (mm)
F1	5.0±0.2
F2	4.9±0.1
F3	5.1±0.2
F4	4.8±0.4
F5	4.7±0.2
F6	5.0±0.6
F7	4.9±0.2
F8	5.1±0.5
F9	4.8±0.7

All value are mean ±SD. (n=3)

Hardness: -The hardness values ranged from 3.2±0.1 to 4.0±0.2 kg/cm^2 for formulation were almost uniform.

Friability test:- The value were found to be well within the approved ranges (<1%) in all designed formulation. The values were found within the limit. Thus the tablets possess good mechanical strength.

Table No 13: Friability:

Formulation code	Friability %
F1	0.42±0.03
F2	0.32±0.01
F3	0.44±0.01
F4	0.43±0.03
F5	0.38±0.03
F6	0.63±0.03
F7	0.62±0.01
F8	0.63±0.01
F9	0.61±0.03

All value are mean ±SD. (n=3)

Weight variation test:- The weight variation for all the formulation is shown in Table No. 14. All the tablets were passed weight variation test as the average percentage weight variation was within the pharmacopoeial limit.

Table No 14: Wt. variation:-

Formulation code	Weight variation (gm)
F1	0.2477±2.09
F2	0.2515±2.98
F3	0.2518±2.67
F4	0.2619±2.85
F5	0.2516±2.44

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F6	0.2582±2.09
F7	0.2601±2.16
F8	0.2611±2.71
F9	0.2551±2.64

All value are mean ±SD. (n=3)

Drug content:- The drug content uniformity was performed for all the nine formulation and results are tabulated in Table No. 15. Three trials from each batch were analyzed by spectrophotometer. The average value and standard deviation of all the formulation were calculated. The drug content of the tablets was found to be in the range of 98 to 102% and 98 to 101%. For domperidone & cinnarizine respectively the results were within the range and that indicated uniformity of mixing [18].

Table No. 15:- Uniformity in drug content:-

Formulation code	Drug content uniformity (mg) CINN	Drug content uniformity(mg) DOM
F1	99.18±0.05	98.23±0.07
F2	99.78±0.02	99.03±0.01
F3	98.35±0.033	98.35±0.02
F4	101.1±0.023	99.23±0.02
F5	99.15±0.043	100.03±0.08
F6	100.4±0.032	99.43±0.05
F7	99.20±0.023	97.98±0.03
F8	99.09±0.084	98.22±0.08
F9	102.5±0.076	101.06±0.03

All value are mean ±SD. (n=3)

Wetting time:- Wettability of tablets was brought to confirm the mechanism for rapid disintegration of the tablets. Wetting time is closely related to the inner structure of tablet. The results of wetting time are shown in Table No. 16, which showed that wetting process is very rapid in almost all formulations. This may be due to ability of swelling and capacity of water absorption.

Table No. 16: Wetting time:-

Formulation code	Wetting Time
F1	43±2.76
F2	40±2.89
F3	39±2.98
F4	35±2.31
F5	30±2.45
F6	36±2.65
F7	26±2.71
F8	24±2.34
F9	22±2.53

All value are mean ±SD. (n=3)

In-vitro disintegration time:- Tablets from all batches showed immediate disintegration. Disintegration time decreased with increase in concentration of disintegrants. The result is shown in Table No. 17, which was determined as per I.P. specification for all the developed formulations. All the formulations showed disintegration time less than 57 seconds.

Table No. 17: In-vitro disintegration time:-

Formulation code	In-vitro disintegration Time in sec
F1	28±1.4
F2	42±1.6
F3	56±2.6
F4	31±2.2
F5	21±1.2
F6	29±1.6
F7	17±1.3
F8	36±1.1
F9	15±1.4

All value are mean ±SD. (n=3)

In-vitro dissolution studies- All the nine formulation were subjected for in-vitro dissolution studies using tablet dissolution tester. The dissolution media pH 6.8 (SSF) was used to study the drug release. The samples were withdrawn at different intervals of time and analyzed at 253 nm and 284 nm using UV spectrophotometer. Cumulative percent drug releases were calculated on the basis of average amount of drug present in the respective formulation. All the formulation showed rapid % drug release due to fast disintegration of tablets. Formulation F1, F2, F3, F4, F5, F6, F7, F8, F9 showed

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99.92, 100.81, 98.93, 97.46, 97.4, 98.48, 95.73, 99.1, 97.46% for drug cinnarizine and 94.18, 99.72, 95.07, 94.73, 96.09, 94..77, 97.21, 98.61% drug release for domperidone respectively, But the rapid drug dissolution was obtained in batch F2 formulation compared to other formulations, which release 67.2 % drug in 10 min. Croscarmellose sodium and crospovidone superdisintegrants showed higher drug release as compare to others with increase in concentration [19, 20].

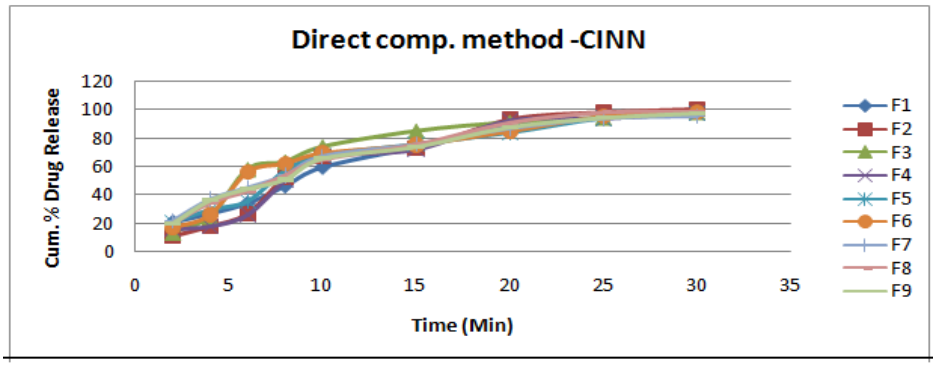

Fig N0 10: In-vitro dissolution studies of cinnarizine

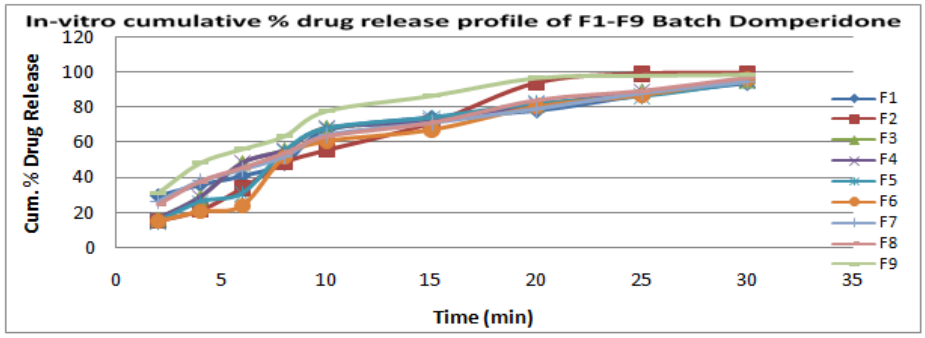

Fig No 11: In-vitro dissolution of domperidone

Stability studies:

Stability studies for the developed formulations ware carried out by storing the selected formulation at $40^0 \pm 5^0$C/75±2% RH up to two months. The formulation F2 was selected on the basis of their high cumulative percentage drug release, as well as results of in-vitro disintegration time, wetting time and in-vitro dispersion studies. On every 7th day the tablets were analyzed for the colour, hardness, drug content uniformity and cumulative % drug release, in-vitro disintegration time up to one month. This formulation showed no significant changes in the values [21].

RESULTS AND DISCUSSION

The results reveal that all batches of domperidone with cinnarizine combination orodispersible tablets prepared by direct compression technique were within the limits for uncoated tablets as per Indian Pharmacopoeia. Hardness of tablets was found to be in range of 3.4±0.2 kg/cm. Friability was observed between 0.32±0.01. Thus the hardness and friability data indicates good mechanical resistance of tablets. F2 batch which contain 8% crospovidone and 10% sodium starch glycolate (F2) was identified as the optimum combination of super disintegrates based on in vitro dispersion time, wetting time, % drug release by using direct compression method Wetting time is determined to get idea of wetting lag time before disintegration. Wetting volume is done to check minimum volume of water required for wetting of tablets. By the mechanism of swelling crospovidone and sodium starch glycolate shows its disintegration effect. The formulation F2 showed best results when compared to other formulations. It was seen that almost 67 % of drug was released in first ten minutes. Thus the release rate of domperidone with cinnarizine in combination orodispersible form was significantly enhanced by using superdisintegrants.

CONCLUSION

It was concluded that enhancement of solubility of cinnarizine by using solid dispersion technique and solvent evaporation method that using the PEG 6000 as a polymer is the best dissolution in 1:4 ratio. superdisintegrants addition technique is a useful method for preparing combination orodispersible

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tablet 8% crospovidone and 10% sodium starch glycolate by direct compression method. It is observed that optimized formulation (F2) which showed rapid disintegration contained. Hence combination of domperidone with cinnarizine ODTs can be formulated by simple technique for effective in treatment of antiemetic action and motion sickness and it can be administered without water for better patient compliance.

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