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Formulation and Evaluation of Orodispersible Tablets Of Domperidone.

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Abstract:- Orodispersible dosage forms are used for accurate dosing, enhanced bioavailability, rapid action, patient compliance, easy of administration, enhanced palatability. Domperidone drug taste was masked with Amberlite IRP 64 (1:3) effectively. Formulations F1,F2,F3,F4,F5,F6 and F7 are formulated with different concentrations of superdisintegrents by direct compression technique. Formulation F5 with crosscaramellose and crospovidone with 2mg, 2mg respectively showed better Water absorption ratio 76.73±2.88%, wetting time 26.66±2.08 sec and disintegration time 25±1.0 sec. By considering disintegration time and dissolution time (102.85±0.23 min.) and other evaluation parameters F5 considered as optimized formula for comparision study with marketed Respiridone conventional tablet 38.02% drug released.
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AIM & OBJECTIVE:

- The aim of this study was to prepare Orodispersible tablets of Domperidone prepared by direct compression Method using different super-disintegrants (alone and in combination) and performing different evaluation tests.
- Choosing the best Formulation among the prepared formulations.
- Finally from all formulations optimized formula was selected and its release characteristics were compared with normal conventional marketed product.

PLAN OF WORK

- To plot standard graph of Domperidone
- To prepare oral disintegrating tablets by direct compression Method using different super disintegrants(alone and in combination)
- The powder blends of formulations are to be characterized for the following parameters:

1.Drug –excipients compatibility
2.Pre compression parameters,
3.Post compression parameters:
4. Choosing the best Formulation among the prepared formulations and comparing it with marketed conventional Domperidone tablets.

I. METHODOLOGY

Determination of □max:

- Weighed an accurate amount 10mg of Domperidone was dissolved in 20ml 0.1N HCl and diluted up to 100 mL by 0.1N HCl to obtain a 100mcg/ml concentration of Domperidone in solution.
- This solutions was subjected to scanning between 200 – 400 nm and absorption maxima at 240 nm for Domperidone is determined.

Standard Stock Solution:

A stock solution containing 1000mcg/mL of pure drug is prepared by dissolving accurately weighed an accurate amount 100mg of Domperidone was dissolved in 20ml of 0.1N HCl and diluted upto 100ml by 0.1N HCl to obtain a 1000mcg/mL concentration of Domperidone in solution

Working standard solution:

- Stock solutions were as such used as working standard solutions
- The working standard solution was diluted serially with sufficient 0.1N HCl to obtain the concentration range of 2–24 mcg/mL for Domperidone. A calibration curve for Domperidone is obtained by measuring the absorbance at the λ_{max} of 240nm.

Formulations

Ingredients (Weight in mg)	F1	F2	F3	F4	F5	F6	F7
Drug	4	4	4	4	4	4	4
Amberlite IRP-64	12	12	12	12	12	12	12
SSG	3.2	-	-	-	-	2	-
CCS	-	4	-	-	2	-	-
CP	-	-	4.8	-	2	2	2
L-HPC	-	-	-	6.4	-	-	2
Mannitol	34.4	33.6	32.8	31.2	33.6	33.6	33.6
MCC	20	20	20	20	20	20	20
Talc	1.6	1.6	1.6	1.6	1.6	1.6	1.6
Magnesium Stearate	0.8	0.8	0.8	0.8	0.8	0.8	0.8
Sodium Sacharain	4	4	4	4	4	4	4
Total weight	80mg	80mg	80mg	80mg	80mg	80mg	80mg

FORMULATION AND EVALUATION OF ORAL DISINTEGRATING TABLETS OF DOMPERIDONE:

Preparation of drug-resin complex:

- The Solvent evaporation method 1:3 ratio of Drug and Resin were taken and dissolved in sufficient quantity of methanol to dissolve the contents. Then the resultant solution was stirred in an open container until the complete evaporation of solvent .Then the wet powder (drug-resin complex) is dried in Hot air Oven.

Preparation of Oral disintegrating tablets by direct compression method:

- Drug-resin complex, MCC, Mannitol, sodium saccharin except lubricant and glidant was mixed in the increasing order of their weights in a mortar. To this mixture talc and magnesium stearate were added. The final mixture was shaken manually for 5-10min in a plastic bag.
- This powder was punched into tablets by using 16-station rotary tabletting machine and 5mm concave punches. The process is similar for all the formulations, which are prepared by direct compression technique

Drug-excipient compatability studies

Fourier Transform Infrared spectroscopic studies:

FT-IR spectra of Domperidone,Domperidone+Amerlite IRP64, Domperidone+CP+CCS were obtained on IR Affinity, Shimadzu. The spectra were scanned over the wave number from 4000 to 400 $cm^{-1.}$

Evaluation tests:

Pre-compression parameters

- Angle of Repose: $\tan(\theta) = h/r$

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

- Bulk Density (D_b): $D_b = M/V_b$
- Tapped Density (D_t): $D_t = M/V_t$
- Carr's index: $I = ((TBD-LBD)/TBD)*100$
- Haussner's ratio: $H = TBD/LBD$

Post compression parameters:

- **Thickness:**

Thickness of tablets was determined using Vernier caliper. Five tablets from each batch were used, and average values were calculated.

- **Tablet Hardness**

For each formulation, the hardness of 6 tablets was determined using the Monsonto hardness tester. The value was noted in kg/cm^2.

- **Weight Variation**

Twenty tablets were selected randomly and weighed. Average weight of the tablet was determined. These tablets were weighed individually and the weight variation was determined by using following formula.

% Deviation = $(W_{avg} – W_{initial}/W_{avg})$ *100

- **Drug content:**

Drug content was determined by ten tablets were weighed and powdered. A quanity of equivalent to 4mg of Domperidone was taken. It was shaken with 70 ml of 0.1 N HCl for 15 min. and then diluted to 100 ml with 0.1 N HCl. It was filtered through whatmann filter paper . One ml of this solution was transferred to 10 ml volumetric flask and final volume was made 10 ml. Absorbance of the resulting solution was measured at 240 nm. The drug content was determined by referring to the calibration curve.

- **Water Absorption Ratio**

$R = (W_a - W_b)/ W_b * 100$

- **Wetting Time:**

Two circular tissue papers placed in petri dish of 10 cm diameter. The dye solution was used two identify the complete wetting of the tablet surface.

A tablet was carefully placed on the surface of the paper in the petri-dish. The time required for water to reach the upper surface of tablet and to completely wet them was noted as wetting time.

- **Friability**

For each formulation, the friability of 10 tablets was determined using the Roche friabilator (Biological museum). This test subjects a number of tablets to the combined effect of shock abrasion by utilizing a plastic chamber which revolves at a speed of 25 rpm, dropping the tablets to a distance of 6 inches in each revolution. A sample of pre weighed 10 tablets was placed in Roche friabilator which was then operated for 100 revolutions i.e. 4 minutes. The tablets were then dedusted and reweighed. Percent friability (% F) was calculated as follows.

%F = (loss in weight/ initial weight)*100

- ***In-vitro* Disintegration Time**

10 mL of water at room temperature was taken in a petri-dish of 10 cm in diameter. The tablet was carefully placed in the centre of petri-dish and time required for the tablet to completely disintegrate into fine particles was noted.

- ***In-vitro* Dissolution Studies**

Dissolution test was carried out using USP type II rotating paddle method. The stirring rate was 50 rpm. 0.1 N HCl was used as dissolution medium (500 mL) and was maintained at 37 ± 10^0 c. Samples of 5 mL were withdrawn it predetermined intervals (2, 4, 6, 8, 10, 12, 14 & 16 minutes), filtered and replaced with 5 mL of fresh medium. Those collected samples were suitably diluted with dissolution fluid and absorbance of sample were noted at 240 nm by using UV Spectrophotometer.

- ***In-vitro* Taste masking evaluation by HPLC Method.**

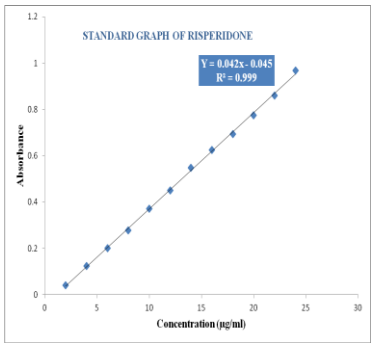
In vitro taste masking was evaluated by determining drug release in simulated salivary fluid (SSF) (pH 6.8) to predict release in the human saliva. Risperidone, equivalent to 12 mg was placed in 10 ml of SSF and shaken for 60 seconds. The amount of drug released was analyzed by proposed HPLC method.

Instrument used	Shimadzu HPLC with UV-detector
Analytical Column	Nuclosil C18, 125x4.6 mm, 5µ or Equivalent
Flow rate	1.0 mL/minute
Temperature	Ambient (25^0C)
Wavelength	240 nm
Injection volume	1 µL
Run time	6 Minute
Retention time	Approximately 2.5 minute for Risperidone
Mobile phase and diluting solvent	Acetonitrile : Water = 60 : 40

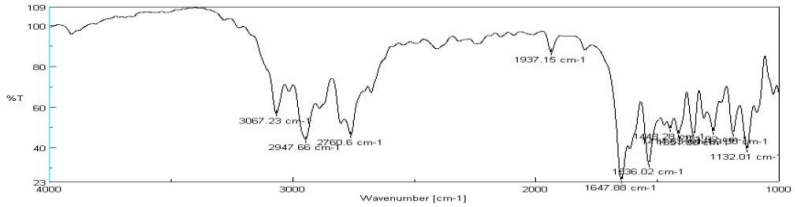
RESULTS AND DISCUSSIONS

Standard Graph of Risperidone

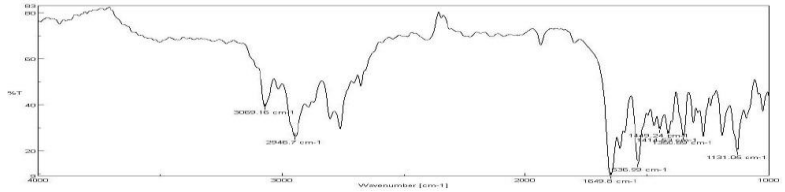
CONCENTRATION	ABSORBANCE
2	0.042
4	0.124
6	0.202
8	0.278
10	0.372
12	0.45
14	0.548
16	0.626
18	0.694
20	0.774
22	0.86
24	0.968



Compatibility studies by FT-IR Spectroscopy

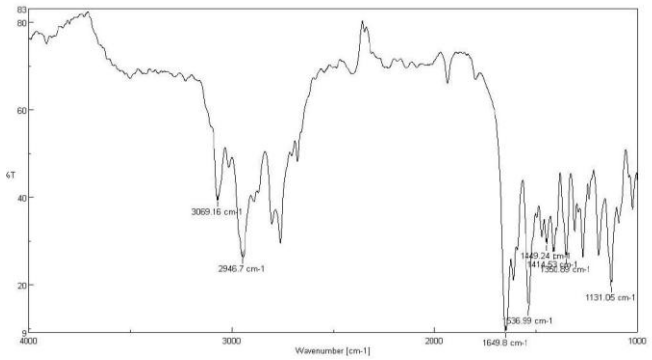


RISPERIDONE



RISPERIDONE + AMBERLITE IRP 64

Compatibility studies by FT-IR Spectroscopy



RISPERIDONE + CROSPOVIDONE + CROSCARMELLOSE SODIUM

Ingredients	Peaks of functional groups (cm^{-1})						
	CH-stretching (Aromatic)	CH-stretching (Aliphatic)	C=C stretching	C=N stretching	C-H bending (Aliphatic)	C-N stretching	C-F stretching
Risperidone	3069.16	2946.70	1536.02	1449.24	1414.53	1350.89	1132.01
Risperidone + Amberlite IRP 64	3067.16	2946.70	1536.99	1449.24	1413.53	1350.89	1131.05
Risperidone + Crospovidone + Croscarmellose Sodium	3067.23	2947.66	1536.02	1449.24	1413.53	1351.86	1132.01

Evaluation data of Pre-compression properties

Batch No.	Angle of Repose (^{0})	Bulk density (gm/cm^3)	Tapped Density (gm/cm^3)	Carr's Index (%)	Haussner's Ratio
F1	29.52±0.63	0.408±0.16	0.52±±0.24	21.5±0.14	1.31±0.16
F2	28.12±1.23	0.416±0.35	0.55±0.28	24.36±0.18	1.33±0.05
F3	25.95± 0.75	0.40±0.18	0.54±0.13	21.92±0.13	1.35±0.02
F4	28.92±1.58	0.38±0.24	0.45±0.19	15.55±0.19	1.19±0.02
F5	30.845± 0.69	0.392±0.27	0.476±0.24	17.64±0.24	1.20±0.07
F6	29.52±0.63	0.416±0.34	0.515±0.32	19.22±0.32	1.24±0.05
F7	28.70±0.91	0.425±0.25	0.522±0.27	18.58±0.27	1.23±0.07

Evaluation of physicochemical parameters of oral disintegrating tablets

Formulations	Thickness (mm)	Hardness (kg/cm^2)	Weight variation (mg)	Friability (%)
F1	4.06±0.090	2.240±0.195	81.05±1.66	0.653±0.1.21
F2	4.18±0.085	2.200±0.235	80.40±1.314	0.625±1.03
F3	4.108±0.096	2.380±0.259	80.45±1.538	0.622±1.36
F4	4.028±0.072	2.300±0.255	76.35±1.606	0.832±1.16
F5	4.104±0.158	2.200±0.158	80.85±1.565	0.830±1.03
F6	4.088±0.125	2.120±0.110	80.55±1.432	0.656±1.04
F7	4.062±0.053	2.260±0.195	80.9±1.804	0.434±1.75

Formulations	Wetting time (Sec.)	Water absorption Ratio (%)	Drug content(%)	*In vitro* disintegration time
F1	51±1.0	53.7±1.29	95.34±0.76	60±1.0
F2	39±1.0	60.49±1.86	98.23±0.43	42.3±2.5
F3	27.6±2.51	72.15±1.98	101.32±0.98	30±1
F4	74.33±4.04	33.75±2.83	97.65±1.12	79±3.6
F5	**26.66±2.08**	**76.73±2.88**	**99.76±1.02**	**25±1.0**
F6	47.33±6.80	56.25±1.52	92.84±0.86	50±0.5
F7	63.33±1.52	41.97±2.66	91.65±1.65	72±2.51

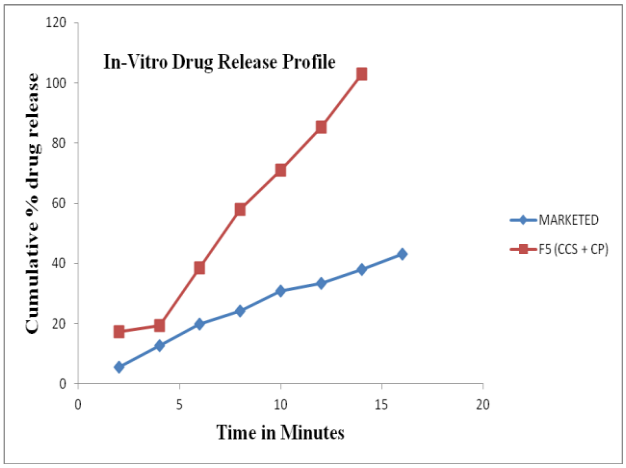
DISSOLUTION DATA

TIME	FORMULATION						
Min	F1	F2	F3	F4	F5	F6	F7
2	15.94±026	15.15±0.29	15.36±0.24	17.14±0.27	17.44±0.30	16.54±0.32	16.24±0.48
4	18.49±0.25	19.38±0.31	20.93±0.33	19.71±0.30	19.41±0.25	21.49±0.28	23.28±0.42
6	41.41±0.33	25.56±0.28	33.18±0.18	33.06±0.20	38.44±0.21	25.59±0.31	25.91±0.06
8	51.39±0.26	41.66±0.31	38.63±0.28	60.01±0.18	57.97±0.33	29.73±0.27	30.95±0.86
10	71.64±0.24	54.34±0.28	60.99±0.26	63.89±0.30	71.11±0.24	57.55±0.35	38.43±0.02
12	77.14±0.24	69.23±0.2	85.06±0.22	75.29±0.32	85.27±0.34	72.47±0.28	64.53±1.04
14	82.67±0.24	96.23±0.24	101.54±0.25	81.71±0.29	**102.85±0.23**	83.65±0.30	85.81±0.56
16	103.52±0.25	102.86±0.21	--	96.86±0.54	--	96.43±0.34	99.51±0.81
18	--	--	--	96.86±0.54	--	96.43±0.34	102.27±0.11

In-vitro drug release data of Risperidone conventional marketed product and optimized formulation F5 (CCS+CP)

Time (min)	Cumulative % drug release	
	Marketed product	F5(CCS+CP)
2	**5.54**	**17.44**
4	**12.83**	**19.41**
6	**19.78**	**38.44**
8	**24.12**	**57.97**
10	**30.85**	**71.11**
12	**33.48**	**85.27**
14	**38.02**	**102.85**
16	**43.10**	

In-vitro drug release data of Risperidone conventional marketed product and optimized formulation F5 (CCS+CP)



Chromatogram of Risperidone

==== Shimadzu LCsolution Analysis Report ====

F:\soumya\res_11232012_4.lcd

Acquired by	: Admin
Sample Name	: Unknown Sample002
Sample ID	: UNK-0002
Tray#	: 1
Vail #	: 3
Injection Volume	: 1 uL
Data File Name	: res_11232012_4.lcd
Method File Name	: soumya.lcm
Batch File Name	: res.lcb
Report File Name	: Default.lcr
Data Acquired	: 11/23/2012 5:50:30 PM
Data Processed	: 11/23/2012 6:28:34 PM

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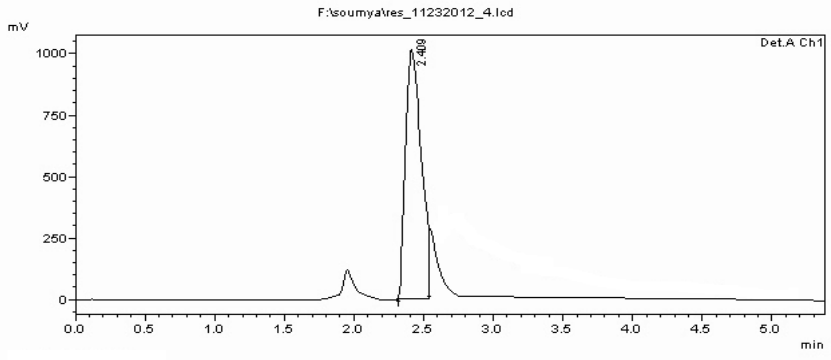
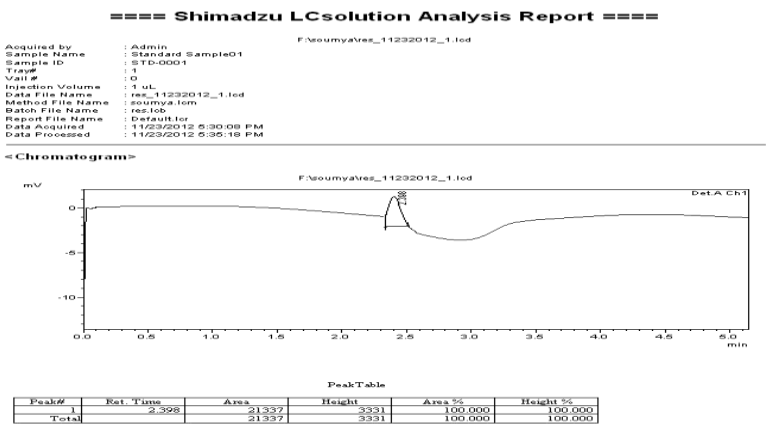


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	2.409	8050758	1013008	100.000	100.000
Total		8050758	1013008	100.000	100.000

Chromatogram of Risperidone+Ameberlite IRP 64



Peak#	Ret. Time	Area	Height	Area %	Height %
1	2.398	21337	3331	100.000	100.000
Total		21337	3331	100.000	100.000

II. CONCLUSION

- Domperidone oral disintegration tablets which were prepared by direct compression with various superdisintegrants (alone and combination) have established good flow properties and compressibility characteristics.
- Drug taste was masked with Amberlite IRP 64 (1:3) effectively.
- FTIR studies showed that there was no interaction between Drug (Domperidone) and excipients i.e., super disintegrants (CCS and CP).
- Water absorption ratio 76.73±2.88%, wetting time 26.66±2.08 sec, disintegration time 25±1.0 sec were found better in F5 i.e., Croscarmellose sodium + Crospovidone.
- From different formulations by taking into consideration of disintegration and dissolution values F5 (i.e., Croscarmellose sodium + Crospovidone) which was having 102.85% drug release at 14min better than other formulation.
- Then comparing with marketed preparation, it was released only 38.02% in 14min. There by it was suggested that Domperidone Oral disintegrating tablets were better than normal conventional tablets because of lesser time for drug release and convenience.

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