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FORMULATION AND EVALUATION OF ONDANSETRON HCL ORALLY DISINTEGRATING TABLETS

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ABSTRACT

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 tablet which has the ability to dissolve into mouth has risen as an option in contrast to regular oral medication use. Based on present work, Oro-dispersible tablets of Ondansetron were structured to expand technique, crospovidone and Croscarmellose sodium in the blend since super disintegrates were utilized alongside straightforwardly miniaturized microcrystalline cellulose to improve mouth feel. The tablets for clumps arranged were assessed for stiffness, friability, sedate substance, consistency, wetting time and water assimilation proportion and *in vitro* dissolution time. In light of *in vitro* scattering time (Approximately 7-30s), All detailing were tried for *in vitro* medication release time (in phosphate buffer). Check the momentary security (for three months at 40^0 C ±2 /75% ±5%RH), and medication excipients connection contemplate. Among all the definition, the definition arranged by Croscarmellose was found to have the least scattering time 7.36s. Momentary dependability examines the best detailing showed that not too much change was there in medication data and in vitro scattering time of span.

KEYWORDS: Crospovidone; Croscarmellose sodium; Ondansetron hydrochloride; Oro dispersible tablets.

INTRODUCTION

Orally disintegrating TABLETS (ODT[s])

These are the tablets which melt and crumble unexpectedly inside the spit to produce their activities in a small number of seconds exclusive of the help of Distilled water. It takes over 15seconds-3minutes to mix into mouth for a mouth dissolving tablet. Primarily the MDT's (mouth dissolving tablets) have superb disintegrates and flavor masking agents. For the administration of medication, the oral way was well thought-out the most frequently used way. Within it process, most normally used orally shipping of medicine, consisting of tablets and capsules. Within this procedure consuming is the most difficulty. The swallowing problem (dysphasia) generally within the event of child's and olds patients believes mainly in compliance choose tablets. Mouth dissolving tablets (MDT) is kinds of solid dosage form of drugs formulation. These are buckle and sublingual capsules. These kinds of pills placed in the oral cavity inside the region in which they discharge their drug contents to get absorption in particular in the course of the mouth mucosa. These pills are typically modest in length and slightly flat and are supposed to be located among the cheek and teeth or within the cheek pouch (buckle pills), or below the tongue (sublingual tablets).

Benefits of orally disintegrating tablets (ODT[S])

- Easy for government to patients that can't swallow the medicines such as hepatitis and geriatric, unconscious and emotionally disabled patients.
- Doesn't want the water to spend the pill throughout travelling (no demand water)
- Quickly breakup of medication generate rapid actions. Drug release of medication be able to be raised through preventing passing of this medication beginning pharynx and oesophagus.
- There's not any danger of suffocation and choking through mouth-melting pills uptake. Mouth dissolving pills are helpful in certain instances like motion sickness, during coughing, etc... ·
- The mouth melt pills are stable for a more extended period until it's consumed.

MATERIALS AND METHOD

Ondansetron hydrochloride was a gift from ambark life science (roorkee, U.K.), Other ingredients like mannitol, crospovidone, Croscarmellose, 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.

Preformulation studies

The angle of Repose

Angle of repose is defined as the maximum angle that can be obtained between the surface of a powder heap and the horizontal plane. Angle of repose has been used as indirect method of quantifying powder flowability, because of their relationship with interpartical cohesion.

The angle of repose is measured by funnel method. The funnel is fixed on a burette stand at a particular height 'h'. A graph paper is placed below the funnel on a table. The powder is pass slowly through the funnel, until if form a pile. The blend powder is stop when the pile touches the tip of the funnel. Circumference of the pile of powder blend is drawn with the pencil without disturbing the pile. The radius of the pile 'r' is noted. The angle of repose was calculated using the following equation.

$\tan \theta = h / r$

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

Where, θ = angle of repose

h = height of the cone

r = radius of the cone base

The results are shown in table.

The lower the angle of repose, better the flow properties, when granules are placed in the hopper & allowed to slide down into the die for compression. It forms tablets. The angle of repose may be calculated by measuring the height (h) of the tablets and the radius of the base (r) with the ruler. The angle of repose shows in between 30-40°C, which is considered as a passable flow of granules.

Bulk density

Bulk density is the ratio of total mass of powder to the bulk volume of powder. It is determine by taken the weighed quantity of blend powder from each formulation in a 50 ml measuring cylinder and the initial volume of the powder in measuring cylinder is noted. The bulk density of powder is calculated by using the formula,

$P_b = M / V_b$

Where.

ρ_b = bulk density

M = Total mass of powder

V_b = bulk volume of powder

Tapped density

Tapped density is defined as total mass of the powder is divided by tapped volume of the powder. It is calculated by taken the powder in measuring cylinder and tapping the powder for 750 times the tapped volume is noted. the difference between tow tapping less than 2%, if the difference more than 2% , the tapping continued for 1250 times and the tapped volume is noted. The tapping continue when the difference between two tapping successive volume is less than 2%. It is calculate by the following formula,

$P_t = M / V_t$

Where,

P_t = Tapped density

M = total mass of powder

V_t = tapped volume of powder

Compressibility Index

The compressibility of the granules was determined by Carr's Compressibility Index.

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:

$$\text{Compressibility Index} = \frac{V_t - V_b}{V_t} X\ 100$$

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 (Table 3.8).

Hausner's ratio: It is the ratio of tapped density to bulk density. It is calculated by the following formula,

Hausner's ratio = tapped density / bulk density.

Preparation of mouth dissolving tablets by direct compression method

Accurately weighed the quantity of Ondansetron, crospovidone, Croscarmellose sodium, other ingredient and passed in 44 mesh sieves. 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/cm^2 for all batches. The weight of tablets of the formulation was 150 mg mention in blow table.

Table: Composition of orally disintegrating tablets of Ondansteron HCl with different batches.

Ingredients(mg/tab)	F_1	F_2	F_3	F_4	F_5	F_6	F_7
Ondansetron HCl	10	10	10	10	10	10	10
Croscarmellose(CS)	10	20			10	20	
Crospovidone (CP)			10	20			10
Mannitol	35	35	35	35	35	35	35
Aspartame	4	4	4	4	4	4	4
Magnesium Stearate	3	3	3	3	3	3	3
Orange flavor	3	3	3	3	3	3	3
Talc	2	2	2	2	2	2	2
M.C.C(Avicel)	83	83	83	83	83	83	83
Total weight	150	150	150	150	150	150	150

Evaluations of post formulation studies of tablets
Psycho-Chemical studies of formulated tablets
Thickness
The thickness of tablets was determined by using venire caliper. There have been handiest five tablets in each batch which are used, and average values had been calculated. The thickness was denoted in millimeter. The result is proven in Table

Test for the weigh variation
To study weigh variation 20 tablets of each formulation were taken and firstly individual tablet were weighed, after that total 20 tablets were weighed using an electronic balance (AW-220 shimadzu), the deviation not more than ± 7% and the test was performed according to the official method.

Drug content
Four tablets were finely powdered; quantity equal to 50 mg of Ondansetron hydrochloride was appropriately weighed and transferred to 100 ml volumetric flask containing 50 ml of methanol. This becomes allowed to stand for six hours to ensure the whole solubility of the drug. Answers had been made as much as quantity, filtered, suitably diluted, and expected for Ondansetron hydrochloride contents at 248 nm, the use of an UV spectrophotometer the usage of methanol as blank.

Hardness
For each formulation the hardness of six tablets was determined using the Monsanto hardness tester (cadaman). The tablets were held along its oblong axis in between two jaws of the tester at this point, reading should be zero kg/cm^2. Then constant force was applied by rotating know until the tablets fractured.

Friability
It is measure of tablets strength. It is related to tablets ability to with stand both shook and abration with crumbling during the handling of manufacture, packing and consumer use.

Method: 6 tablets have been weighed and placed in Roche's friabilator where the tablets were exposed to rolling at 25 rpm, and repeated shocks are resulting for free falls inside the equipment. After 100 revolutions, the tablets were de-dusted and weight again. The friability is known through the loss of percent of the weight of the tablet. Best less than 1 percent losses are relevant.

***In-vitro* test of finished formulated tablets of Ondansetron hydrochloride**
Determination of swelling index
The swelling index of drugs have been decided in phosphate buffer (ph 6.8), at room temperature up to 8 hours. The bloated burden of this tablet has been ascertained via as soon as intervals15. The swelling equation may be determined without difficulty through using this equation:

$$\text{Percentage of water uptake polymer swelling} = \frac{Ws - Wi}{Wi} \times 100$$

Ws define the Wight of matrix at time t, W is the initial weight of the Matrix.

***In-Vitro* drug Release Studies (Dissolution study)**
In-vitro drug release look at for the prepared matrix pills become performed for 10-12 hours the use of six-station USP type II (paddle) equipment at 37ºc ± 0.5 ºC and 50 rpm speed. The dissolution studies have been done in triplicate for 2 hours in phosphate buffer P^H 6.8. Eight under spout condition, first of all half an hour one hour after which in line with one hour length forms of 5 ml were pulled from dissolution slight and substituted with a new medium to hold the quantity constant. Right dilution is there at once afterward filtration, the pattern solution changed into analyzed at 248 nm for Ondansetron HCl by means of a UV-spectrophotometer for determining its cumulative % drug release or amount gift within the pattern.

Disintegration test
Disintegration time was measured by disintegration test apparatus. Which have the six tube basket, the bottom surface of the basket was made up of stainless steel with steel screen (mesh no. 10). The tablets are placed in six tube of basket and distilled water was used as dissolution media. The test carries out at 37±0.5ºC in disintegration equipment and the speed was 100 rpm. When the tablet was completely disintegrated, the time was noted. The disintegration time was expressed in second.

***In vitro* dispersion time**

Take 10 ml of distilled water in a measuring cylinder. Five tablets were taken from each formulation and Tablets are added in distilled water at 37 ± 0.5^{0}C. Determined the tablets for completes dispersion at time require.

Ratio of wetting time and absorption

Taken 5 cm petridish. Two-piece of tissue paper is placed in a petridish. Water soluble eosin dye is added to petridish. The tablets are placed on the floor of tissue paper. After some time, the purple or pink shade is produced at the surface of tablet, the time is cited. It is a wetting time. The identical technique is accompanied by the water absorption ratio. It's far determined by using the subsequent equation,

$$R = \frac{W_b - W_a}{W_a} \times 100$$

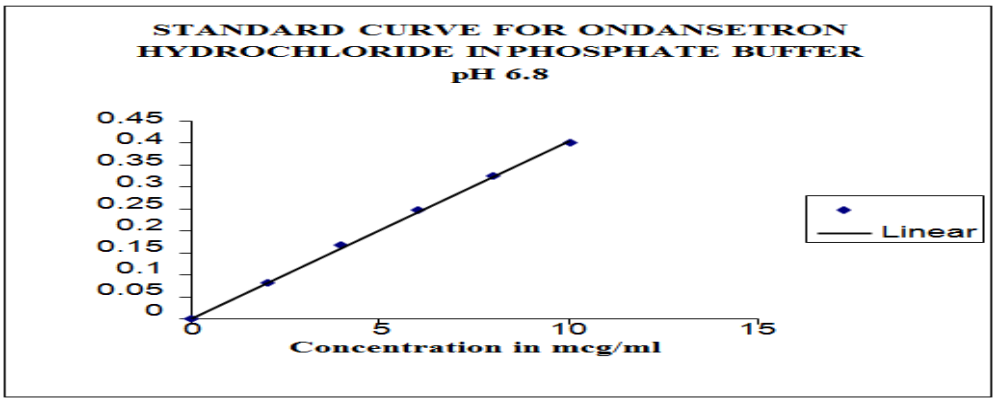
Stability studies

The selected formulation became examined for three months at the storage conditions at room temperature and 40°c at 75% RH were analyzed for their drug content. The residual drug contents of formulations had been located to be in the permissible limits, as shown in the desk. The tablets showed excellent bodily stability at room temperature and forty °c at 75% RH. No appreciable changes were determined in any of the formulations. The drugs were additionally subjected to IR studies to determine well matched the drug with the recipients used within the pills. Their studies confirmed that there are no interactions.

RESULTS AND DISCUSSION

Standard calibration curve of Ondansetron hydrochloride in phosphate buffer pH 6.8:

Concentration in (µg/ml)	Absorbance at 248 nm
0	0
2	0.084
4	0.168
6	0.250
8	0.332
10	0.403
Slope	0.042
Correlation	0.9995



FT-IR SPECTRAL STUDIES

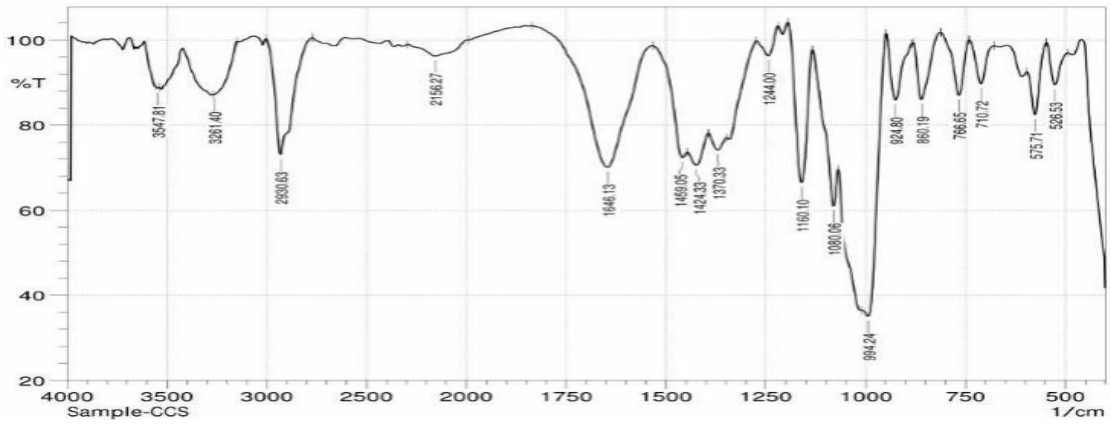


Fig.: FT-IR Spectrum of pure drug Ondansetron hydrochloride.

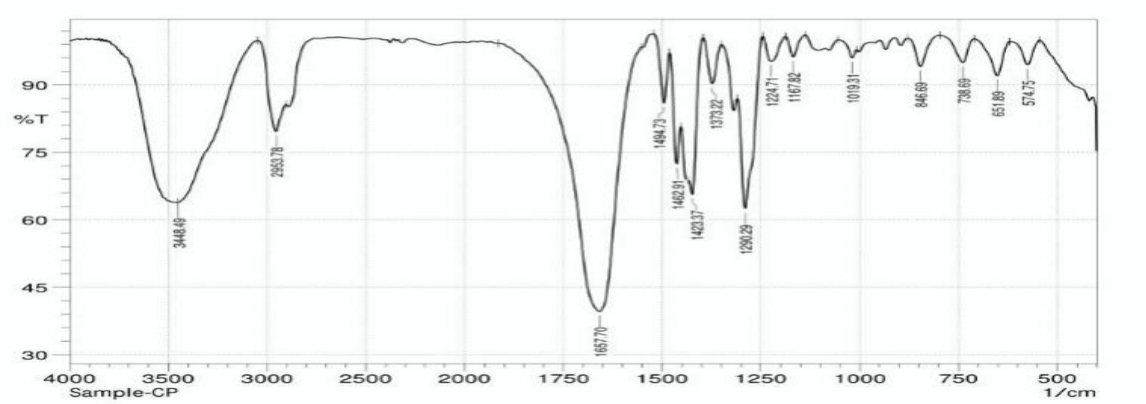


Fig.: FT-IR spectrum of Croscarmellose sodium.

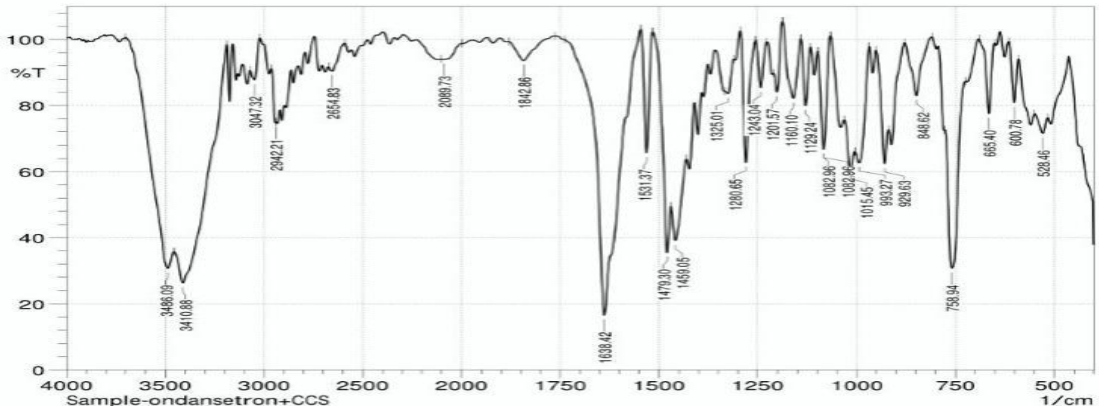


Fig.: FT-IR spectrum of crospovidone.

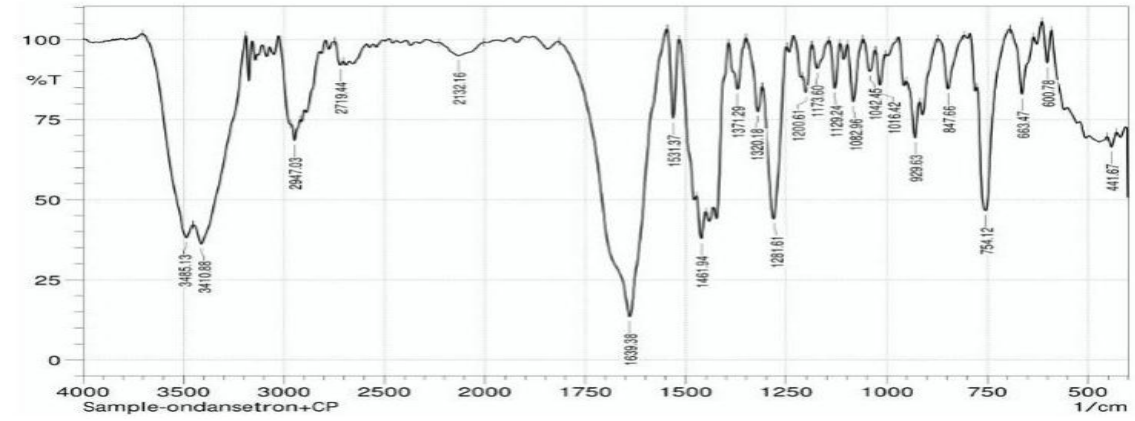


Fig.: FT-IR spectrum of Ondansetron hydrochloride + crospovidone.

Table: comparative FT-IR Spectral data of drug and super disintegrate.

Table: Evaluation of pre-compression parameters of all formulation.

Formulation	Angle of repose (θ)	Bulk density (g/cm^1)	Tapped density (g/cm^1)	Compressibility Index (%)	Hausner's ratio
F_1	$31^0.15'$	0.630	0.755	14.10	1.17
F_2	$29^0.16'$	0.405	0.368	12.99	1.15
F_3	$28^0.01'$	0.320	0.377	13.25	1.15
F_4	$28^0.95'$	0.315	0.358	13.32	1.12
F_5	$26^0.32'$	0.365	0.388	13.70	1.16
F_6	$25^0.10'$	0.388	0.398	15.90	1.14
F_7	$22^0.93'$	0.390	0.325	15.31	1.17

*Calculated average mean of above three values.

Compound	Functional Group				
	OH (cm^1)		OH (cm^1)		OH (cm^1)
Drug (Ondansetron hydrochloride)	3410	Drug (Ondansetron hydrochloride)	3410	Drug (Ondansetron hydrochloride)	3410
Drug + CCS	3490	Drug + CCS	3490	Drug + CCS	3490
Drug + CP	3491	Drug + CP	3491	Drug + CP	3491

The angle of all Repose: The F_1 formulation have $31^0.15'$ angle of repose indicate good flow properties. Other formulation was found $22^0.93'$ -$29^0.16'$ angle of repose indicate good flow properties. Angle of repose mansion in the above table.

Bulk density: The Ascertain worth of bulk density of formulation was Cite in above table. The obtained values are 0.315-- 0.630g/cm^1.

Tapped density: The ascertain values of exploited density of formation were cited in above table. The obtained values are 0.325-- 0.755 g/cm^1.

Compressibility index: The ascertain values of compressibility of the formulation are mention in above table 14. The ascertain values are 12.99%- 15.90%.

Hausner's ratio: The acquired Hauser's ratio values are 1.12-- 1.17, which Mention in preceding (table3.8)

Table: Evaluation of physical properties of all formulation.

Formulations	Thickness (mm)	Hardness (kg/cm^2)	Weight variant (mg)	Friability (%)
F_1	3.31±0.044	3.85 ± 0.35	143±1.22	0.25
F_2	3.35±0.012	4.16 ± 0.24	141±0.66	0.43
F_3	3.25±0.014	3.66 ± 0.32	141±0.45	0.51
F_4	3.41±0.012	4.18 ± 0.22	142±0.44	0.47
F_5	3.41±0.018	4.22 ± 0.44	143±0.97	0.33
F_6	3.22±0.055	3.60 ± 0.30	142±0.97	0.21
F_7	3.33±0.008	3.01 ± 0.25	140±0.46	0.16
Marketed sample	2.80±0.011	3.60 ± 0.32	140±0.88	0.27

Form of tablets: The invented tablets of batches are circular, and it's no cracks at microscopic evaluation.

Thickness: The thicknesses of invented tablets were uniform in character. The depth values of the formulation are 3.22±0.055 mm - 3.41±0.018 mm. The values cited in above (table).

Hardness: The every formula of formulated ablates possess the hardness together with the Array of 3.01 ± 0.25 kg/cm^2- 4.22 ± 0.35 kg/cm^2. Which mention in above (table).

Weight Variation test: The obtained value of weight variation all batches be shows in above (table). The all formulated tablets are passed in weight variant test. The values have been 140±0.46 mg to 143±0.97 mg (table).

Friability: The obtained values of friability evaluation of formulation were cited in preceding (table 3.8). The values are 0.16-- 0.51. The friability of pills of the formulation is not greater than 1 percent.

Table: Evaluation of Ondansetron hydrochloride tablets.

Formulation Code	Disintegration Test (Sec)	Wetting Time (Sec)	Water Absorption Ratio	*In vitro* Dispersion Time (Sec)	Fineness of Dispersion
F_1	27±0.32	101±1.44	81.23±0.62	49±0.15	Passed
F_2	23±0.22	91±1.45	86.37±0.48	38±0.13	Passed
F_3	16±0.15	49±2.38	93.18±0.39	27±0.32	Passed
F_4	23±0.50	87±0.81	78.26±0.20	39±0.16	Passed
F_5	24±0.62	80±0.20	88.13± 0.10	37±0.53	Passed
F_6	21±0.45	57±0.31	87.97±0.22	28±0.77	Passed
F_7	13±0.62	46±0.37	92.25±0.53	24±0.44	Passed
Marketed Sample	18±0.43	55±0.55	95.32±0.32	28±0.35	Passed

Disintegration time: disintegration time of Ondansetron hydrochloride is found in range between 13 to 27 second. The values are shows in above table.

Wetting time: That the obtained wetting time of pills of all formulation cites in above table 16. Tablets were formulated using Ondansetron HCl +crospovidone + Croscarmellose sodium. The Wetting time was 46 - 101 seconds.

Water Absorption ratio: The water absorption of the formulation ratio is mention in the above table. 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 78.26 – 93.18 Seconds.

***In vitro* Dispersion time:** The *in vitro* dispersion period was found range between 24 - 49 seconds. All batches of formula have less than 30 seconds of dispersion t

***In vitro* dissolution dtudies**

Table: drug release percentage of ondansetron hydrochloride ODT^{s}.

Time (min)	Percentage drug release (%)						
	Formulation code						
	F_1	F_2	F_3	F_4	F_5	F_6	F_7
2	21.60±0.50	25.86±0.38	31.50±0.23	18.52±0.31	22.44±0.29	30.11±0.60	35.31±1.20
4	31.24±0.69	34.75±0.59	42.59±0.56	31.18±0.30	31.55±0.50	48.51±0.49	54.16±0.60
6	42.59±0.60	49.90±0.27	61.55±0.19	48.66±0.42	46.63±0.07	59.91±0.42	72.29±0.23
8	66.99±1.24	69.62±0.58	79.55±0.45	58.95±0.69	62.80±0.30	74.18±0.68	85.62±0.53
10	72.29±0.15	76.29±0.49	84.45±0.10	70.71±0.59	73.19±0.08	81.61±0.10	99.86±0.08

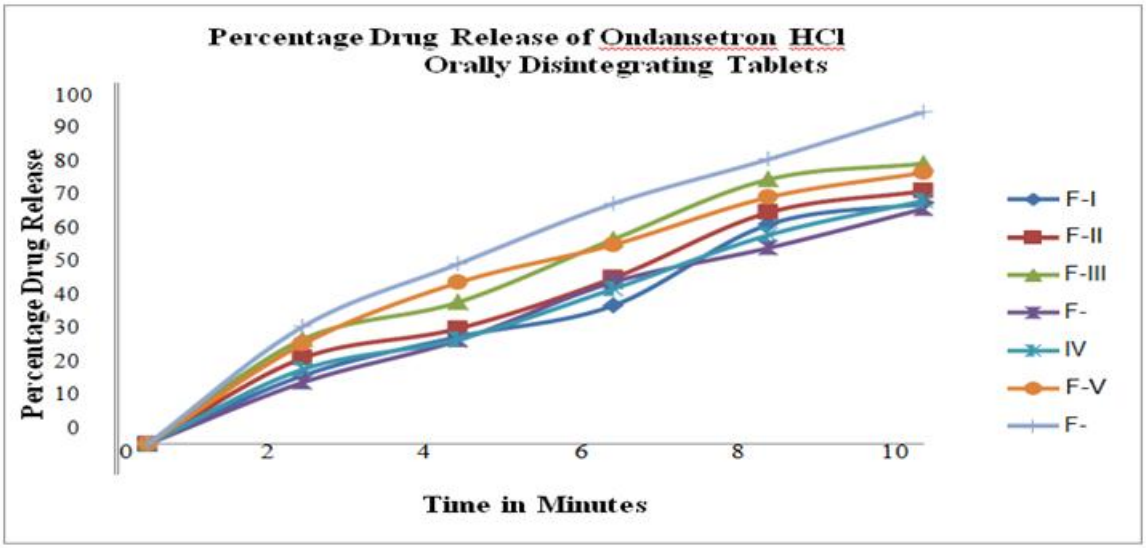


Fig.: comparative In vitro drug release picture of Ondansetron HCl oral disintegration tablets.

Table: sta bility data of Ondansetron hydrochloride oral disintegration tablets stored at 40±2^{0}C/75%±5% RH.

S.No.	Storage conditions: 40±2^{0}C/75%±5% RH				
	Test	**Initial period**	**1st month**	**2nd month**	**3rd month**
1	Physical appearance	complies	complies	Complies	Complies
2	Average weight	142.49	141.99	142.29	141.30
3	Thickness (mm)	3.33	3.38	3.33	3.32
4	Hardness (kg/cm^{1})	3.01	3.1	3.01	3.01
5	Friability (%)	0.16	0.21	0.18	0.20
6	Disintegration test (sec)	11	11	9	07
7	In vitro dispersion time (sec)	23	23	23	22
8	Fineness of dispersion	Passed	passed	Passed	Passed
9	In vitro drug release at the end of 10 min (%)	99.86	99.76	99.74	99.73
10	Assay (Limit 99-110%)	99.93	99.88	99.82	99.80

CONCLUSION

According to the previous work, Oro-dispersible tablets of Ondansetron hydrochloride were invented with superb disintegrates such as crospovidone, Croscarmellose sodium independently and also mix together, tablet are prepared by direct compression technique. Ondansetron hydrochloride is a water-soluble drug but has limited bioavailability. Bioavailability of medication is raised via this method. In equipped tablets device $F_{7\backslash}$ very own dispersion time about 7-24 second, and disintegration time 13 to 27 second and wetting time 46 to 101 seconds. Short-time period stability of method F_7 has not any alternate change in physical appearance, average weight, thickness, hardness, friability, disintegration test, in vitro dispersion time, fineness of dispersion, in vitro drug release at 10 min and assay, stored for the three month at 40±2^{0}C/75%±5% RH. The maximum drug release

percentage of over 99.93 of formulation F_7. The most formulation of tablets has a minimal wetting time and the highest water absorption ratio. The most batches of tablets have <1 per cent friability, which signaled the fantastic mechanical resistance.

REFERENCES

1. Brahmanker D.M, Sunil B. Jaiswal. Bio Pharmaceutics and Pharmacokinetics-A treatise: 8th Ed; New Delhi, Vallabh Prakashan, 2003; 18.
2. Kalyan Babu P.G, Vital M, Nirupama K, Gayatri Devi M, and Uma Devi P. Solid dosage forms. International Research Journal of Pharmaceutical Sciences, 2012; 3(4): 47-51.
3. E.A. Rawlin. Bentley's Text Book of Pharmaceutics 8th Ed; London, Bailliere Tindall, 2010: page no: 269.
4. Lippincott Williams & Wilkins, Edward Rudnic, Alfonsa R.Gennaro. Remington's Pharmaceutical Sciences.18thEd; Pennsylvania, Mack publishing company, 2011; 1633.
5. Kaur Harbir. Processing technologies for pharmaceutical tablets. International Research Journal of Pharmacy, 2012; 3(7): 20-23.
6. Leon Lachman, Herbert A.Lieberman. The Theory and Practice of Industrial Pharmacy, S Prasanth VV, Sidhyartha Sarkar, Sourav Tribedi, Rinku Mathappan and Sam T Mathew. Formulation and evaluation of Oro dispersible tablets of Salbutamol Sulphate. Research and reviews: Journal of Pharmacy and Pharmaceutical Sciences, 2013; 2: 26-36.
7. Akula Nikhil Prashant, J. Sharma V. C, Nagaraju Potnuri and Srinivas Martha. Formulation and evaluation of oral disintegrating tablets of Nateglinide. Scholars Research Library Der Pharmacia Lettre, 2015; 7(2): 49-59.
8. Balakrishna T, Vidyadhara S, Murthy T. E. G. K, Viswanadh K, Tejasri M. Formulation and evaluation of Oro dispersible tablets of Zolmitriptan. Asian Journal of Pharmaceutics, 2016; 10(4): 683-687.
9. Sandhyarani G, Sarangapani M. Formulation and evaluation of oro dispersible tablets of Domperidone. IOSR Journal of Pharmacy, 2016; 6(9): 39-47.
10. Bharathi A, Ramakrishna V, Sowjanya K. and Shobha Deepthi K. Formulation development and *in vitro* evaluation of orally.