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DEVELOPMENT AND EVALUATION OF MOUTH DISSOLVING ORO-DISPERSIBLE PELLETS OF MECLIZINE HCL USING EXTRUSION AND SPHERONIZATION TECHNIQUE

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ABSTRACT
Among all the dosage forms conventional forms are convenient way to administer, and even more easy when preparation like Oro dispersible tablets or pellets administered which directly get into systemic circulations. Pellatization is a technique which achieves control release rate of drugs when coated with suitable polymers. For formulation, drug-excipients incompatabilities were carried out by FTIR and DSC. Among all the F2(SD-1:2) was having std results for particle size (2.57), Bulk density(0.406±0.004), Tapped density(0.498±0.003), Cars index(8.535±0.002), Hausners ratio(1.023±0.001). Pellet were evaluated for F2, Pellet size(0.80±0.015mm), Disintegration(50.9±0.020sec), Wetting time(4.0min), Friability(0.7±0.036%). *In vitro* dissolution test reveals the release increase from 50% to a maximum of almost 100% for 30 min. The release is in the following order of Formulation F2> F1> F5> F3> F4.

KEYWORDS: Oro dispersible, FTIR, DSC, Pellet, Disintegration.

I. INTRODUCTION
Oral route of administration is the most important method of administering drugs for systemic effects. Many pharmaceutical dosages are administered in the form of tablets, hard gelatin capsules, granules, powders, and liquids. Many patients, particularly pediatric and geriatric and bed ridden patients have difficulty in swallowing or chewing solid dosage forms. This problem is also applicable to active working or travelling people who do not have ready access to water. Recent advances in novel drug delivery systems (NDDS) aim to develop fast dissolving /disintegrating tablets to improve patience compliance. Dispersible tablets (DTs) Dissolve or disintegrate in saliva within a minute without the need of water or chewing.[1]

The various technologies used to prepare ODTs include conventional methods like direct compression, wet granulation, and moulding, spray drying, freeze drying and sublimation. Direct compression represents a simple and cost effective tablet manufacturing technique. The basic approach used in the development of the dispersible tablets is the use of Superdisintegrants. Superdisintegrants facilitate the break upon disintegration of tablet content into smaller particles that can dissolve more rapidly than conventional dosage form. The commonly used superdisintegrants are Croscarmellosesodium, Crospovidone, Kollidon CLM and sodium Starch glycolate.[2,3]

Pellets
The word "pellet" is used to describe a variety of systematically product geometrically defined agglomerates obtained from diverse starting material. It consist of small discrete unit and exhibit some derived characteristics produced by agglomeration of fine powder with binder solution normally the size of the pellets varies from 0.5 – 1.5 mm for oral dosage form.[1,4]

An innovative use of pellet in pharmaceutical field are given as[2]

- Improve aesthetic appearance of products.
- Achieve control release rate of drugs when coated with polymers.
- Improve flow properties and flexibility in formulation development and manufacturing.
- It has less variance in transient time through the gastro intestinal tract (GIT) than a single Unit dosage form like tablet.

II. Experimental Methods and Discussion
Preparation of Solid Dispersion
Solid dispersions of meclizine Hcl in polyethylene glycol-6000 [PEG-6000]1:1, 1:2, 1:3 w/w were prepared by the solvent evaporation method. Meclizine Hcl and the polymer were dissolved in a minimum amount of

methanol. The solvent was removed by evaporation on magnetic stirrer at the temperature of 40°C for 1 h. The resulting mass was dried for 2 h at room temperature and stored overnight in a dessicator. After drying, the mass was sieved through a mesh # 60. The resultant solid dispersions were stored in dessicator until further investigation.[5]

Characterization of solid dispersion

Practical Yield

Percentage practical yield were calculated to know about percent yield, thus it helps in selection of appropriate ratios of solid dispersion. Solid dispersions were collected and weighed to determine practical yield from the following equation.

$$\text{Percentage Yield} = \frac{\text{Practical Mass (SD)}}{\text{Theoretical Mass (Drug + carrier)}} \times 100$$

Drug content

The content of meclizine Hcl in PEG 6000 solid dispersion was estimated by UV spectrophotometric method using Shimadzu spectrophotometer. An accurately weighed quantity of solid dispersion (equivalent to 10 mg of meclizine Hcl) was taken and dissolved in 100ml of 0.1N Hcl, from this solution 1ml of solution was diluted to 10ml and assayed for drug content at 232 nm.[6]

Particle size

Particle size determination

Particle size analysis was done by sieving method using Indian standard sieves ≠ 10, 12, 16, 22, 28, 44. Weighed quantity of the solid dispersion was shifted into the sieve shaker. The machine was run for five minutes after which all the meshes were taken out and retained solid dispersion were collected by respective mesh and the % retention of solid dispersion by that mesh was calculated. Average particle size was calculated using the formula where n is frequency weight and d is the mean diameter.[7,9]

$$davg = \sum dn / \sum n$$

Rheology properties

Angle of repose, Carr's index and Hausner's ratio were determined to assess the flow ability of the prepared solid dispersion.

Bulk density

The bulk density of a powder is the ratio of the mass of an untapped powder sample (W) is taken in a graduated measuring cylinder and volume (V_0) including the contribution of the interparticulate void volume. Hence the bulk density depends on both density of powder particles and the spatial arrangement of particles in the powder bed. The bulk density can be expressed in grams per millilitre (g/ml).

Bulk density is calculated using the equation:

$$\text{Bulk density (BD)} = \frac{\text{weight of the powder}}{\text{Volume of powder}}$$

Tapped density

The tapped density is obtained by tapping a measuring cylinder containing a powder sample and the volume is measured as initial volume. Measuring cylinder was fixed in the 'Tapped Densitometer' and tapped for 750-1250 times until the difference between succeeding measurements is less than 2%. The final reading was denoted by (V_f). The Tapped density can be expressed in grams per millilitre (g/ml).

$$\text{Tapped density (TD)} = \frac{W}{V_f}$$

Carr's compressibility index

Carr's compressibility index is an indication of the flowability of a powder.

$$\text{Carr's index} = \frac{\text{Tapped density-poured density} \times 100}{\text{Tapped density}}$$

Hausner's ratio

It indicates the flow properties of powder and is measured by the ratio of tapped density to bulk density.

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

***In vitro* drug release study**

In vitro release studies were carried out for the formulations in dissolution test apparatus USP type II. The medium used was 900ml 0.1N Hcl. Solid dispersion equivalent to 25 mg of the pure drug were used. The tests were carried out for 12 hrs and at 50rpm at 37° ± 0.5°C. 5ml of the aliquots were withdrawn at different predetermined time intervals and filtered. The required dilutions were made with dissolution medium and the solution was analyzed for the drug content spectrophotometrically at 232 nm against suitable blank. 5ml of the dissolution medium was replaced in the vessel after each withdrawal to maintain sink condition. From this % drug release was calculated and this was plotted against time to study the pattern of drug release.[7,9,13]

Preparation of Meclizine Hcl solid dispersion loaded pellets

The compositions of the various formulations are shown in Table:1. Extrusion-spheronization was evaluated as a granulation technique to obtain desired pellet characteristics for preparation of Meclizine Hcl solid dispersion pellets. The first step in this process was to study the effect of the formulation and process variables on pelletized product characteristics so as to get pellets with best possible yield, good flow ability and desired particle size distribution. Meclizine Hcl solid dispersion (SD F3, 1:3) equivalent to 25 mg of Meclizine Hcl and combination of different superdisintegrants (Sodium Starch Glycolate, Croscarmellose, Crospovidone) were

used by Hirajau et al.14. All materials were blended in a polybag using geometric dilution principle and kneaded into wet mass of required plasticity using distilled water in which PVP K30 was dissolved which helped as binder and granulating agent. The cohesive mass was extruded through extruder which resulted in extrudate. The extrudates were rotated in spheronizer using optimum process conditions of spheronizer speed of 900 rpm and residence time of 5 min. Lubrication was done using magnesium stearate during spheronisation for 1 minute to avoid sticking and to facilitate smooth discharge of pellets from spheronizer. The pellets obtained were dried on paper lined trays in hot air oven at 45^0C for 1 h.[15,16]

Table No. 1: Formulation of Meclizine Hcl solid dispersion loaded pellets.

S.No	Ingredients (mg)	F1	F2	F3	F4	F5
1	Meclizine Hcl (SD)	25	25	25	25	25
2	Lactose	18	16	16	18	16
3	Microcrystaline Cellulose (MCC)	48	45	45	48	45
4	Sodium Starch Glycolate	5	10	-	-	-
5	Croscarmellose sodium	-	-	10	-	-
6	Crospovidone	-	-	-	5	10
7	Saccharin	2.5	2.5	2.5	2.5	2.5
8	Polyvinyl Pyrrolidone (PVP)	1.5	1.5	1.5	1.5	1.5
9	Distilled Water	q.s	q.s	q.s	q.s	q.s

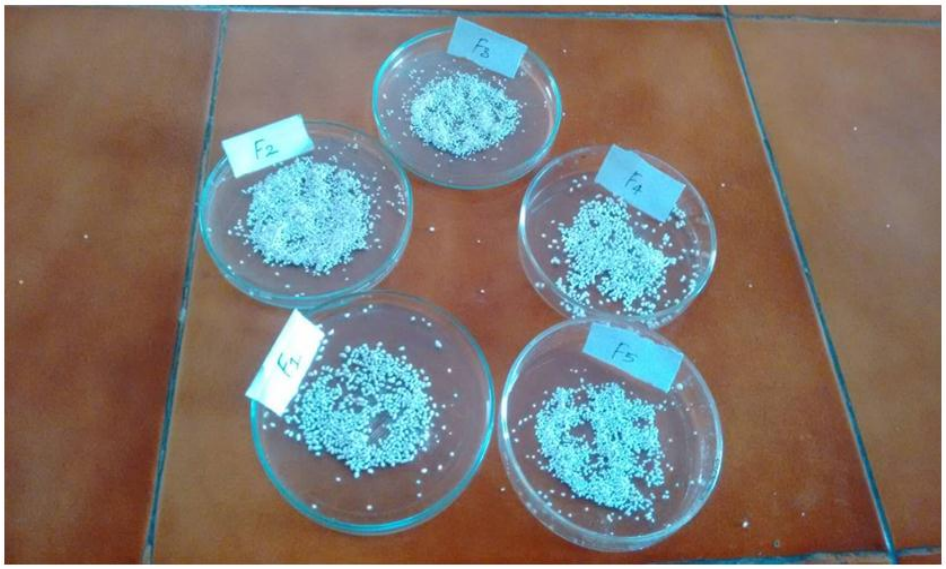

Fig. 1: Formulation of Meclizine Hcl solid dispersion loaded pellets.

Characterization of solid dispersion pellets

Determination of Sphericity

In order to determine the sphericity of the pellets, the tracings of pellets (magnification 45x) were taken on a block paper using camera lucida (model -Prism type, Rolex, India) and circulatory factor was calculated using the equation;

$$S = p^2 / (12.56 \times A)$$

Where, A is the area [cm2] and p is the perimeter[cm].

Friability

The friability test was performed on the pellets to ensure their mechanical strength. Lower friability values indicate good mechanical strength. Pellets of known mass (1000 – 1400 m) were placed in a Roche Friability tester (Electro lab Friability tester) and subjected to impact testing at 25 RPM for 5 min. Pass the pellets through a sieve of mesh size 16 (1000µm), weight of pellets retained on the sieve was noted and the friability was calculated using the following equation;

$$\text{Friability (\%) } F = 100 \times (1 - w / w_0)$$

Where w_0 = weight of pellets before friability

W = weight of pellets after friability

Drug content

Meclizine Hcl content of the manufactured pellets was determined spectrophotometrically at 232 nm in a triplicate. Pellets were crushed in a porcelain mortar and about 25 mg of the crushed pellets was dispersed in 20 ml of methyl alcohol under sonication for 5 min. The supernatant was filtered and measured spectrophotometrically at 232 nm. The Meclizine Hcl content was calculated using a pre-constructed calibration curve.[12,25]

Pellet size

The pellet size and pellet size distribution were estimated by sieve analysis (Sieve Shaker, Electro Lab, India.). Each batch of the pellets was sieved before the subsequent test in order to remove the lumps larger than 1000 µm. About 20 g of the sample was sieved employing a set of standard trembling at amplitude of 2 mm for 5 min. All results presented were the mean of three determinations. Pellets ranging between 800 and 900 µm in size were selected for the *In-vitro* dissolution test so that the effect of the particle size on the dissolution rate is excluded Ramu et al.[12][24]

Evaluation parameters

The pellets were evaluated for bulk density, tapped density, compressibility index, and Hausner's ratio.[22,23]

Bulk density

The bulk density of a powder is the ratio of the mass of an untapped powder sample (W) is taken in a graduated measuring cylinder and volume (V_0) including the contribution of the inter particulate void volume. Hence the bulk density depends on both density of powder particles and the spatial arrangement of particles in the powder bed. The bulk density can be expressed in grams per millilitre (g/ml).

Bulk density is calculated using the equation,

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Tapped density

The tapped density is obtained by tapping a measuring cylinder containing a powder sample and the volume is measured as initial volume. Measuring cylinder was fixed in the 'Tapped Densitometer' and tapped for 750-1250 times until the difference between succeeding measurements is less than 2%. The final reading was denoted by (V_f). The Tapped density can be expressed in grams per millilitre (g/ml).

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It indicates the flow properties of powder and is measured by the ratio of tapped density to bulk density.

$$\textbf{Hausner's ratio} = \frac{\textbf{Tapped density}}{\textbf{Bulk density}}$$

***In vitro* Dissolution studies**

Dissolution of the pellets of each batch was carried out using USP type II apparatus using paddle. 900 ml of 0.1 N Hydrochloric acid was filled in a dissolution vessel and temperature of the medium were set at 37±0.5^{0}C. Pellets were placed in each dissolution vessel and the paddle rotational speed was set at 50 rpm. 10 ml of sample was withdrawn from the dissolution apparatus at every hour for 12 hours and same volume of fresh medium was replaced into the dissolution flask every time. Absorbance of this solution was measured at 232 nm using a UV spectrophotometer.[18,20,24,25]

Release kinetics

The release kinetics methods are based on different mathematical functions, which describe the dissolution profile. Once a suitable function has been selected the dissolution profiles are evaluated depending on the derived model parameters in order to determine the suitable drug release kinetic model describing the dissolution profile by Sharma A et al.[21]

III. RESULTS AND DISCUSSION

Calibration curve for Meclizine Hcl

The calibration curve of Meclizine Hcl in 0.1N hydrochloric acid was derived from the concentration and corresponding absorbance. Values of linear regression analysis gave the equation for the line of best fit as y= 0.0401x- 0.0178. Linearity was observed in the concentration range between 5 to 25 µg/ml. The values were show in Table 1 and represented graphically in Fig.2.

Table 2: Standard Calibration Curve of Meclizine Hcl.

Concentration [µg/ml]	Absorbance
0	0
5	0.215
10	0.429
15	0.641
20	0.853
25	0.98

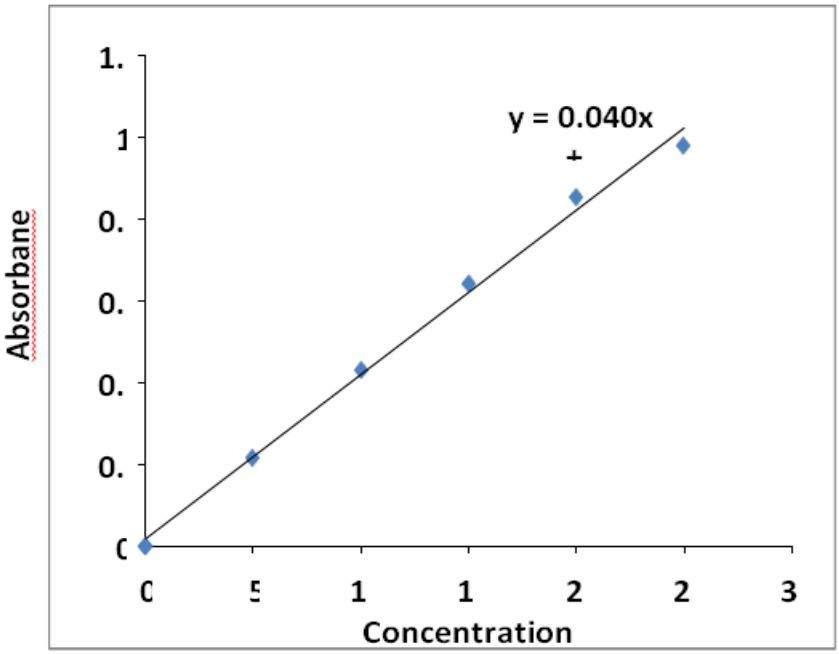

Fig. 2: Calibration curve of Meclizine Hcl.

Evaluation of Solid Dispersion

Table 3: Comparison of Micrometric properties of solid Dispersion.

Formulation	Particle Size (µm)	Bulk density (gm/cm^3)	Tapped Density (gm/cm^3)	Cars index	Hausners ratio
SD F1 (1:1)	3.26	0.449±0.008	0.557±0.005	9.467±0.003	1.357±0.004
SD F2 (1:2)	2.57	0.406±0.004	0.498±0.003	8.535±0.002	1.023±0.001
SD F3 (1:3)	2.98	0.425±0.012	0.476±0.005	7.622±0.003	0.902±0.002

The Solid Dispersions were subjected to different parameters and results were represented in the (Table 3). The Solid Dispersion of Meclizine Hcl were characterized with respect to Bulk density, Tapped density, cars index and hausners ratio. Cars index values were less than 10 for all the Solid dispersions which indicating good flowability. Hausners ratio was less than 1.5 indicating good flow properties.

Table 4: Drug Content, Practical Yield and In vitro release of Solid Dispersion.

Formulation	Practical Yield (%)	Drug Content (%)	Percentage drug release (%)
SD F1 (1:1)	96.87	91.37±1.56	70.33
SD F2 (1:2)	95.03	98.54±2.62	74.87
SD F3 (1:3)	94.02	96.04±1.06	78..06

The practical yield solid dispersion was found in the range of 94 to 97%. (Table 4). The practical yield, drug content was found to be good.

SEM analysis of Meclizine Hcl solid dispersion

The SEM of Meclizine solid dispersion appeared in the form of irregular particles in which the original morphology of both components disappeared and tiny aggregates of amorphous pieces of irregular size were present. The results revealed the reduced particle size, increased surface area, and the close contact between the hydrophilic carriers and Meclizine might be responsible for the enhanced drug solubility found for the solid dispersion particles.

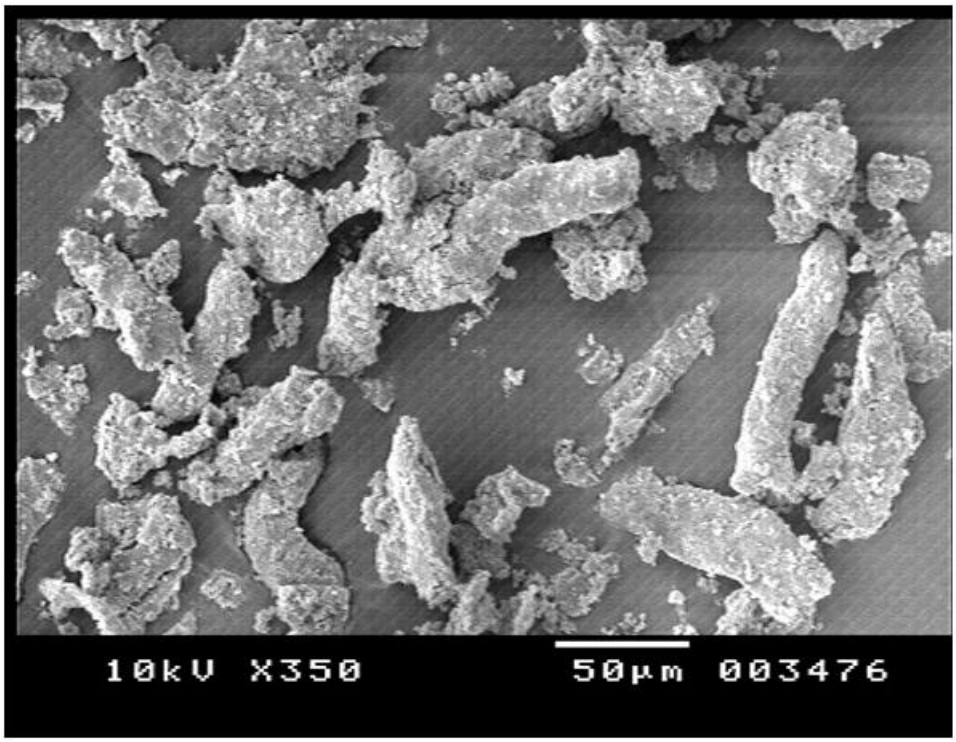

Figure 3: SEM analysis of Meclizine Hcl solid dispersion.

In vitro release of Solid Dispersion.

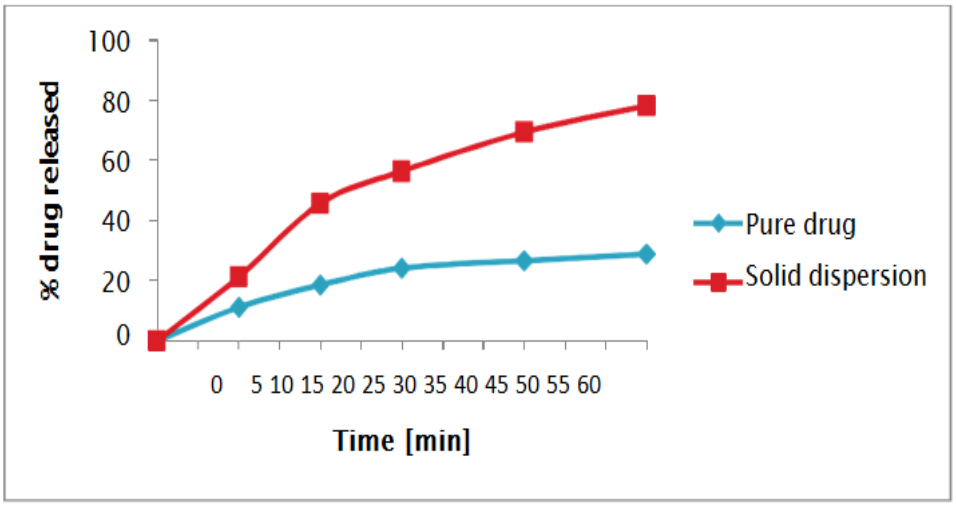

Figure 4: In vitro release of solid dispersion.

The invitro release data revealed that percentage drug release was significantly improved in solid dispersion formulation when compared to pure drug. Invitro drug release of SD was increased when compared to pure drug because of larger surface area of Solid dispersion. Based on the data Solid dispersion (1:3) ratio was selected for the preparation of OD pellets.

Drug Excipient Compatibility Study

FTIR analysis

Drug and excipients interaction was checked out by comparing the FTIR spectra of pure drug and FTIR spectra of the physical mixture of drug and excipients. FTIR spectrum of Pure Meclizine showed the characteristic peak at 1649cm^{-1} which can be assigned to the C=O stretching in the aromatic ring and a peak at 1612cm^{-1} which can be assigned to the C=N in the aromatic ring, a peak at 1533cm^{-1} which can be assigned to the N-H stretching and a peak at 1201cm^{-1} which can be assigned to the stretching of C-C n the aromatic ring. FTIR spectrum of formulation showed the peaks at 1649, 1612, 1462, 1201 cm^{-1} confirming the functional groups in the formulation proving no interactions. IR spectra result indicates that no significant difference in characteristic peak at wave numbers of the drug in presence of the excipients. From the results it can be concluded that drug and excipients are compatible.

FTIR Spectroscopy
Meclizine Hcl

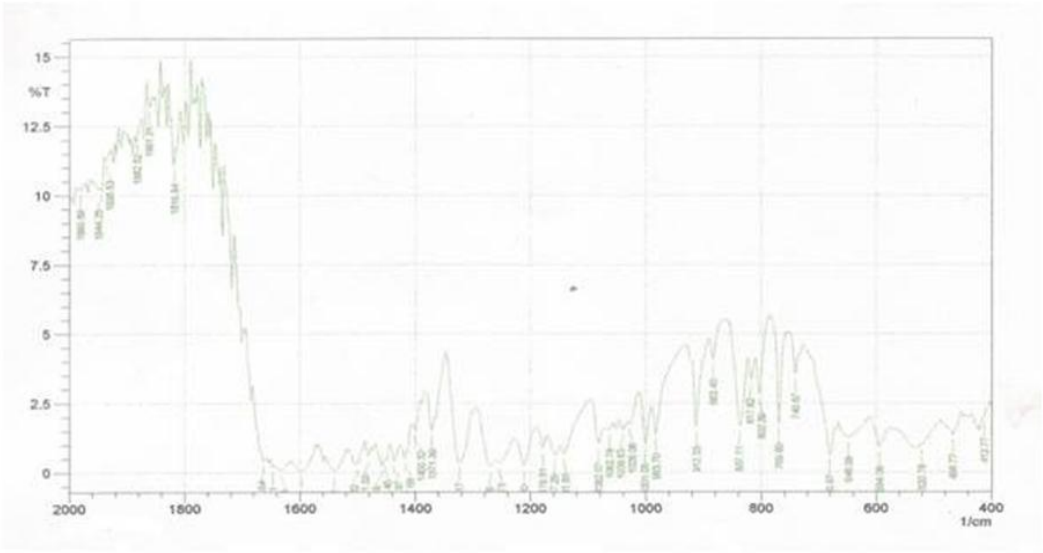

Fig. 5: FTIR spectrum of Meclizine Hcl.

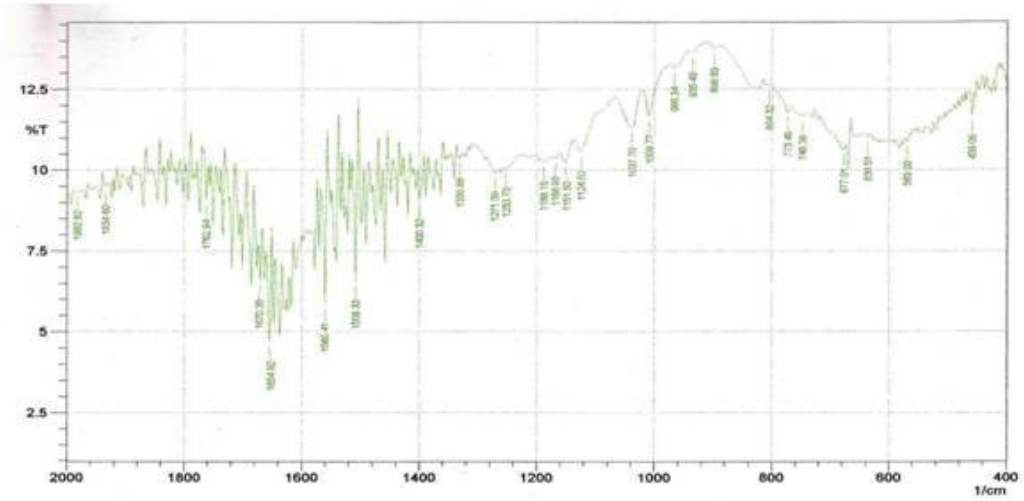

Fig. 6: FTIR spectrum of PEG 6000.

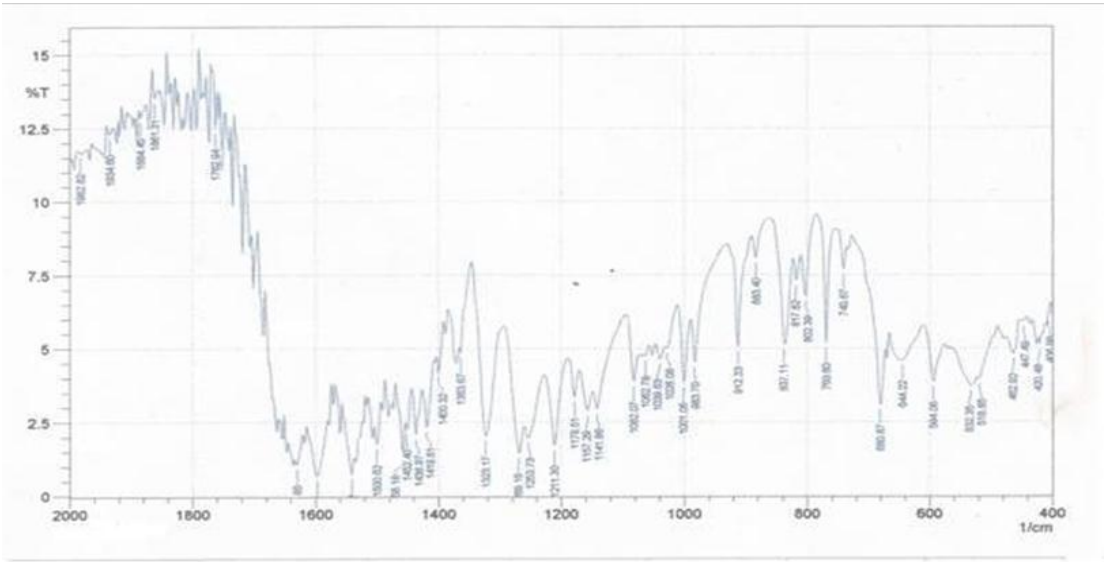

Fig. 7: FTIR spectrum of Formulation of Meclizine Hcl.

DSC Analysis

DSC thermograms obtained for pure drug and OD pellets formulations were shown in Figure. The DSC thermogram of Meclizine Hcl showed endothermic peak at 154.6ºC whereas thermogram of the OD pellets formulation did not show any significant shift in the endothermic peak of drug. Thermogram of the OD pellets formulation did not show any significant shift in the endothermic peak when compared to pure drug, indicating that there was no change in MCZ in the OD pellets.

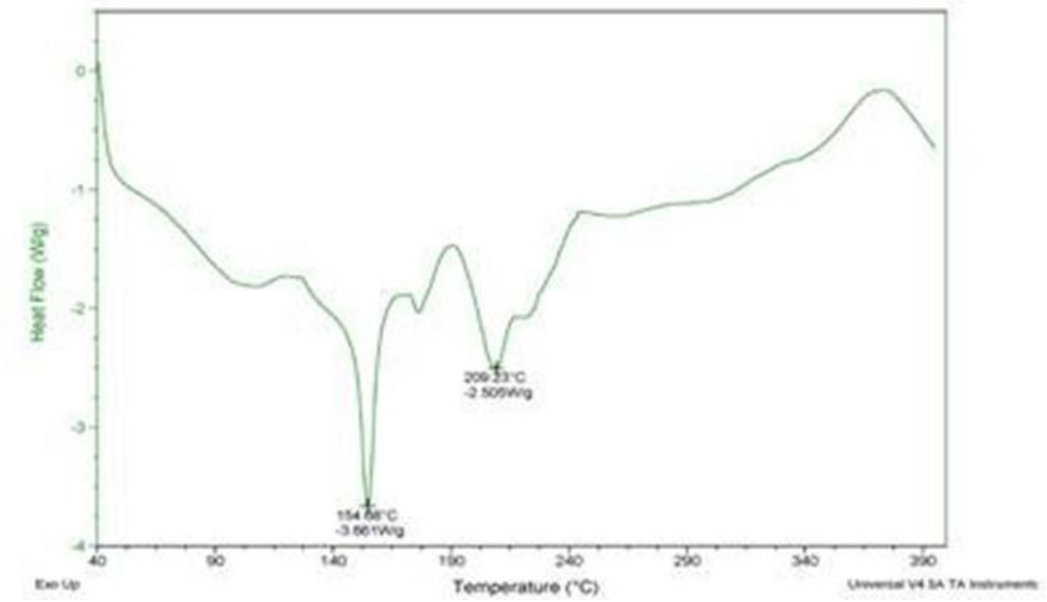

Fig. 8: DSC thermogram of pure Meclizine Hcl.

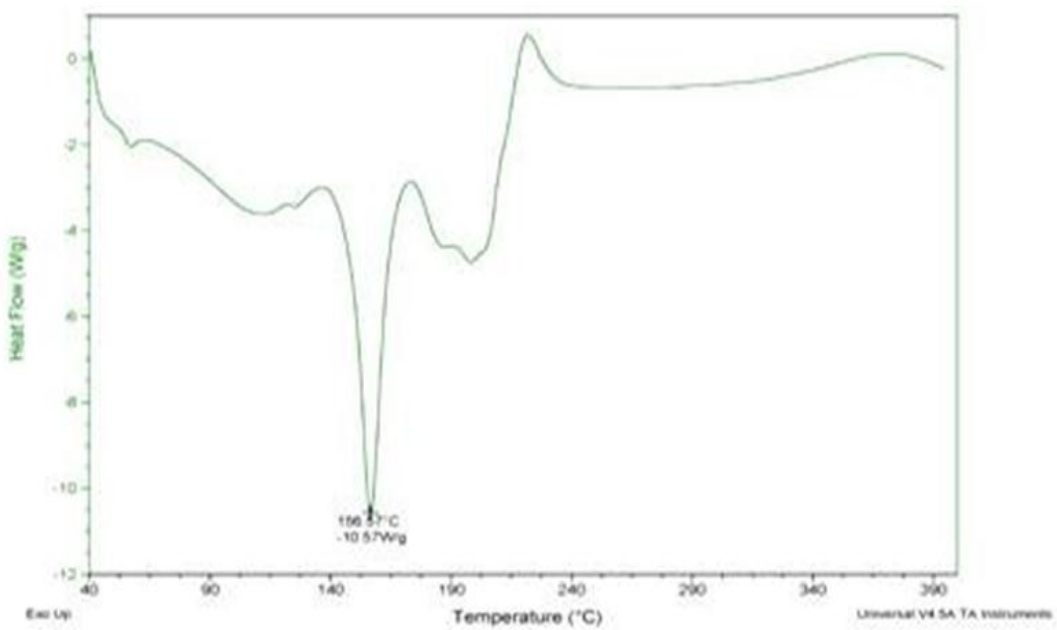

Fig. 9: DSC thermogram of Formulation of Meclizine Hcl.

Evaluation of Powder

The result of the evaluation of the powder blend was done. Angle of repose ranged from 20.2 to 29.95 and the compressibility index from 11-15. The LBD and TBD of the prepared granules ranged from 0.59 to 0.65 and 0.50 to 0.75 respectively. Hausner's ratio was found to be 1.02 or less than 1.4. The results of angle of Repose indicated good flow property of the granules and the value of the compressibility index further showed support for the flow property.

Flow properties of pellets

Table 5: Flow Property values of powder blend.

Parameters	F1	F2	F3	F4	F5
Bulk Density	0.01±0.015	0.64±0.20	0.61±0.14	0.56±0.11	0.65±0.25
Tapped Density	0.59±0.021	0.76±0.036	0.65±0.21	0.59±0.19	0.59±0.10
Carr's Index	11.52±1.11	13.66±1.33	12.2±1.02	11.9±0.97	10.9±0.52
Hausner's Ratio	1.22±0.025	1.37±0.018	1.2±0.011	1.07±0.009	1.02±0.1
Angle of Repose	28.70±1.23	29.95±1.16	26.5±1.01	24.4±0.89	20.2±0.24

Evaluation of Pellets

The results of the evaluation of pellets were shown in Table No:5. The size of the pellets was found in the range of 0.7 to 0.9 mm for all the formulations. All the formulations exhibited less than 1% friability. The results were found to be within the content of uniformity limits (95 to 100.5%). It shows that the drug was uniformly distributed throughout the pellets. The wetting time for all the formulation was found to be between 03 to 05 minutes. All the formulations were passed the dispersibility test.

SEM analysis of Meclizine Hcl OD pellets

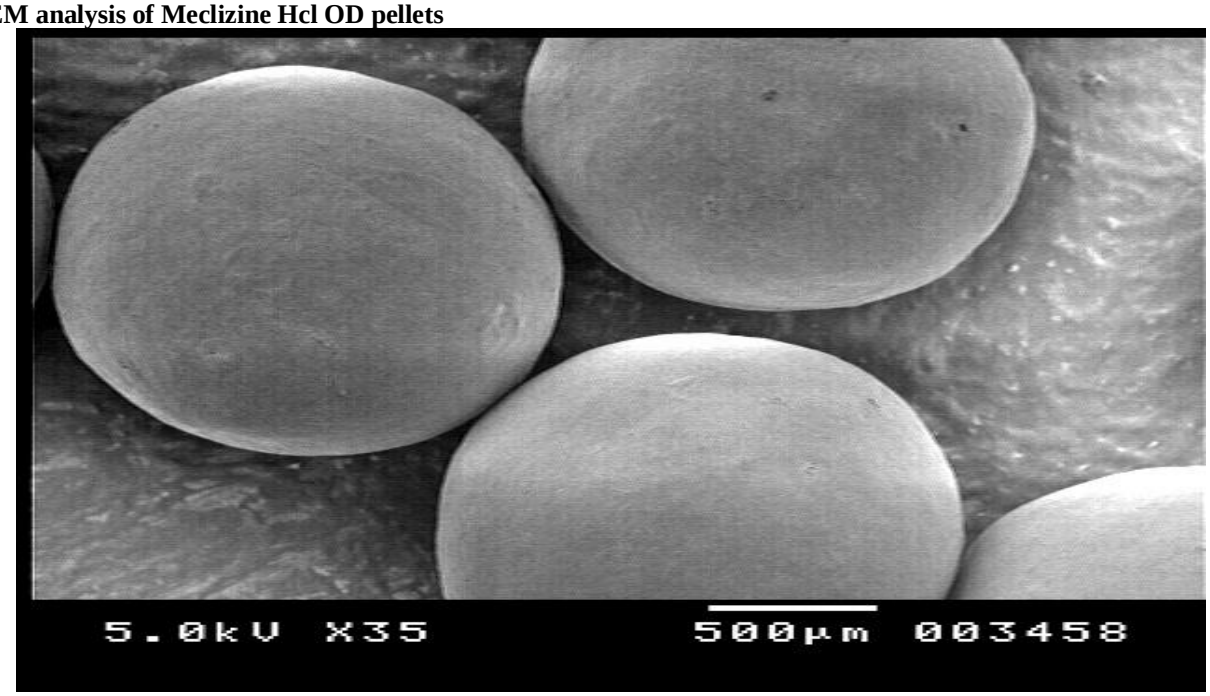

Fig. 10: SEM analysis of Meclizine Hcl OD pellets.

SEM studies were carried out on final optimized formulation to determine the surface morphology. Prepared pellets were of uniform size and spherical in shape with small porous and little rough surface was observed in prepared pellets. The rough surface is caused due to the rapid loss of moisture from the wet mass with the high liquid content that results in a porous surface structure.

Disintegration Test

The results of the disintegration test were found. Disintegration is the most important characteristic test of dispersible pellets, formulation F6 with Sodium starch Glycolate (SSG) 10% shows an excellent disintegration time of 48 seconds when compared with other formulations.

Evaluation of pellets

Table 6: Pellets Size, Disintegration, Wetting time and Friability of Meclizine Pellets Swelling Ratio.

Formulation Code	Pellet Size (mm) Mean±S.D (n=10)	Disintegration (sec) Mean±S.D (n=10)	Wetting time (min) Mean±S.D (n=10)	Friability (%) (n=10)
F1	0.92±0.010	60±0.017	4.2	0.5±0.041
F2	0.80±0.015	50.9±0.020	4.0	0.7±0.036
F3	0.92±0.012	68±0.012	3.9	0.72±0.024
F4	0.91±0.02	74±0.010	3.2	0.62±0.022
F5	0.88±0.42	56±0.02	3.2	0.52±0.04

The optimized formulation (F2) of Meclizine Hcl OD pellets showed very high percentage of swelling index than other formulations F1, F3, F4 and F5.

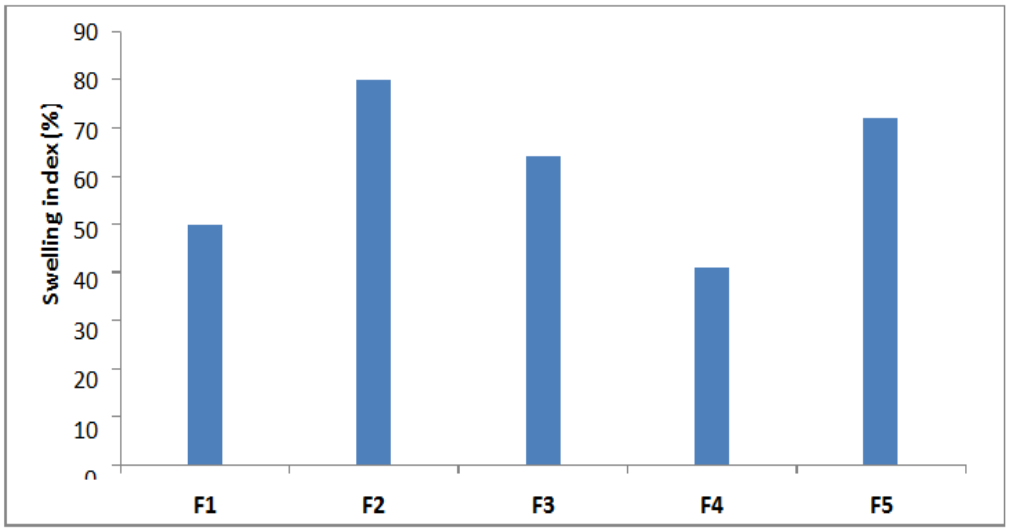

Fig: 11: Swelling ratio.

***Invitro* Dissolution Studies**

The results of the in vitro dissolution studies were shown in above table 7 and in Figure 12. In vitro dissolution test reveals the release increase from 50% to a maximum of almost 100% for 30 min. The release is in the following order of Formulation F2> F1> F5> F3> F4. The maximum in vitro dissolution was found to be with formulation F2. The formulation with Sodium starch Glycolate 10% shows maximum in vitro dissolution of 100% and the formulation F2. It clearly shows that disintegrant (Sodium starch Glycolate 10%) is the best when compared to other disintegrants. The reason may be high porous structure and water wicking mechanism into porous network of pellets hence increases in concentration of Sodium starch Glycolate accounts for rapid release.

Dissolution Data for the Formulations F1 – F5

Table 7: Dissolution data for the formulations F1-F5.

Time (Minutes)	F1	F2	F3	F4	F5
0	0	0	0	0	0
5	17.4	20	15	11.3	16.7
10	39.8	44	34	22	35.3
15	62.6	70	55.3	32.4	60.45
30	89.4	99.5	78.2	50	87.56
45	100.2		99.6	71.7	99.8
60				95.2	

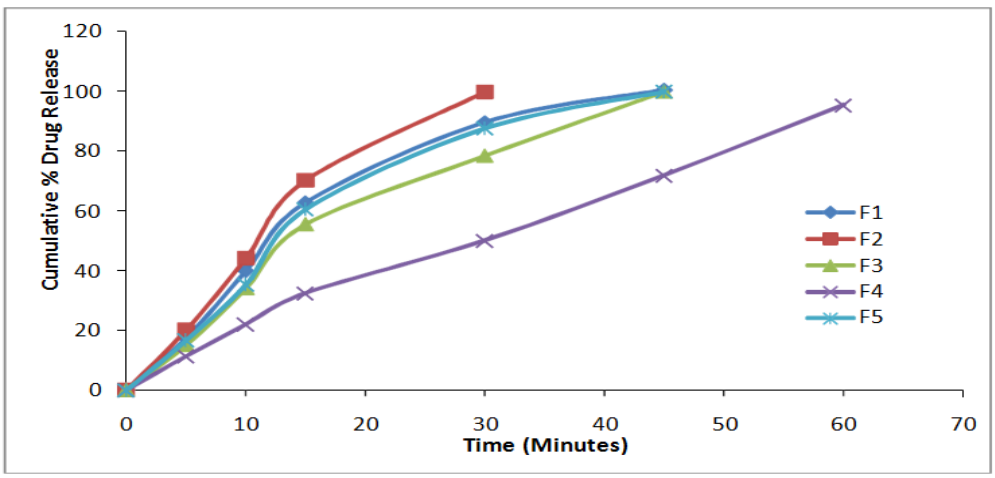

Fig. 12: *In vitro* dissolution profile of formulations F1 to F5 In vitro drug release kinetic parameters.

The release data were analyzed by any one method as per Zero order, First order, Higuchi's, Hixson- Crowel and Peppas equation models to know the pattern of drug release and mechanism of drug release from the pellets. The invitro release kinetic parameters of formulation SDPF1to SDP**.** The various kinetics release graph such as Zero order, First order, Higuchi's and Peppas models. The in vitro release profiles of drug from the formulations (SDP F1to SDP F5) could be best expressed by Higuchi as the plots showed highest linearity (r^2 = 0.96 and 0.98). It confers that drugs are released by diffusion. To confirm the release mechanism, the data were fitted into Korsmeyer-Peppas equation. Both the formulations showed good linearity (0.92 to 0.99) with slope (*n*) values ranging from 0.53 to 0.73 indicating that diffusion was the predominant mechanism of drug release from these formulations indicating that the release mechanism was non-Fickian or anomalous release (0.45< n <0.89). It can be inferred that the release was dependent on both drug diffusion and polymer relaxation, which appears to indicate a coupling of diffusion and erosion mechanisms-so called anomalous diffusion.

Table 8: In vitro drug release kinetic parameters.

Formulation	Zero order		First order		Higuchi model		Peppas model		Hixson-Crowel model	
	K_0	R^2	K_1	r^2	K_H	r^2	*n*	r^2	K	r^2
SDP F1	1.979	0.893	0.076	0.986	18.67	0.96	0.533	0.924	0.045	0.796
SDP F2	3.064	0.937	0.078	0.950	24.73	0.981	0.734	0.995	0.07	0.855
SDP F3	2.007	0.946	0.051	0.991	18.65	0.986	0.612	0.963	0.048	0.848
SDP F4	1.467	0.995	0.044	0.873	14.74	0.983	0.673	0.99	0.043	0.931
SDP F5	2.023	0.907	0.071	0.983	19	0.966	0.596	0.922	0.047	0.818

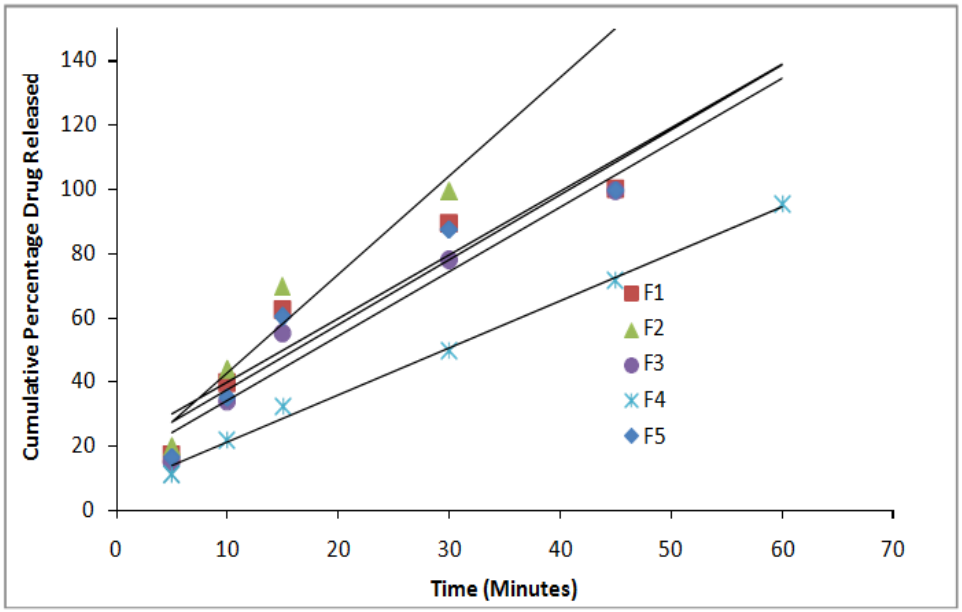

Fig. 13: In Vitro Zero Order Release Kinetics.

IV. CONCLUSION

Formulated Meclizine Hcl Oral Disintegrating pellets observed satisfactory results for various evaluations of physical parameters like size, friability, weight variation, content uniformity and disintegration were found within the permissible range. The assay of the product was found within the limit. The prepared pellets were also shown quick disintegration and faster dissolution rate and good taste masking of the drug. From the dissolution studies of all formulations, F2 formulation showed rapid disintegration time as well as fast dissolution rate. The Dissolution efficiency was increased by 1.3-fold with F2 OD pellets compared to marketed tablets. The in vitro dissolution release pattern followed Non-Fickian Diffusion. It was concluded that fast disintegrating meclizine Hcl pellets successfully prepared with enhanced disintegration/dissolution of the drug and hence can be provide better patient compliance and effective therapy. Further in vivo study has to be performed to prove the efficacy of the formulations. The study may suggest that meclizine Hcl Oral Disintegrating pellets with solid dispersion could be an alternative choice for the preparation of oral rapid disintegrating pellets dosage form of Meclizine Hcl.

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