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# Enhancing the Solubility and Dissolution Rate of Meclizine Hydrochloride by Inclusion Complex

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## ABSTRACT

Meclizine Hydrochloride is an Anti-Histamine drugs with very low bioavailability that can be improved by increasing its solubility and dissolution rate. The aim of this study is to enhance dissolution of Meclizine Hydrochloride as a model hydrophobic drug through application of inclusion complex technology. It was formulated as inclusion complex compact, and its dissolution property is evaluated and compared with marketed product of Meclizine Hcl tablet. The newly formulated drug and the interaction between excipients was examined by, Fourier-transform infrared spectroscopy, and differential scanning colorimetry, respectively. Both DSC and SEM results suggested loss of crystallinity of Meclizine Hydrochloride upon conversion into a inclusion complex formulation. The dissolution efficiency of Meclizine Hydrochloride at 45 min was increased from directly compressed tablet to 98.0% for marketed product to 97.2% at 45 minutes for the inclusion complex formulation. The increase in the dissolution rate was also found to be significant compared to the marketed product. The inclusion complex technique appears to be a promising approach for improving the dissolution of poorly soluble drugs like Meclizine Hydrochloride.

**Keywords:** *Meclizine Hydrochloride*, inclusion complex, Avicel pH 102, Talc, Lactose, ethanol

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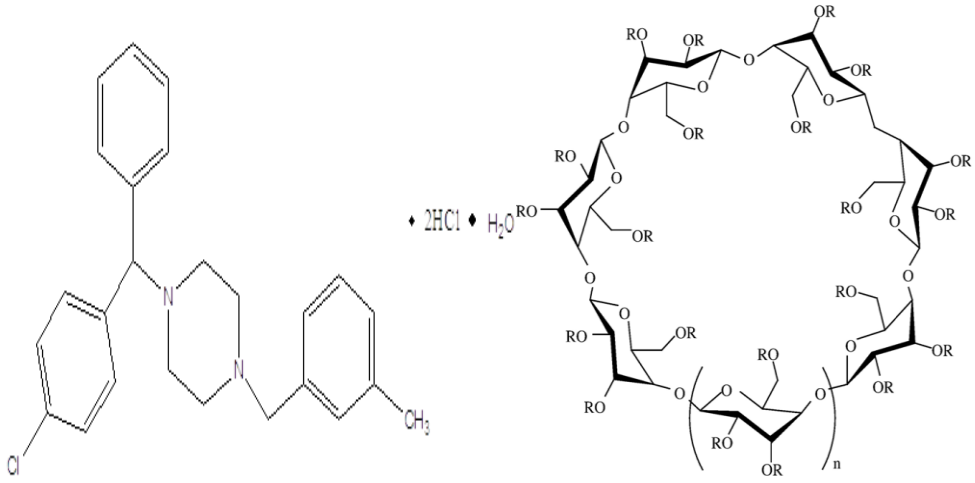
## 1.0 INTRODUCTION

Cyclodextrins (CD) inclusion complexation, which is the arrangement of host–guest inclusion complexes by weak intermolecular interaction, has been shown to be a promising technique in enhancing solubility and bioavailability of poorly BCS class II drugs. The molecular structure of cyclodextrins appears to be a truncated cone, arries a hydrophilic exterior surface and a non-polar interior cavity. The central cavity of the cyclodextrins molecule is lined with skeletal carbons and ethereal oxygens of the glucose residues. It provides a Lipophilic microenvironment into which suitably sized API drug molecules may enter and be included. This method has been shown to improve the solubility of various drugs such as celecoxib and natamycin etc. The commonly available cyclodextrins are, α-, β- and γ-cyclodextrins, which consist of 6, 7 and 8 glucopyranose units, respectively. β-Cyclodextrins (β CD) and their derivatives, such as hydroxypropyl-βCD (HPβCD) and methyl βCD (MβCD), are the main excipients commonly used in pharmaceutical formulations. In general, chemical modification of CDs can alter their physical properties, especially their solubility. The solubility of βCD in water is relatively low (approximately 18.5 mg/mL at 25 °C), whereas it's derivative HP βCD has a higher aqueous solubility (approx. 600 mg/mL at 25 °C). There are different methods to prepare cyclodextrins inclusion complexes. These methods encompass co-precipitation, kneading, lyophilization, spray drying, freeze drying and supercritical fluid technology. Meclizine Hydrochloride is an Anti Histamine drugs. It is used mainly in the treatment of motion sickness and vertigo. The poor solubility of Meclizine Hydrochloride reduces the bioavailability to around 30 to 40%. Figure. 1 shows the chemical structures of Meclizine Hydrochloride and βCD. In the present study, solubility and dissolution enhancement of β-cyclodextrins (βCD) on Meclizine Hydrochloride was compared. Inclusion complex was prepared using three different methods, namely, physical mixture, kneading and Co-precipitate method. The inclusion complex was characterised using scanning electron microscopy, infrared spectrophotometer, powder X-ray diffractometry, and differential scanning calorimetry.




**(A)** **(B)**

Fig. 1 - Chemical structures of (A) Meclizine HCl (B) βCD

## 2.0

## MATERIALS AND METHODS

**Materials:** Meclizine Hydrochloride was a gift sample from Srikem Labatories Limited Mumbai. Other materials were purchased from different sources like β Cyclodextrins from Gangwal chemicals Mumbai Lactose and Talc from signet chemicals, Mumbai, Micro crystalline cellulose PH 102 and crosspovidone and ethanol from SR Chemi Mumbai India and all other reagents used were of analytical grade and obtained from S.D. Fine Chemicals, Mumbai, India. Doubled distilled water was used during entire research work.

**Phase Solubility Studies:** [6,7,8]

The phase-solubility technique permits the evaluation of the affinity between β-CD and Meclizine HCl in water. It gives not only the solubilising ability of CD's, but also the stability constant of the complexes by analyzing the solubility curve. Phase solubility studies were performed according to the method reported by Higuchi and Connors. This methodology was based on the solubility variation of the guest molecule (drug) upon increase of the host molecule (β-CD/) concentration. For phase solubility studies of Meclizine Hydrochloride, an excess of drug (200 mg) was added to 20 ml portions of distilled water, each containing variable amount of β-cyclodextrin such as 2, 4, 6, 8, and 10 m Moles. All the above solutions with variable amount of β-cyclodextrins were shaken for 72 hours. After shaking, approximately 0.5 ml of the solution was withdrawn by the syringe and filtered through a 0.22 µm membrane filter (Millipore) and suitably diluted with water. Drug concentration was determined spectrophotometrically using (*UV-1240, Shimadzu, Japan*) at 230 nm. The phase solubility plot was prepared by plotting the total dissolved drug concentration against the total β Cyclodextrin concentrations separately. The apparent complexation constant ($K_{1:3}$) of the complex was calculated by the following equation (***Eq. 1***) from phase solubility curve, where the intercept is the intrinsic solubility of drug in the absence of polymer.

$$K_{1:3} = \left( \frac{\text{Slope}}{\text{Intercept (1-slope)}} \right) \qquad \text{Eq. ------- (1)}$$

**Preparation of complexes with β-cyclodextrin:** [9,10,11]

Complexes of Meclizine Hydrochloride with β-cyclodextrin (β-CD) were prepared by different methods using different molar concentrations of β-CD. The molar concentration used and methods adopted are mentioned below.

**a) Physical mixture:** Meclizine Hydrochloride with β-CD in different molar ratios (i.e. 1:1M, 1:2M and 1:3M) were mixed in a mortar for about 30 minutes with constant trituration, passed through sieve No. 60 and stored in a desiccators over fused calcium chloride.

**b) Kneading method:** Meclizine Hydrochloride with β-CD in different molar ratios (i.e. 1:1M, 1:2M and 1:3M) was taken. First cyclodextrin is added to the mortar, small quantity of 50 % ethanol is added while triturating to get slurry like consistency. Then slowly Meclizine Hydrochloride is incorporated into the slurry and trituration is further continued for 30 minutes. Slurry is then air dried at 25$^0$C for 4 hours, pulverized and passed through sieve No. 60 and stored in desiccators over fused calcium chloride.

**c) Co-precipitate method:** Meclizine Hydrochloride was dissolved in ethanol at room temperature and β-CD was dissolved in distilled water. Different molar ratios (i.e. 1:1M 1:2M and 1:3M of Meclizine Hydrochloride and β-CD were taken respectively. The mixture was stirred at room temperature, for 30 minutes and then slowly evaporated on a boiling water bath. The inclusion complex precipitated as a crystalline powder was pulverized and passed through sieve No. 60 and stored in a desiccator till free from any traces of the organic solvent.

Sifted material Mix with other Prelubricant material and for 10 minutes and then add Magnesium Stearate and mix for 2 minutes.

**Differential Scanning Calorimetry (DSC)** [12]

DSC analysis was performed using a DSC 822e with a robotic sampler from Mettler Toledo and thermal characteristics of the drug and solid dispersions were determined. The instrument was calibrated using indium as the standard. Approximately 5 mg of each sample was placed in 100 µL aluminum pans which were sealed and initial and final temperature were set and heated from 25°C to 300°C at a rate of 10°C/min under nitrogen flow of 30 ml/min.

***Scanning electron microscopy***

The surface morphology of the Meclizine Hydrochloride and inclusion complex was determined using scanning electron microscopy (LEO 435 VARIABLE PRESSURE SEM), operated at an accelerating voltage of 20 kV (beam current of 30–40 mA, filament current of 1.75 lA, and probe current of 250 pA) Robinson detector and at magnification ranging from minimum magnification-4x and maximum magnification of 5000x.

**Fourier transform infrared spectroscopy [12,13]**

Fourier transform IR spectra were recorded on FT/IR-8400 S Shimadzu. The spectra were recorded for Meclizine HCl and inclusion complex system. Samples were prepared in a KBr disc (3mg of the sample in 300mg KBr). The pinch of the powder sample was inserted in the sample holder and the spectra were run from 3800 $cm^{-1}$ to 650 $cm^{-1}$.

**In vitro dissolution studies [13]**

The dissolution patterns of the inclusion complexes were compared with those of a market product. The dissolution studies were performed according to the USP XXIII Dissolution apparatus (ELECTROLAB TDL-08L), Type-I (Basket). The dissolution medium was 900 ml of 0.01N HCl (pH 1.2). The stirring speed of the basket was 100 rpm, and the temperature was maintained at 37 ± 0.5°C. The samples (5 ml) were withdrawn at various time intervals, which was filtered through a 0.45 µm membrane filter and analyzed by a HPLC spectrophotometer at 230 nm.

**Formulation of tablets by direct compression method [9, 10, 11]**

Tablet compacts were prepared using a Fluid pack 10 ton laboratory press 10.5 x 5.49 mm, Oval shaped Embossed Tooling (Upper punches: Embossed with "ET3", Lower punches: plain). Tablets weighing 360 mg ± 5% were compressed to 2 kN for 3 seconds and ejected from the die.

***Table 1: Batches of Meclizine Hydrochloride Tablets by Inclusion Complex.***

| S.No | Ingredients | CD1 (mg) | CD2 (mg) | CD3 (mg) | CD4 (mg) | CD5 (mg) | CD6 (mg) | CD7 (mg) | CD8 (mg) | CD9 (mg) |
|---|---|---|---|---|---|---|---|---|---|---|
| **Intra Granular Materials** | | | | | | | | | | |
| Complex Ratio | | 1:1 | 1:2 | 1:3 | 1:1 | 1:2 | 1:3 | 1:1 | 1:2 | 1:3 |
| 1 | Meclizine Hydrochloride | 25.0 | 25.0 | 25.0 | 25.0 | 25.0 | 25.0 | 25.0 | 25.0 | 25.0 |
| 2 | β Cyclodextrins | 58.8 | 117.6 | 176.4 | 58.8 | 117.6 | 176.4 | 117.6 | 176.4 | 58.8 |
| 3 | Ethanol | Q.s | Q.s | Q.s | Q.s | Q.s | Q.s | Q.s | Q.s | Q.s |
| 4 | Lactose regular | 136.1 | 77.3 | 18.5 | 136.1 | 77.3 | 18.5 | 77.3 | 18.5 | 136.1 |
| 5 | Microcrystalline Cellulose PH 102 | 114.0 | 114.0 | 114.0 | 114.0 | 114.0 | 114.0 | 114.0 | 114.0 | 114.0 |
| 6 | Crospovidone | 20.0 | 20.0 | 20.0 | 20.0 | 20.0 | 20.0 | 20.0 | 20.0 | 20.0 |
| 7 | Talc | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 |
| **Lubrication** | | | | | | | | | | |
| 8 | Magnesium Sterate | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 |
| **Weight of core tablet** | | **360.0** | **360.0** | **360.0** | **360.0** | **360.0** | **360.0** | **360.0** | **360.0** | **360.0** |

**Micromeritic properties of blend [12, 13, 14, 15, 16, 17,]**

The flow properties of powder plays vital role in the manufacturing of tablets. The flow properties were studied through measuring the angle of repose, Carr's index. Powder mixtures of different formulations were evaluated for angle of repose, bulk density, tapped density Hausner's Ratio and compressibility index. It is usually determined by the fixed funnel method and is the measure of the flow ability of powder/granules. A funnel with 10 mm inner diameter of the stem was fixed at a height of 2 cm. Over the platform. About 10 mg of sample was slowly passed along the wall of the funnel till the tip of the pile formed and touches the stem of the funnel. A rough circle was drawn around the pile base and the radius of the powder cone was measured. Angle of repose was calculated from the average radius, using the following formula.

$$\theta = \text{Tan}^{-}[h/r] \qquad \text{Eq. ------- (2)}$$

In which, θ is the angle of repose, h is the height of the cone and r is radius of base. To measure the angle of repose

The bulk density (δb) of a powder was determined by measuring the volume of a known mass of powder sample into a 100 ml graduated cylinder. Tapped density (δtap) of powder samples were determined by a tap density apparatus. Tap the cylinder 10, 500 and 1250 taps on the same powder sample and read the corresponding volume $V_{10}$, $V_{500}$ and $V_{1250}$ to the nearest graduated unit. The Carr's Index is a measure of the propensity of a powder to be compressed and it is calculated using the following formula:

$$\text{Carr's Index} = [(\delta tap - \delta b) / \delta tap] / \times 100 \qquad \textbf{Eq. ------- (3)}$$

**Evaluation of post compression parameters of tablets**

The prepared tablets were evaluated for tablet hardness using a Monsanto Tablet tester, friability of a sample of 6.5 g tablets was measured using a Roche Friabilator (Electro lab), the weight variation test was done by weighing 20 tablets (USP) individually and calculating the average weight with comparing the individual tablet weight to the average weight, disintegration time of the tablet was measured in water (37±2°C) according to the disintegration test apparatus with a disk (Electro lab).

## 3.0 RESULTS

**Phase solubility study**

The solubility method is useful for studying inclusion compounds for poorly soluble drugs with CDs in water because it gives not only the solubilizing ability of CDs but also the stability constant (Ks) of the complexes by analyzing the solubility curves.

The phase solubility curves of Meclizine Hydrochloride in the presence of ß-CD are presented in Figure.2. This curve

indicated a linear increase in solubility of Meclizine Hydrochloride with increase in concentrations of β-CD in water. Increasing amounts of β-CD increased the aqueous solubility of Meclizine Hydrochloride.

The shape of solubility diagram represents linear host–guest correlation ($A_L$ Type) with a slope less than 1 indicating the formation of a 1:2 complex with respect to β-CD concentrations. It was observed that the Meclizine HCl/β-CD system shows greater solubility and this may be attributed to the fact that the contact surface and cavity size of β-CD thus, β-CD is selected for further formulation and evaluation studies.

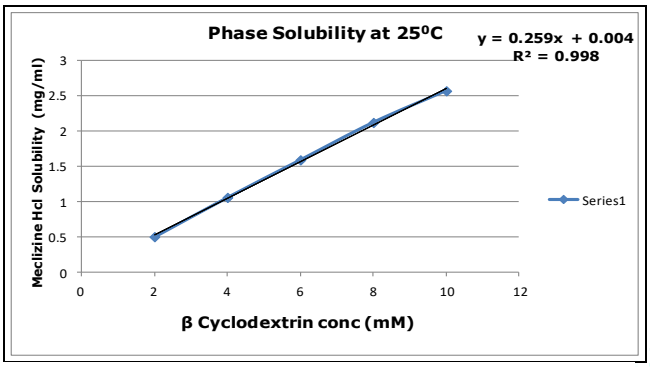



**Fig.2: Phase Solubility curve of Meclizine Hydrochloride with different concentration**

## Differential scanning calorimetry

Differential scanning calorimetry (DSC) was used to identify the inclusion complex between the drug and β-CD. Some evidence of inclusion complexation was obtained from thermal analysis. When guest molecules were embedded in β-CD cavities, their melting, boiling, or sublimation point generally could shift to a different temperature or disappear within the temperature range where β-CD was decomposed. As seen from Figure 3, the DSC thermogram of Meclizine HCl alone showed a sharp endothermic peak at 220.03 °C, corresponding to the melting point of the drug, while β-CD showed a very broad endothermic effect, which attained a maximum around 86.06 °C, The endothermic peaks of Meclizine HCl (205 °C) and β-CD (98.08 °C) observed in the physical mixture were significantly different from their endotherms in pure forms (lowering of the endothermic peak) indicating that complex formation has taken place only partially that also indicates decrease in drug crystallinity due to complexation. The same was the case for the complex prepared by a co-precipitation method where endothermic peaks of Meclizine HCl (185.26°C) and β-CD (99.11°C) were observed which indicates complex formation is not complete but has taken place to a greater extent. The complete disappearance of the Meclizine HCl endothermic peak was observed for the inclusion complex prepared by the kneading method Figure 4, since Meclizine HCl was contained within the cavity of the β-CD ring molecule. This demonstrated that an inclusion complex of Meclizine HCl could be obtained by the Kneading method.

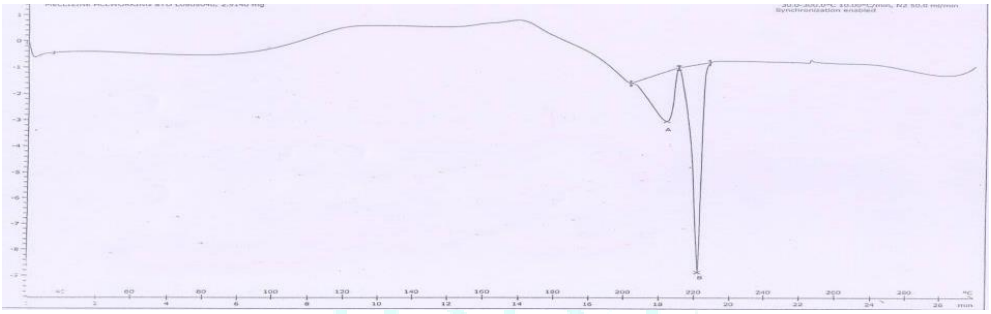


**Fig 3: DSC Thermogram of Meclizine Hydrochloride**

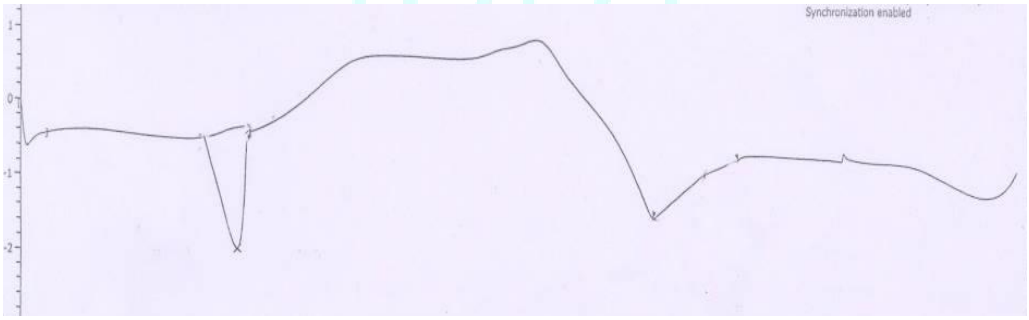



**Fig 4: DSC Thermogram of Meclizine Hydrochloride β CD inclusion Complex**

## Fourier transform infrared spectroscopy

IR spectrum of Meclizine HCl Figure 5 is characterized by 2420cm$^{-1}$ (–$NH_3$– stretch), 2300cm$^{-1}$ ($CH_2$–$CH_2$), 1450cm$^{-1}$ (C = C stretch), 1080$^{-1}$ (C–N stretch), 910 cm$^{-1}$ (C–Cl stretch). The IR spectrum of pure b-CD is characterized by prominent peaks at 3410cm$^{-1}$ (O–H), 2930.13cm$^{-1}$ (C–H), 1620.73cm$^{-1}$(H–O–H bending), 1060.28cm$^{-1}$ (C–O–C). No significant alterations in the IR bands of the pure drug were detected in the physical mixture. However, some of the peaks of Meclizine HCl were slightly shifted and found to be attenuated. The IR spectrum of the physical mixture could be diagnosed as a superimposition of the bands of pure drug and β-CD. Significant changes were recorded in the IR spectrum of the inclusion complex prepared by the kneading Figure 6 Almost all peaks of Meclizine HCl were smoothened indicating a strong physical interaction between pure drug and β-CD. However, the broad peak of O–H of β-CD was consistently appeared in binary systems. All the binary systems of Meclizine HCl-β-CD did not show any new peaks, indicating non covalent interaction in inclusion complex.

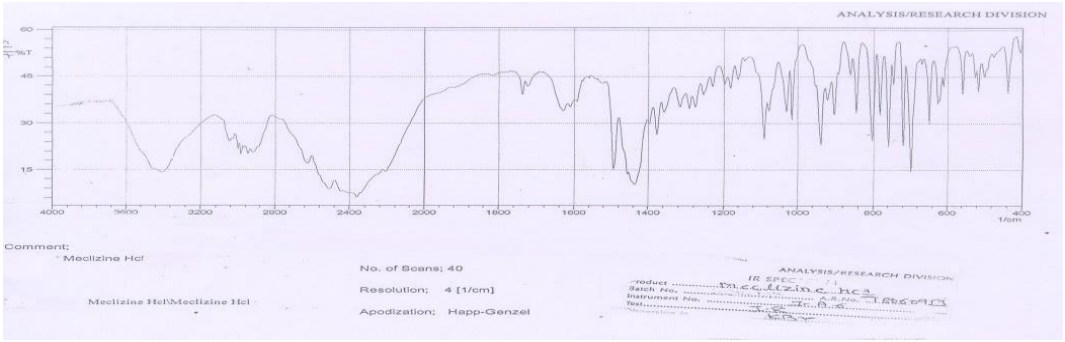



**Fig 5: Infra Red Spectrum of Drug**

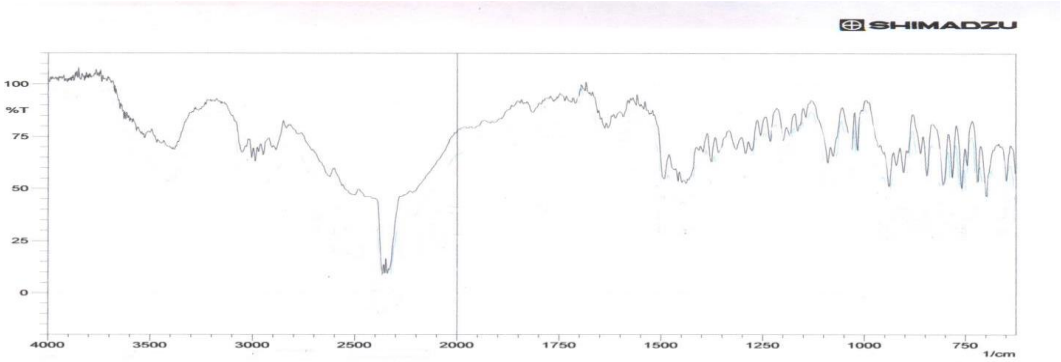



**Fig 6: Infra Red Spectrum of Drug Mix (CD)**

**Scanning electron microscopy**

Fig shows the scanning electron photomicrographs of Meclizine Hcl, βCD and physical mixture of Meclizine Hcl β-CD inclusion complexes prepared using the three methods. βCD appears to be thick solid with non-smooth surface. Meclizine Hcl appears to be a solid with smooth surface. The scanning electron photomicrographs of Meclizine Hcl β-CD produced from physical trituration method showed similar surface morphology of mixtures of Meclizine Hcl and βCD Figure.7. No complexation occurred between Meclizine Hcl and cyclodextrins using physical trituration method, indicating that inclusion complex could not be produced using physical trituration method. For kneading method, there was formation Meclizine Hcl / βCD complex with rough surface and irregular shape.

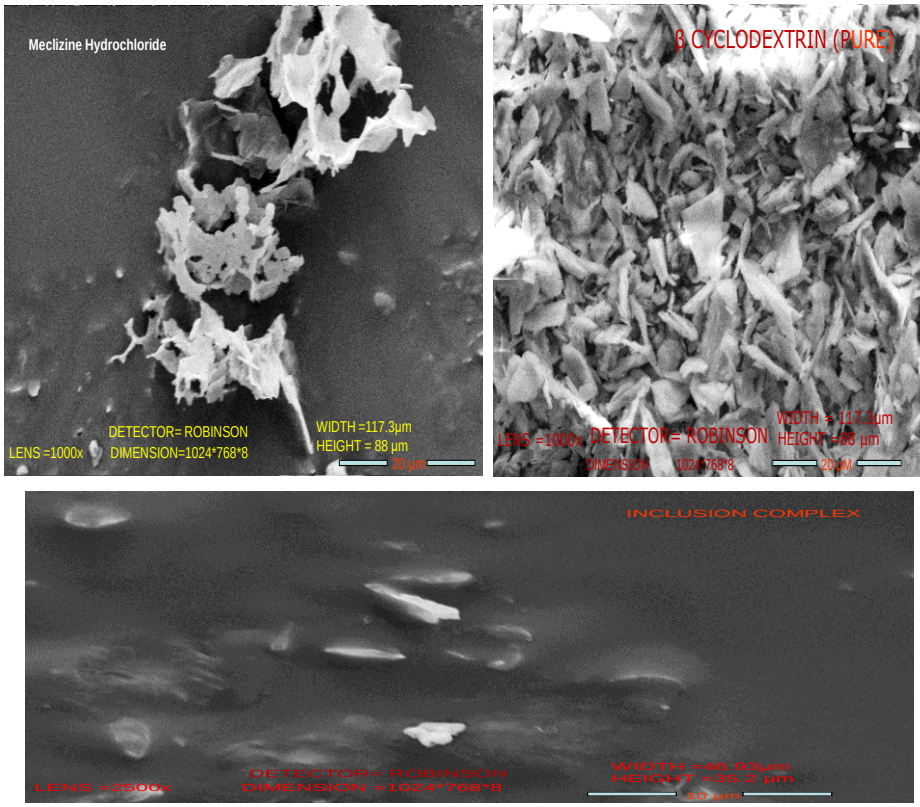



**Fig-7(A) scanning electron photomicrographs of pure Meclizine Hydrochloride (B) Beta Cyclodextrins. (C) Inclusion Complex**

**Drug content**

The HPLC method with a UV-detector was used to determine the drug content of the binary system of the β-CD: Meclizine HCl molar ratio of 1:2, in all system samples of the binary system (equivalent to about 50 mg of Meclizine HCl), were dissolved in the mobile phase. The β-CD drug ratio would therefore remain 1:2] in the final solution to calculate the drug content. The potency content of drug in all the formulation was found to be 97.0 to 101.0%.

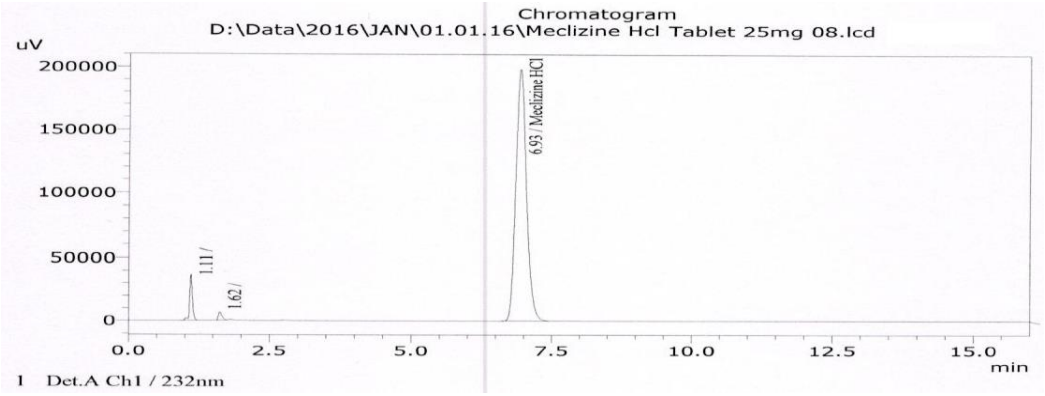



**Fig 8: chromatogram of Potency Assay**

**In vitro *dissolution studies***

The release rate profile was drawn as the cumulative percent release on the *y*-axis and time on the *x*-axis shown in Figure 9. It showed that the inclusion complex (CD5) of Meclizine HCl prepared by the kneading method released 75.5% drug in 10min, and up to 98.0% drug in 45 min while the inclusion complex prepared by the co-precipitation method showed 70% drug release in 10min and up to 86 % drug release in 45 min. Physical mixtures show release up to 50% in 10 min and up to 70% drug release in 45 min, whereas the Market product exhibited the release of 81% in 10min and 97% drug release in 45 min. It was evident that the complex exhibited the faster dissolution rate than Marketed Product. The very high increase of Meclizine HCl dissolution rate in the case of inclusion complex might be due to several reasons. The formations of soluble inclusion complex are consequently solubility increase, better wettability and reduction of particle size.

**Table 2: %Cumulative drug release**

| Time in min | %Cumulative drug release (Avg. ± RSD; n=6) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Innovator | CD1 | CD2 | CD3 | CD4 | CD5 | CD6 | CD7 | CD8 | CD9 |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 10 | 81.6±2.12 | 56.5±4.65 | 64.8±2.69 | 71.0±2.41 | 74.6±1.64 | 75.5±2.07 | 74.4±2.96 | 73.5±2.51 | 72.0±1.83 | 72.0±2.91 |
| 20 | 93.8±1.04 | 65.3±4.53 | 73.0±3.86 | 79.0±1.32 | 80.1±1.27 | 80.0±1.50 | 79.3±1.14 | 78.9±1.90 | 74.6±2.11 | 81.4±2.56 |
| 30 | 95.4±0.84 | 81.7±4.15 | 84.2±2.27 | 86.7±1.62 | 85.3±1.62 | 86.3±0.76 | 86.2±1.61 | 83.3±2.05 | 79.8±0.56 | 88.2±1.35 |
| 45 | 97.2±0.74 | 87.3±1.35 | 92.9±2.92 | 93.6±1.59 | 92.0±1.26 | 98.0 ±0.67 | 92.7±0.81 | 89.9 ±0.71 | 85.0±0.57 | 93.7±2.56 |
| 60 | 98.5±0.46 | 98.6±0.70 | 99.6±0.69 | 99.6±0.95 | 99.7±0.57 | 99.8±0.47 | 98.7±0.63 | 99.2±0.48 | 93.1±0.71 | 99.8±0.93 |

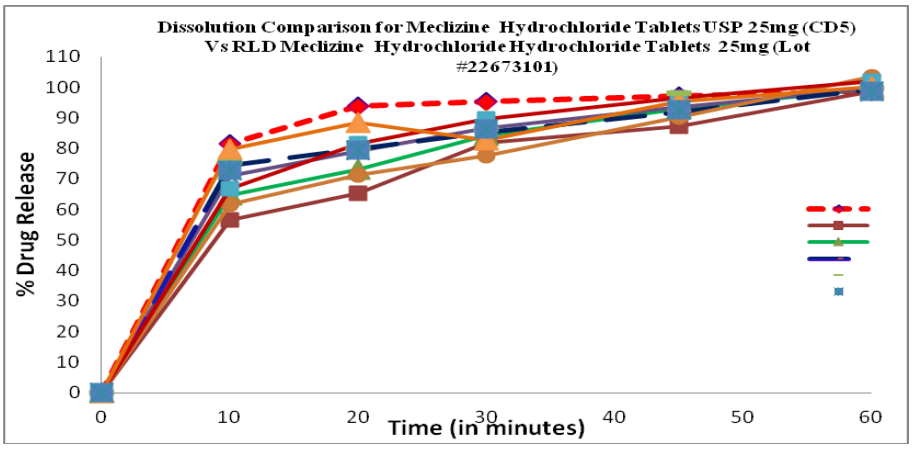



**Fig 9: Dissolution comparison between RLD and different IH formulation.**

**Evaluation of precompression parameters of powder blend**

The angle of repose of the powder blend (CD5) was found to be 19.46°. The bulk density and tapped bulk density of all the batches were varied from 0.44 to 0.48 gm/ml and 0.60 to 0.66 gm/ml, compressibility index of all the trial batches ranged from 09.182% to 11.387% and the Hausner's ratio of all the batches prepared ranged from 1.106 to 1.126.

**Table 3: Flow characters and compressibility of the prepared formulation powder blends**

| Formulation codes | Bulk density | Tapped density | Carr's Index | Hausner's ratio | Angle of repose |
|---|---|---|---|---|---|
| CD1 | 0.45±0.00 | 0.65±0.00 | 11.045 ± 0.46 | 1.127 ± 0.00 | 21.12 ± 0.55 |
| CD2 | 0.44±0.02 | 0.63±0.00 | 11.387 ± 0.52 | 1.121 ± 0.01 | 19.32 ± 0.15 |
| CD3 | 0.47±0.00 | 0.64±0.01 | 10.632 ± 0.61 | 1.112 ± 0.00 | 24.52 ± 0.36 |
| CD4 | 0.45±0.00 | 0.62±0.01 | 11.281 ± 0.74 | 1.126 ± 0.01 | 22.35 ± 0.25 |
| CD5 | 0.48±0.01 | 0.62±0.01 | 09.812 ± 0.54 | 1.106 ± 0.01 | 19.46 ± 0.74 |
| CD6 | 0.45±0.01 | 0.66±0.01 | 11.274 ± 0.32 | 1.125 ± 0.01 | 24.12 ± 0.23 |
| CD7 | 0.44±0.00 | 0.62±0.00 | 10.097 ± 0.44 | 1.118 ± 0.01 | 23.38 ± 0.45 |
| CD8 | 0.44±0.01 | 0.60±0.01 | 09.182 ± 0.68 | 1.109 ± 0.01 | 19.28 ± 0.81 |
| CD9 | 0.42±0.00 | 0.71±0.00 | 12.112 ± 0.61 | 1.119 ± 0.00 | 22.12 ± 0.36 |

**Evaluation of postcompression parameters of tablets**

The hardness of the prepared tablet (CD5) was found to be 10.08±0.60 kg/cm². Friability was found to be 0.0%, which were below 1% indicating sufficient mechanical integrity and strength of prepared tablets. The disintegration time was found to be 02:50 to 04:02. Weight variation was found to be 365.0±0.92 mg which was within the permissible limit of ±7.5%. The *in vitro* dissolution studies showed that almost 75.5% of the drug was released within 10min and almost 98.0% of the drug was released at the end of 45min. The prepared tablets were compared with the marketed tablet, and the dissolution parameters of both formulations are shown in Table 4 and Figure 10. The drug content was found to be 99.5%.

Table 4: Results of evaluation tests of Meclizine Hydrochloride tablets of all formulations

| Formulation code | Hardness ($Kg/cm^2$) | Average Weight (mg) | Disintegration time (minute: second) | Friability (%) |
|---|---|---|---|---|
| CD1 | 9.75±0.74 | 362.0±1.04 | 04:02 to 05:20 | 0.1 |
| CD2 | 10.30±0.79 | 364.0±0.62 | 03:25 to 04:54 | 0.2 |
| CD3 | 9.92±0.73 | 362.0±1.07 | 02:18 to 07:09 | 0.0 |
| CD4 | 9.95±0.67 | 363.0±1.21 | 01:38 to 02:30 | 0.0 |
| CD5 | 10.08±0.60 | 365.0±0.92 | 02:50 to 04:02 | 0.0 |
| CD6 | 9.87±0.69 | 364.0±1.26 | 01:48 to 02:06 | 0.0 |
| CD7 | 9.93±0.71 | 361.0±0.82 | 02:55 to 04:50 | 0.0 |
| CD8 | 9.58±0.56 | 359.0±1.06 | 03:57 to 04:49 | 0.0 |
| CD9 | 9.33±0.22 | 361.0±1.11 | 04:21 to 06:01 | 0.1 |

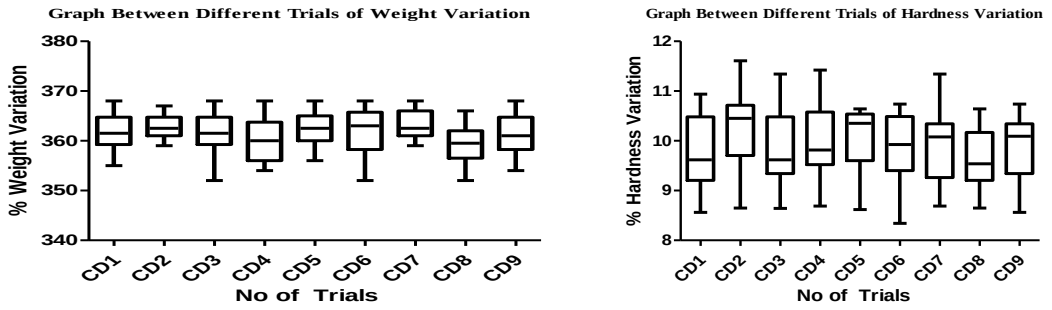



**Fig 10: Graph Between different trials of (A) Weight variation (B) Hardness variation**

## 4.0 DISCUSSION

From the result it is observed that the solubility of Meclizine HCl in the presence of β-cyclodextrin can be classified as the $A_L$ type. This indicated that the complexes at 1:2 ratios are adequately stable and also the extent of solubility enhancement being higher for β-CD. While the DSC thermogram of the kneading complex shows the complete disappearance of the Meclizine HCl endothermic peak and flattening of endotherm which indicates the formation of true complex and conversion of a drug-to-amorphous form. The dissolution rate increase for the physical mixture, kneaded and co-precipitation mixtures is due to the wetting effect of the β-CD, this effect is more evident for the kneaded product, where the mixing process between the two components is more intensive. The effect of complexation with β-CD on the solubility of Meclizine HCl can be explained in terms of the reduction in the crystallinity of the drug and

conversion to amorphous form by inclusion into the hydrophobic cavity of the β-CD.

The FTIR spectra for Meclizine Hcl and the optimum formula showed the main characteristic absorption bands of functional groups of C-CL, C-N amine and C=C stretching . As shown in characteristic absorption peaks of Meclizine Hydrochloride appear almost at the same region. These results indicate that there is no chemical interaction between the API and the excipients and this confirms the compatibility of the drug with the excipients of the optimum formula. *In vitro* drug release from prepared tablets shows significantly improved drug dissolution as compared to the marketed tablet of Meclizine HCl. Hence, it could be concluded that the solubility enhancement of Meclizine HCl could be successfully achieved by the inclusion complexation technique and inclusion complex based fast dissolving tablets of Meclizine HCl would provide quick-onset of action.

Thus, it can be summarized that stable Formulation CD5 were prepared successfully by using Inclusion complex in 1:2 ratio by kneading technique.

## 5.0 CONCLUSIONS

The Kneading methods could increase the solubility and dissolution rate of Meclizine Hydrochloride via formation of inclusion complex with βCD. Kneading method was the most effective method in terms of Meclizine Hydrochloride solubilization. Meclizine Hydrochloride was converted from crystalline to amorphous form through inclusion complexation.

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