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FORMULATION AND EVALUATION OF ORAL DISINTEGRATING TABLETS OF DIPHENHYDRAMINE BY DIRECT COMPRESSION METHOD

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ABSTRACT

Orally disintegrating tablets (ODTs) improve patient compliance, particularly in pediatric and geriatric populations who experience difficulty swallowing conventional tablets. The present study focuses on the formulation and evaluation of diphenhydramine hydrochloride orally disintegrating tablets prepared by the direct compression method. Diphenhydramine HCl, a first-generation antihistamine with anticholinergic and sedative properties, was characterized using differential scanning calorimetry (DSC), Fourier transform infrared spectroscopy (FTIR), and UV–Visible spectroscopy to assess purity and compatibility with excipients. Various super-disintegrants such as sodium carboxy methyl cellulose (SCMC), sodium alginate, polyvinyl pyrrolidone (PVP), and polyethylene glycol (PEG) were evaluated at different concentrations. Pre-compression and post-compression parameters including angle of repose, compressibility index, Hausner's ratio, weight variation, hardness, friability, thickness, disintegration time, and wetting time were assessed. Sodium carboxy methyl cellulose demonstrated superior disintegration efficiency and mechanical strength compared to other super-disintegrants. The optimized formulation containing 10% SCMC exhibited rapid disintegration (≈10 seconds), acceptable wetting time, and satisfactory mechanical properties. Stability studies conducted under varying temperature and humidity conditions confirmed that the formulation remained stable with drug release between 90–110% as per

USP standards. The study concludes that diphenhydramine HCl ODTs formulated using SCMC via direct compression are stable, effective, and suitable for pediatric and geriatric use.

KEYWORDS: Diphenhydramine hydrochloride, Orally disintegrating tablets, Direct compression, Super-disintegrants, Sodium carboxy methyl cellulose, Stability studies.

1. INTRODUCTION

Oral drug delivery remains the most preferred route due to its convenience, safety, and cost-effectiveness. However, conventional solid dosage forms present swallowing difficulties for pediatric, geriatric, and dysphagic patients. Orally disintegrating tablets (ODTs) were developed to overcome these limitations, as they rapidly disintegrate in the oral cavity without the need for water, enhancing patient compliance and onset of action.

Diphenhydramine hydrochloride is a first-generation antihistamine widely used in the treatment of allergic disorders, motion sickness, and as a sedative. Despite its therapeutic efficacy, its bitter taste and conventional dosage forms limit its acceptability among sensitive patient groups. Formulating diphenhydramine HCl as an ODT provides a promising approach to improve ease of administration and patient adherence.

The direct compression method is a simple, economical, and scalable technique for ODT preparation. The selection of appropriate super-disintegrants plays a crucial role in ensuring rapid tablet disintegration while maintaining adequate mechanical strength. The present study aims to formulate diphenhydramine HCl ODTs using different super-disintegrants, evaluate their physicochemical properties, optimize the formulation, and assess stability under various environmental conditions.

2. DRUG PROFILE: DIPHENHYDRAMINE

- **Chemical Name:** 2-(Diphenylmethoxy)-N,N-dimethylethanamine
- **Molecular Formula:** $C_{17}H_{21}NO$
- **Molecular Weight:** 255.35 g/mol
- **Appearance:** White or almost white crystalline powder
- **Odor:** Odorless or faint characteristic odor
- **Taste:** Bitter

- **Solubility:** Freely soluble in water (as diphenhydramine hydrochloride), Soluble in alcohol and chloroform, Slightly soluble in ether, Practically insoluble in non-polar solvents (free base).
- **State:** Solid (at room temperature)
- Melting Point: 168–172°C
- **Generic Name:** Diphenhydramine
- **Brand Names:** Benadryl, Nytol, Sominex, Unisom (certain formulations) Others depending on country.
- **Drug Class:** First-generation antihistamine**,** Ethanolamine derivative**,** Anticholinergic agent
- **Mechanism of Action: H_1 receptor antagonist:** Blocks histamine H_1 receptors, preventing the effects of endogenous histamine (e.g., vasodilation, increased capillary permeability, and itching). **Anticholinergic activity:** Blocks muscarinic acetylcholine receptors, leading to drying effects (e.g., reduced secretions) and sedation. **Sedative effects:** Due to its ability to cross the blood–brain barrier and cause central nervous system (CNS) depression.
- **Routes of Administration:** Oral (tablets, capsules, syrup), Intramuscular (IM), Intravenous (IV)
- **Absorption:** Well absorbed orally
- **Onset:** 15–60 minutes
- **Duration:** 4–8 hours
- **Metabolism:** Liver
- **Excretion:** Urine
- **Half-life:** ~4–9 hours (longer in elderly)
- **Drug Interactions:** Alcohol (↑ CNS depression), Sedatives, benzodiazepines, opioids, MAO inhibitors (↑ anticholinergic effects), Other anticholinergic drugs.

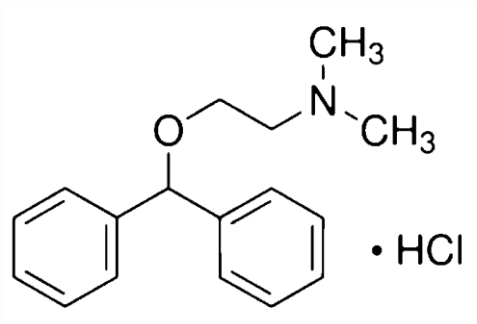

Fig. 1: Diphenhydramine HCl.

3. MATERIALS AND METHODS

3.1 METHODS ANALYSING

Diphenhydramine HCl Analysis: A DSC model 822e with a TS0801R0 Robot from Mettler-Toledo was used to analyze the diphenhydramine HCl sample for its thermal behavior. Samples (10 mg) were weighed in 100 ul aluminum pans and a lid crimped to the top with a hole punched at the top. The thermo grams were recorded from 25-250°C at a rate of 10°C/min under nitrogen gas purge at 50 ml/min. Mettler Toledo STARe software (version 10.0) was used to collect and analyze the data.

FTIR Analysis of Diphenhydramine HCI: Diphenhydramine HCl, and a 1:1 mixture were each individually analyzed. The samples were mixed with potassium bromide in approximately 1:100 ratio and formed into a pressed disc. The resulting disc was placed in a vacuum to expel air trapped between particles. The FTIR spectra of the samples were collected using a Germanium ATR (Attenuated Total Reflection) crystal in the Digi lab Excalibur FTS 4000 FTIR spectrometer from Bio-Rad Laboratories fitted with a UMA 600 microscope. The spectra for these samples were obtained by accumulating 256 scans with a resolution of 4 cm- in the range of 800-4000 cm-1.

UV-VIS Analysis of Diphenhydramine HCI: UV- vis model Genesys 6. Thermo Fisher Scientific Madison was used to analyze the quantin of diphenhydramine Plastic one-centimetre path length curettes were used in the analysis The wavelength (m) where diphenhydramine HCT has the highest absorption was determined by wanning the dissolved sample of pure diphenhydramine HCI in deionised water from 200 to 300 was analyzed at the experimental lambda max of diphenhydramine HCl to determine if absorption occurred at that wavelength.

A calibration curve was plotted using the Beer-Lambert law. Several diphenhydramine HCl concentrations were analyzed between 0.2-0.8 absorbance. Linear regression was used to correlate absorbance to diphenhydramine HCI concentration at its lambda max. The resulting Beer-Lambert equation was used to quantify the diphenhydramine HCl concentration in the sodium alginate: diphenhydramine HCI mixture to determine if degradation of diphenhydramine HCl occurred in a known sample.

3.2 PREPARATION OF SUPER DISINTEGRANTS POWDER MIXTURES

Composition of 110 mg Blank Tablets Prepared on the manesty A 28

Table 1: Formulation Table.

S.NO	INGREDIENTS	F1	F2	F3	F4
1	DPH	2.5	2.5	2.5	2.5
2	SCMC	1	1.5	1	1.5
3	Sodium Alginate	1.5	1	1	1.5
4	Glucose	4	4	4	4
5	PVP	1	1	1	1
6	PEG	1	1	1	1

Procedure: Take 2.5gms of diphenhydramine active drug. its get grinded in mortar and pestle then this powder is mixed with sodium carboxy methyl cellulose about 1.0gms. Make a fine powder form. get continuous triturating by adding sodium alginate for 1.5gms.then adding a poly vinyl pyrrolidine and poly ethylene glycol each one add about 1.0 gms. Make a fine powder finally get mixed with glucose as sweetening agent. for taste masking purpose. about 4.0gms.2.5gms of diphenhydramine active drug. its get grinded in mortar and pestle then this powder is mixed with sodium carboxy methyl cellulose about 1.0gms. Make a fine powder form. get continuous triturating by adding sodium alginate for 1.5gms. then adding a poly vinyl pyrrolidine and poly ethylene glycol each one add about 1.0 gms. Make a fine powder finally get mixed with glucose as sweetening agent. for taste masking purpose. about 4.0gms.

Fig. 2: Diphenhydramine HCI ODT Packaging.

4. RESULTS AND DISCUSSION

4.1 DIPHENHYDRAMINE HCL ANALYSIS

DSC thermogram in Figure 9.1 illustrates the purity of diphenhydramine HCI with a single sharp peak at 170°C for melting and subsequent degradation above 200°C.The experimental melting point is consistent with literature values.

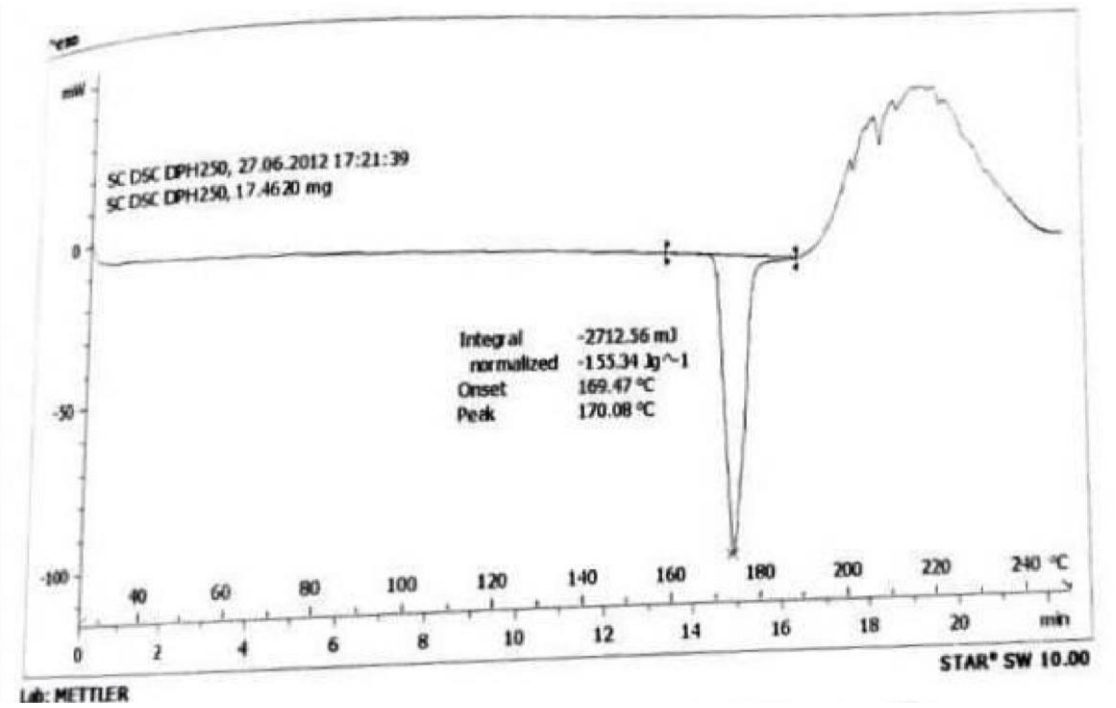

Fig. 3: DSC Thermogram For Diphenhydramine.

4.2 FTIR ANALYSIS OF DIPHENHYDRAMINE HCL

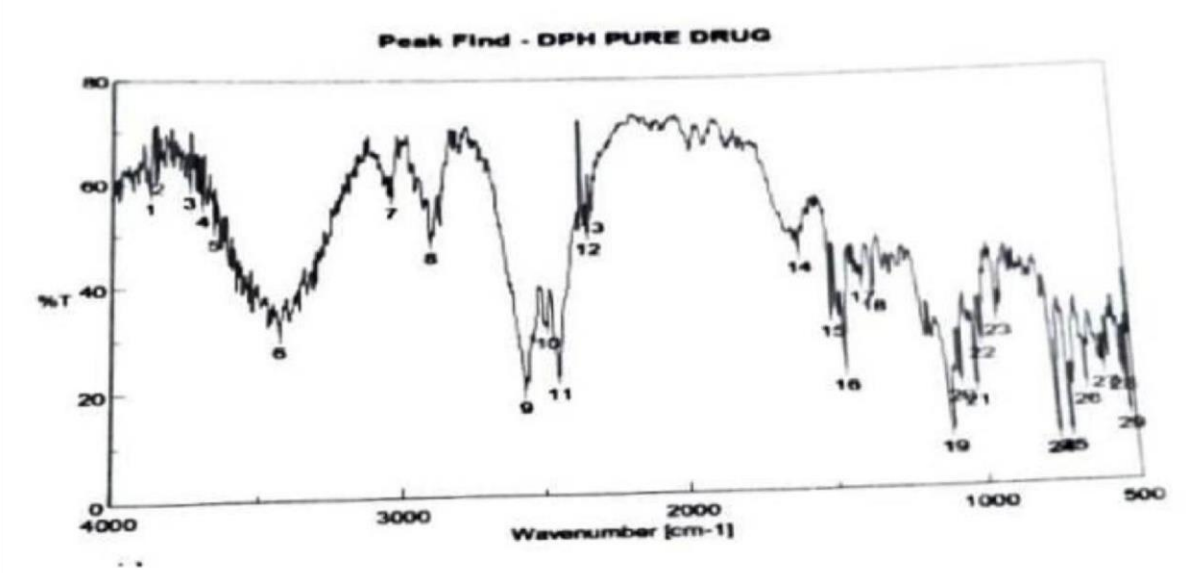

Fig. 4: FTIR Spectra for Diphenhydramine HCI.

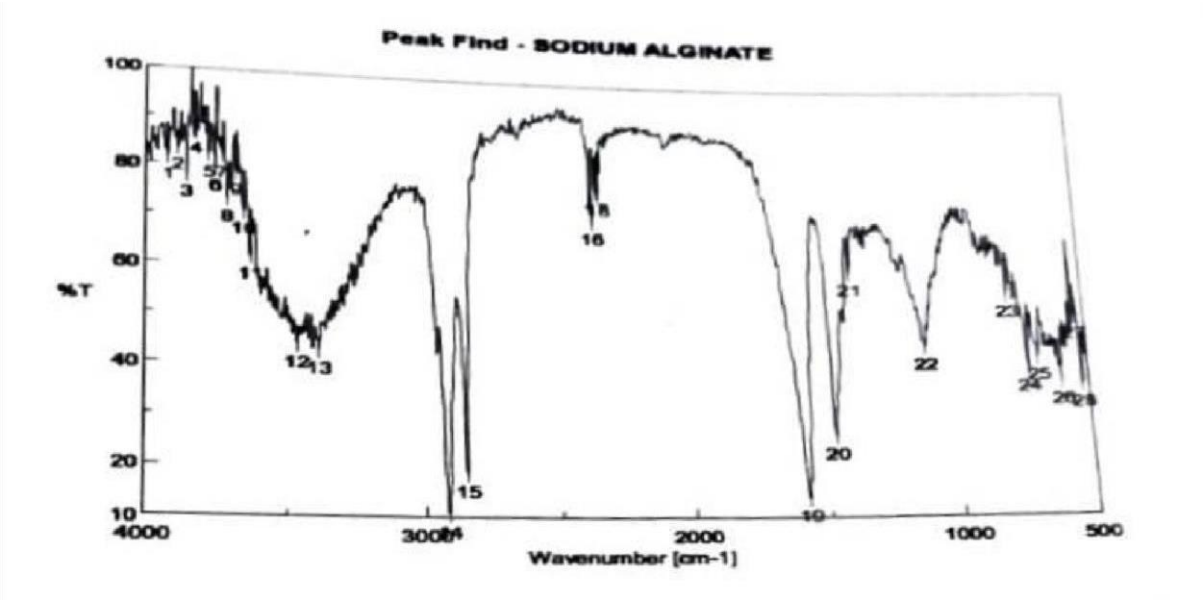

Fig. 5: FTIR Spectra for Sodium Alginate.

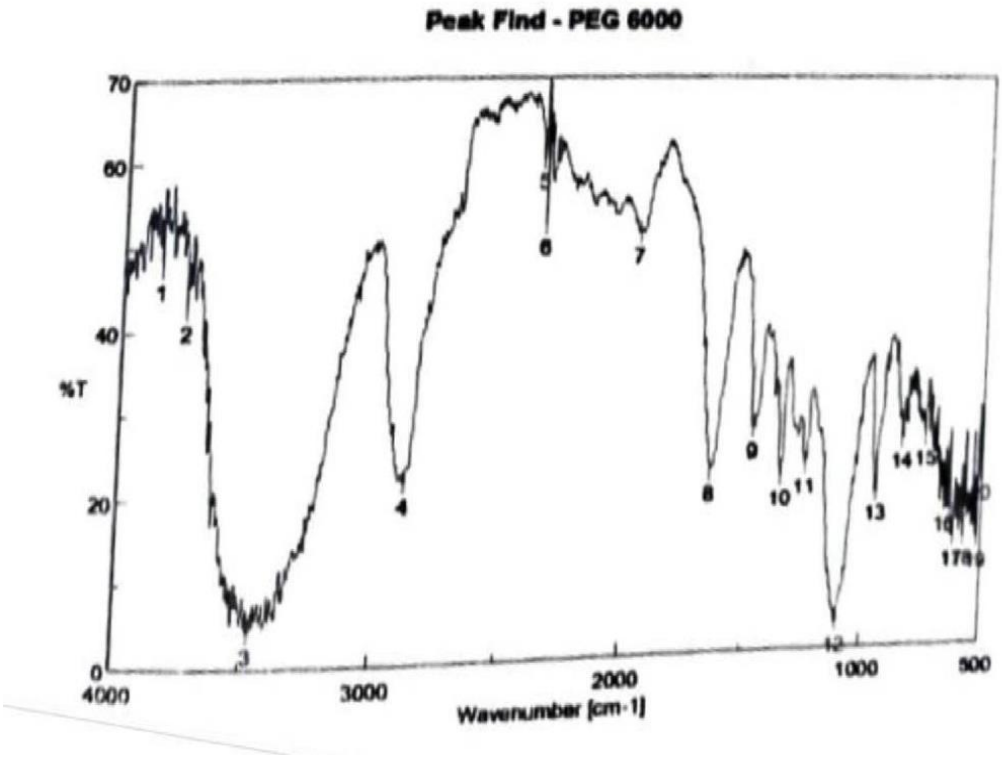

Fig. 6: FTIR Spectra for PEG 6000.

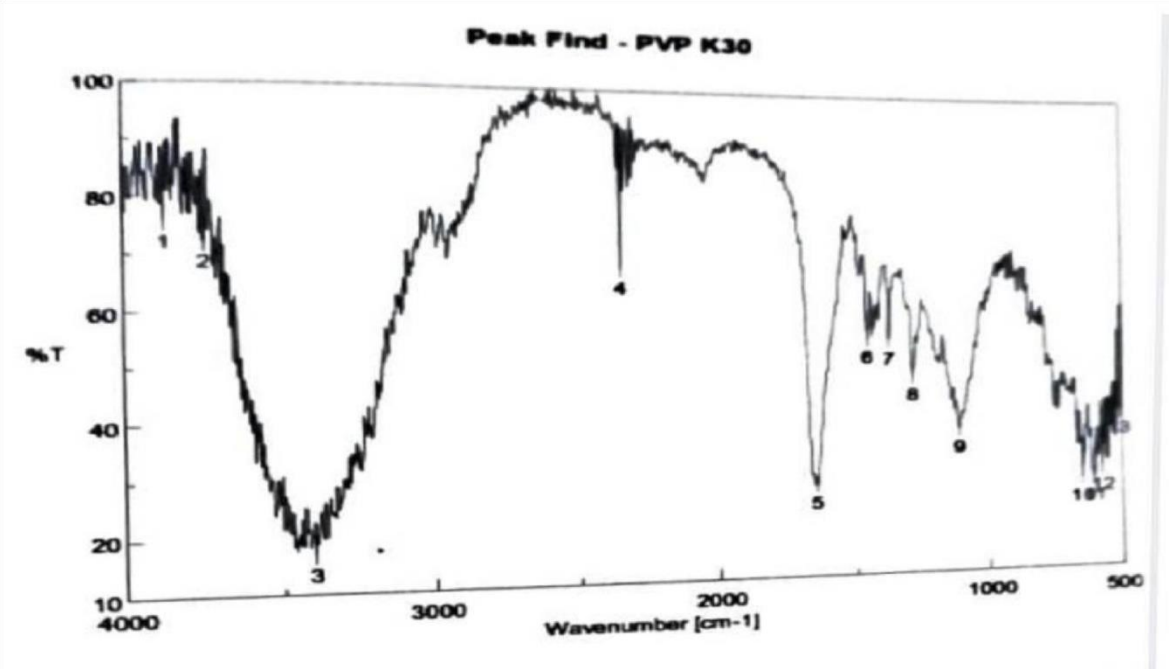

Fig. 7: FTIR Spectra for PVP K30.

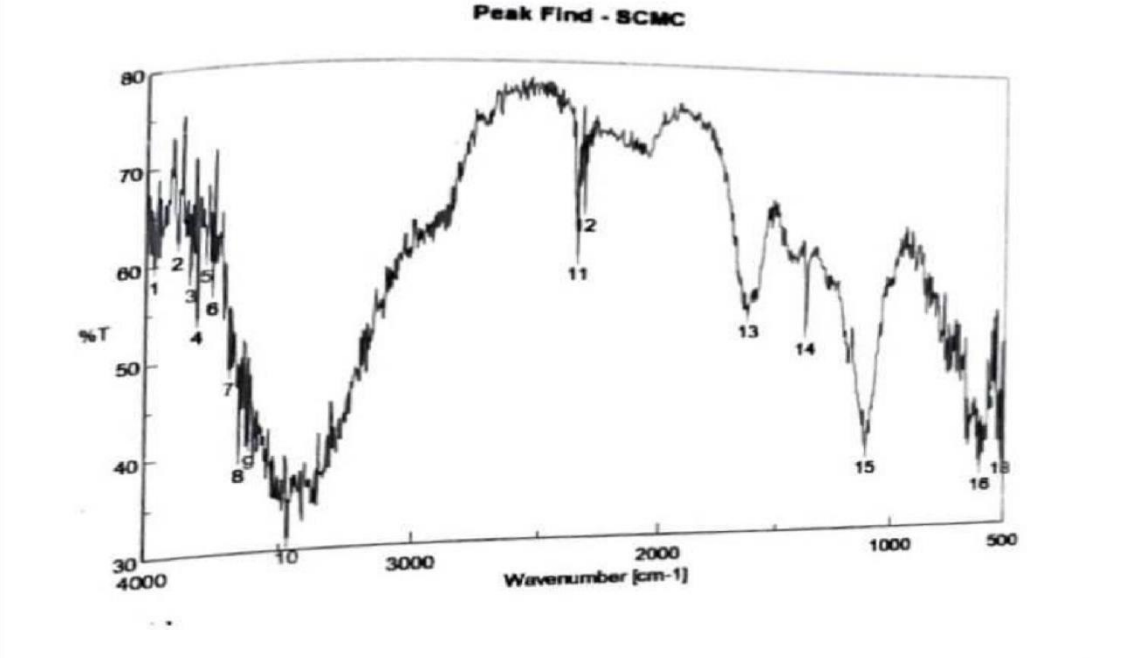

Fig. 8: FTIR Spectra for PVP SCMC.

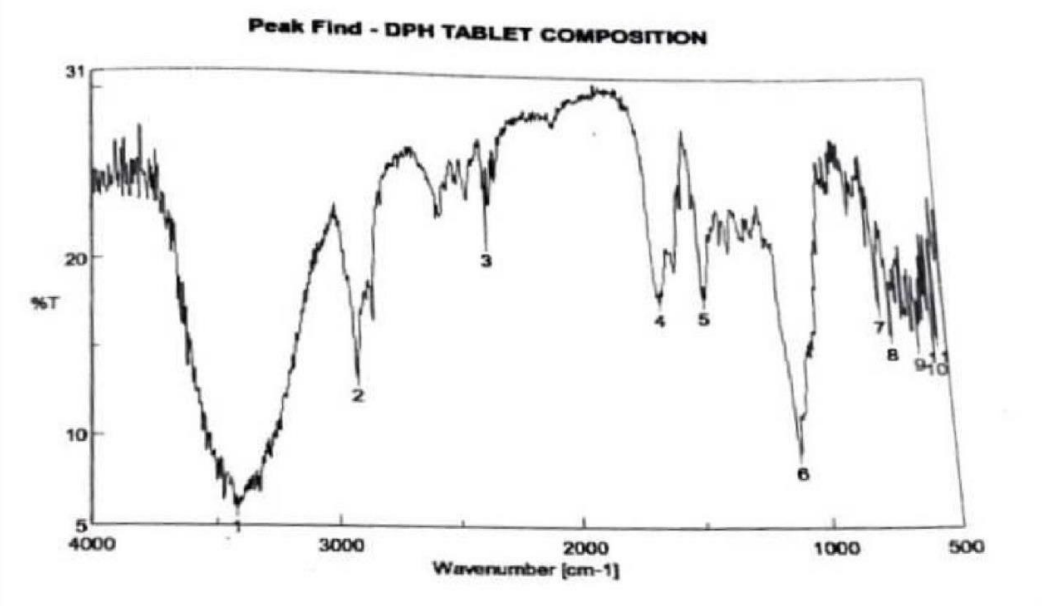

Fig. 9: FTIR Spectra for DPH Tablet.

4.3 UV -VIS ANALYSIS OF DIPHENHYDRAMINE HCI

The wavelength (max) where diphenhydramine HCl has the highest absorption was Determined by scanning the dissolved sample of pure diphenhydramine HCI in deionized water from 200 to 300 nanometers. The max for diphenhydramine HCl is 258 nm sodium alginate was Evaluated at 258 nm and displayed no significant absorption. SCMC, PVP, and PEG are all insoluble in deionised water and were filtered out before evaluation. None of the excipients registered a UV absorption at 258 nm. This wavelength will be used for the quantitative analysis of diphenhydramine HCI.

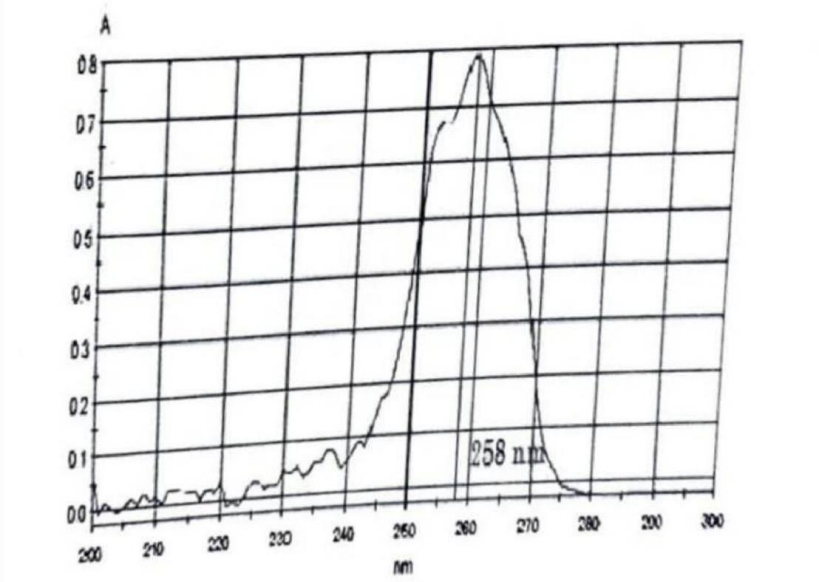

Fig. 10: UV -VIS Analysis Of Diphenhydramine HCI.

A 1:1 physical mixture of diphenhydramine HCI and sodium alginate was Mended using a mortar and pestle. The mixture was dissolved in 100 ml. of deionized water and analyzed at 258 nm. The absorbance of the mixture was 0.210 A. Using the calibration curve of diphenhydramine HCl in deionised water, the theoretical concentration of diphenhydramine HCl is 0.0005217 M. The percent error of diphenhydramine HCL in the 1:1 mixture is 0.0687%. Therefore, no degradation of diphenhydramine HCI has occurred when physically mixed with sodium alginate in a mortar and pestle. PVP can be used as the primary excipient in the orally disintegrating tablets of diphenhydramine HCI because there is no negative reaction occurring between the two components.

Calibration curves for diphenhydramine HCI were prepared according to the Beer-Lambert Law using both deionised water and simulated gastric fluid without enzymes. illustrates the linear relationship that was found and used to quantify diphenhydramine HCI in deionised water, while illustrates the calibration curve which will be used for the simulated gastric fluid without enzymes. Water at 258 nm where slope = 445.61; intercept-0.0096; and R2 = 0.9999

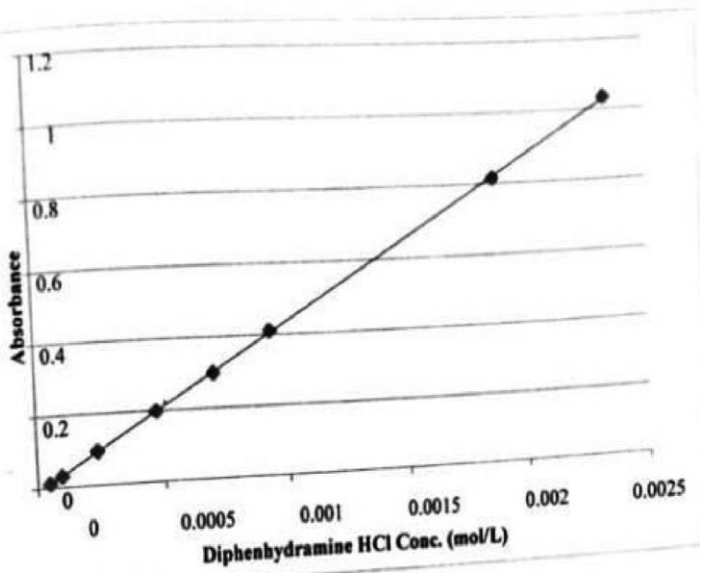

Fig. 11: Calibration Curve.

4.4 SUPER-DISINTEGRATE TABLET TESTING

Tablets prepared according to Sections 11.2.5 Preparation Super-disintegrant Powder Mixtures and 11.2.6 Super-disintegrant Tableting and were analyzed for weight variation; friability; thickness; hardness; disintegration time and wetting time. includes the average weight of ten tablets, the average hardness of six tablets, and the average thickness of six tablets.

Table 2: Tablet Testing.

	Weight Variation, g	Hardness, N	Thickness, mm
3%	0.0986 ± 0.0018	18.2±2.8	3.46±0.01
4%	0.1010± 0.0028	23.8±1.9	3.58±0.01
5%	0.1025± 0.0016	17.3±3.1	3.59±0.02
6%	0.1012± 0.0022	16.0±2.8	3.61±0.01
	Weight Variation, g	**Hardness, N**	**Thickness, mm**
2%	0.1035± 0.0020	22.3±1.8	3.51±0.01
3%	0.1129± 0.0011	21.2±1.9	3.77±0.01
4%	0.1119± 0.0010	22.5±4.2	3.77±0.01
5%	0.1117± 0.0017	20.2±3.1	3.78±0.01

The disintegration times for the four different types of super-disintegrants. Poly ethylene glycol has significantly longer disintegration times than sodium carboxy methyl cellulose,poly vinyl pyrrolidine and sodium alginate. Sodium carboxy methyl cellulose has the shortest average disintegration times of 5.83 seconds.

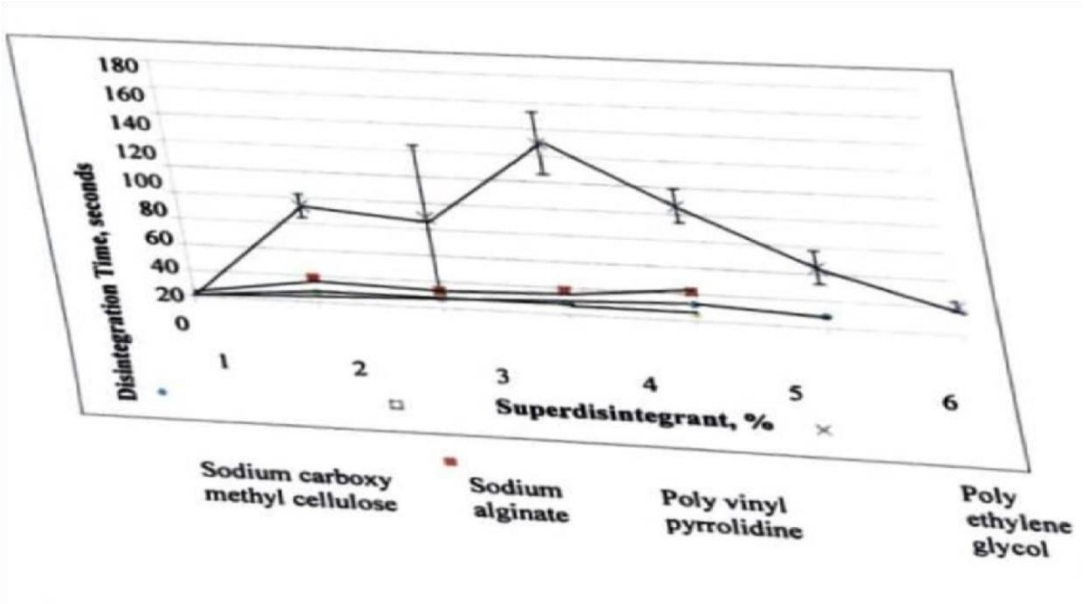

Fig. 12: Disintegration Time.

The wetting times for super-disintegrant sodium carboxy methyl cellulose. Sodium alginate, poly vinyl pyrrolidine, and poly ethylene glycol with diphenhydramine tablet selection are shown in Figure 9.26. sodium carboxy methyl cellulose has shortest average wetting time of 31.1 seconds.

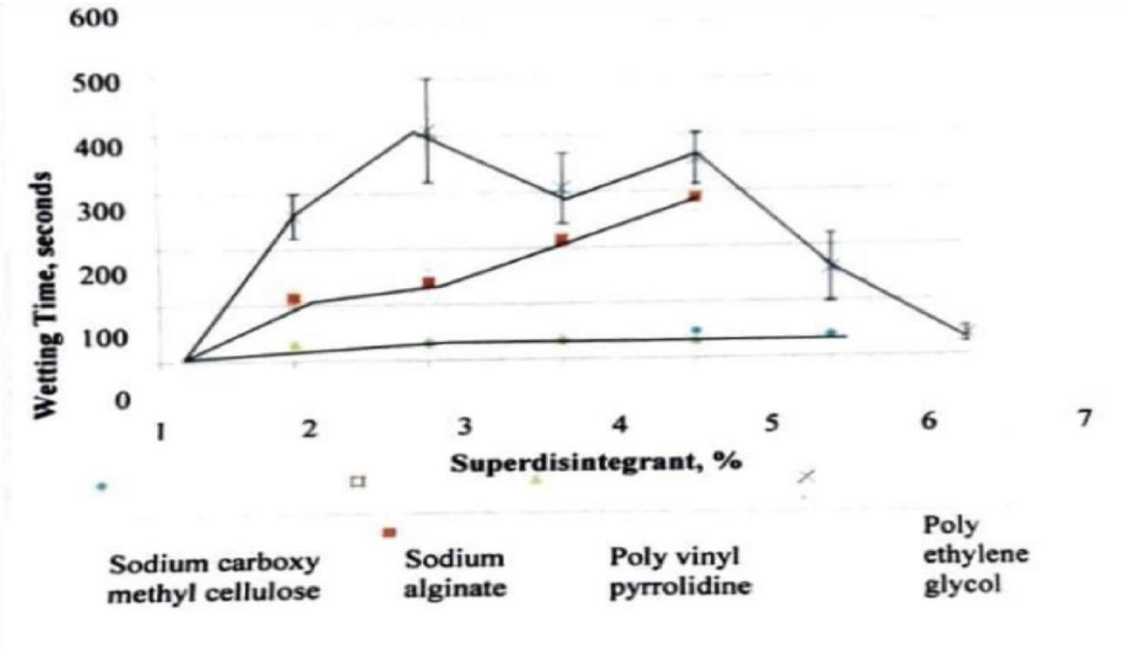

Fig. 13: Wetting Time.

Disintegration in the oral cavity would likely require more time than the disintegration test described in Section 11.2.7 Super-disintegrant Tablet Testing and less time than the wetting test. The disintegration test incorporates agitation in a large volume of water while the wetting test more closely resembles the oral cavity but lacks the closed environment and agitation the tongue would contribute. Both parameters illustrate specific qualities of the orally disintegrating tablet that allow it to uptake water and disintegrate in the presence of aqueous fluid.

Poly ethylene glycol failed the friability test for all concentrations analyzed by resulting in tablet capping and breakage. All concentrations of sodium carboxy methyl cellulose, sodium alginate, poly vinyl pyrrolidine, passed the friability test with less than 1% weight loss. These super-disintegrants also possess binding properties that are essential to forming a rigid tablet that can withstand the rigors of manufacturing and shipping stress. Sodium carboxy methyl cellulose was selected as the ideal super-disintegrant because it out performed poly vinyl pyrrolidine, sodium alginate, poly ethylene glycol in the disintegrating and wetting tests. The optimal concentration of sodium carboxy methyl cellulose is 5% in the 110 mg tablets.

4.5 POWDER PROPERTIES FOR THE OPTIMAL CHOICE OF SUPERDISINTEGRANT AND ITS CONCENTRATION

The following powder mixture was analyzed for its flow properties:

- 5% sodium carboxy methyl cellulose
- 91% sodium alginate
- 3% poly vinyl pyrrolidine
- 1% poly ethylene glycol

Table 3.5.1 contains the angle of repose data for the optimal concentration of super-disintegrant, namely 5% sodium carboxy methyl cellulose . The average angle of repose for this mixture is 32.56° and has good flow properties based on the USP 30 standard method.

Table 3: Results For Five Trials For 5% Sodium Carboxy Methyl Cellulose Angle Of Respose.

Height (cm)	Width (cm)	Angle (degree)	Flow
3.3	9.3	35.36	Good
2.9	8.9	33.24	Good
3.4	10.9	31.96	Good
3.0	9.8	31.48	Good
3.6	12.1	30.75	Excellent

The densities were calculated according to Equations Compressibility index was calculated according to Equation . The average compressibility index was 17.450 and classified as fair flowing properties. The Hausner's ratio was calculated according to Equation. The average Hausner's ratio was 1.211 and classified as fair flowing properties.

Table 4: Compressibility Index And Hausner's Ratio For Three Trials For 5% SCMC.

Trial	(g/ml)	g/ml	Compressibility index I =1-(v-v0)100	Flow	Hausner's ratio	Flow
1	0.9017	0.7469	17.164	Fair	1.207	Fair
2	0.9092	0.7408	18.519	Fair	1.227	Fair
3	0.9087	0.7572	16.667	Fair	1.200	Fair

The Flow rate apparatus was used to determine the smallest orifice that allowed the 5% sodium carboxy methyl cellulose powder mixture to freely flow through the opening. The 7 mm orifice was the smallest opening that allowed free flowing powder to pass through on three consecutive attempts.

4.6 DIPHENHYDRAMINE HCI TABLET TESTING

Since the addition of diphenhydramine HCl in 110 mg tablets using 5% SCMC slowed the disintegration time and wetting time for the tablets by hindering the water uptake capacity, the concentration of the superdisintegrant had to be increased. Further studies were performed to optimize the superdisintegrant concentration used with diphenhydramine HCl. Tablets prepared according to Sections of Preparation of Diphenhydramine HCI Powder Mixture with SCMC and Diphenhydramine HCI Tableting were analyzed for weight variation; friability; thickness; hardness; disintegration time and wetting time. Table includes the average weight of ten tablets, the average hardness of six tablets, and the average thickness of six tablets. 12.5 mg Diphenhydramine HCL Tablets with sodium carboxy methy cellulose.

Table 5: The Weight Variation, Hardness, And Thickness For Diphenhydramine HCl Tablets Containing SCMC.

	Weight Variation, g	Hardness, N	Thickness, mm
5%	0.10170 ± 0.0020	24.8± 3.7	3.56 ± 0.04
6%	0.0983± 0.0018	20.0± 2.1	3.53± 0.02
7%	0.1052± 0.0011	19.7±1.8	3.74± 0.01
8%	0.1016± 0.0016	22.2± 2.3	3.67 ± 0.03
9%	0.1021± 0.0014	17.7± 1.2	3.69 ± 0.01
10%	0.1024± 0.0012	16.2± 1.6	3.71 ± 0.01
11%	0.1013± 0.0021	21.3± 4.0	3.67 ± 0.04
12%	0.1025± 0.0011	22.8± 2.8	3.64 ± 0.02

The disintegration times for each concentration of SCMC in diphenhydramine HCI tablets. The 10% SCMC has the shortest average disintegration time of 10.3 seconds.

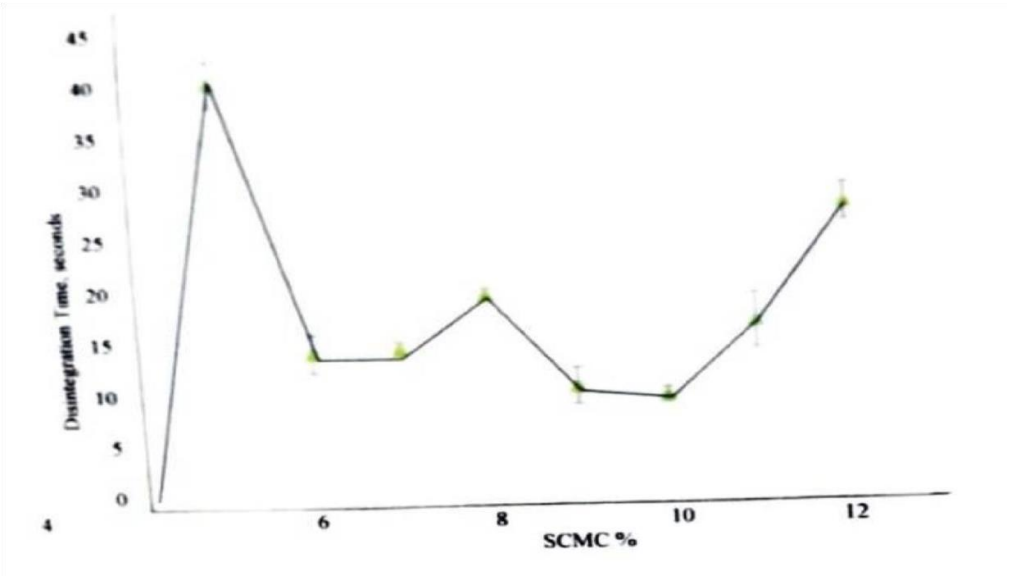

Fig. 14: Disintegration Time And Variation For Tablets Of 12.5 Mg.

Diphenhydramine HCl with SCMC. The wetting times for diphenhydramine HCI tablets containing sodium carboxy methyl cellulose. The 10% sodium carboxy methyl cellulose has the shortest average wetting time of 234.6 seconds in the presence of diphenhydramine HCl. All concentrations greater than 5% sodium carboxy methyl cellulose with diphenhydramine HCI passed the friability test with less than 1% weight loss.

Larger concentrations of the ideal super-disintegrant were used to account for the change caused by the addition of diphenhydramine HCl to the blank formulation and optimized the disintegration and wetting time for the tablets while passing friability standards.

4.7 POWDER PROPERTIES FOR THE OPTIMAL SODIUM CARBOXY METHYL CELLULOSE CONCENTRATION WITH DIPHENHYDRAMINE HCI:

The following powder mixture was analyzed for its flow properties:

- 10% SCMC
- 73.5% poly vinyl pyrrolidine
- 3% sodium alginate
- 1% poly ethylene glycol
- 12.5% Diphenhydramine HCI

The angle of repose data for the optimal concentration, namely 10% sodium carboxy methyl cellulose in the diphenhydramine HCl tablet mixture. The average angle of repose for this mixture is 31.87° and has good flow properties based on the USP 30 standard method.

Table 6: Angle Of Repose For Five Trials Of Powder Containing 10% Sodium Carboxy Methyl Cellulose And Diphenhydramine HCI (0.25 Mg/110 mg Tablet).

Height (cm)	Width (cm)	Angle (degree)	Flow
3.7	11.2	34.45	Good
3.3	10.6	31.91	Good
3.5	11.0	32.47	Good
3.0	10.3	30.22	Excellent
3.1	10.2	31.29	Good

The densities were calculated according to Equations 12.1 and 12.2. Compressibility index was calculated according to Equation 11.2. The average Compressibility index was 20.705 and classified as fair flow properties. The Hausner ratio was calculated according to Equation. The average Hausner ratio was 1.262 and classified as passable flowing properties.

Table 7: Compressibility Index And Hausner Ratio For Three Trials Of The 10% SCMC And Diphenhydramine HCI Powder Mixture.

Trial	(g/mL)	(g/mL)	Angle Of Repose	Flow	Hausner Ratio	Flow
1	0.8265	0.6712	18.792	Fair	1.231	Fair
2	0.8547	0.6623	22.517	Passable	1.291	Passable
3	0.8475	0.6712	20.805	Passable	1.263	Passable

The Flow rate apparatus was used to determine the smallest orifice that allowed the 10% SCMC powder mixture containing diphenhydramine HCl to freely flow through the opening. The 12 mm orifice was the smallest opening that allowed free flowing powder to pass through on three consecutive attempts.

4.8 STABILITY TESTING

The final formulation containing 10% SCMC and 12.5 mg of diphenhydramine HCI per tablet was analyzed for weight variation; friability; thickness; hardness; disintegration time; wetting time and dissolution of the active ingredient. Table 12.9 contains the average data of ten tablets for each parameter.

Table 8: Tablet Parameters For The Final ODT Diphenhydramine HCL Formulation.

Weight variation, g	0.095± 0.0012
Friability	Pass
Thickness, mm	3.57±0.02
Hardness, N	18.1±3.9

Disintegration Time, S	20.1±4.4
Wetting Time, s	242.3±30.3

Dissolution of the tablets at time-zero was assessed in both deionized water dissolution medium and simulated gastric fluid without enzymes. Both sets of dissolution data provided the same release profile. Deionized water dissolution medium was selected for subsequent studies because USP 30 recommends deionized water as the dissolution medium for diphenhydramine HCI tablets and capsules (since there is no protocol in place for diphenhydramine HCl orally disintegrating tablets). Furthermore, the log P value for diphenhydramine HCI is greater than I and diffuses into the epithelium of the upper gastrointestinal tract or the oral cavity where water is the primary dissolution medium.

Accelerated stability studies using extreme environmental conditions were implemented to determine how the orally disintegrating tablets would perform over time. The percent diphenhydramine HCl dissolved was calculated by adjusting the volume after each sample until the tablets disintegrated completely (12 min). Additionally, the filter paper used to remove solid particulates affected the UV-Vis absorption and was corrected in the percent dissolved evaluation. The dissolution of the tablets kept under refrigerated conditions (3°C) is illustrated in Figure. The dissolution profile was consistent over the nine week testing period and suggests the final formulation of 110mg diphenhydramine HCI orally disintegrating tablets are viable in similar conditions for at least nine weeks.

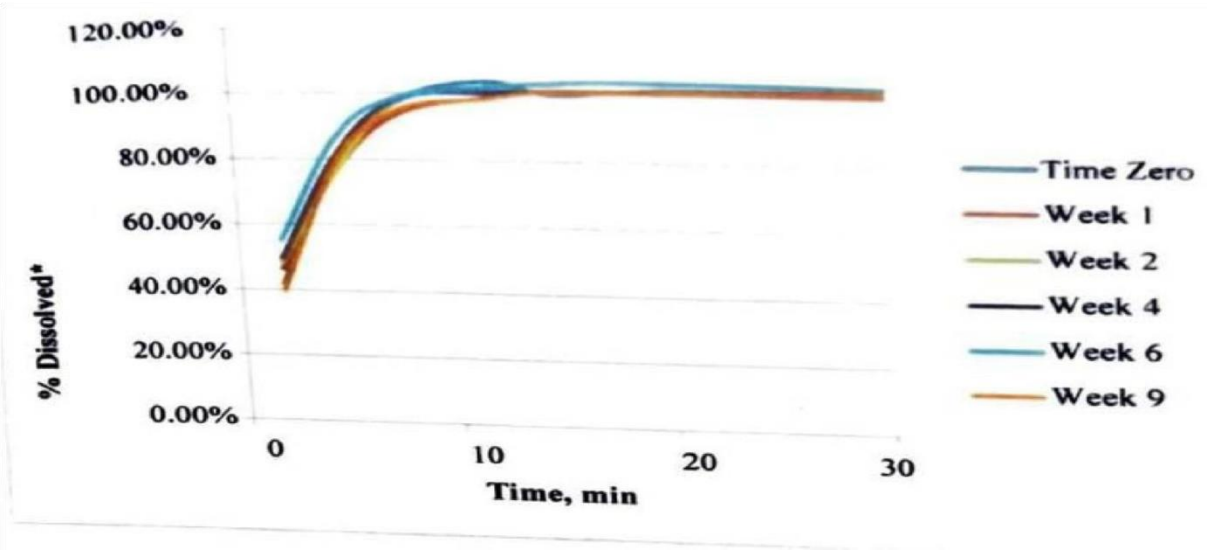

Fig. 15: Dissolution Testing For The Refrigerated (3°C) 110 mg Diphenhydramine HCI Tablets.

The dissolution of tablets kept at room temperature (21°C) is illustrated in Figure . The dissolution profile showed slight variation over the nine week testing period but remained consistent in the final percent diphenhydramine HCI dissolved. Tablets of the final formulation kept in a comparable environment are suitable for up to and perhaps beyond nine weeks after manufacture.

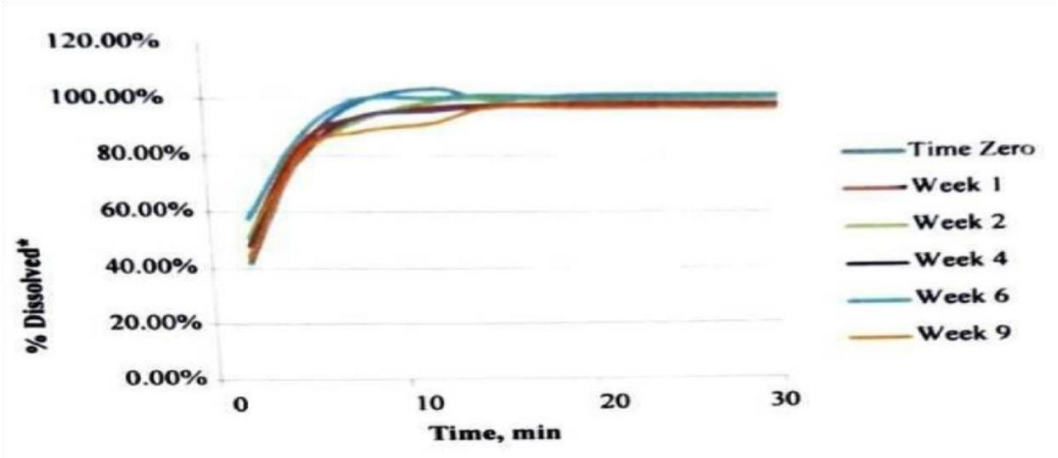

Fig. 16: Dissolution Testing For The 110 mg Diphenhydramine.

HCI Tablets at Room Temperature (21°C) displays the results for the dissolution testing for tablets stored at an elevated temperature (40°C) for nine weeks. The dissolution profile showed some variation over time, however the percent of diphenhydramine HCl dissolved remained within acceptable limits defined in USP 30 standards. This indicates that tablets stored under less thermal stress would be viable for a longer period of time.

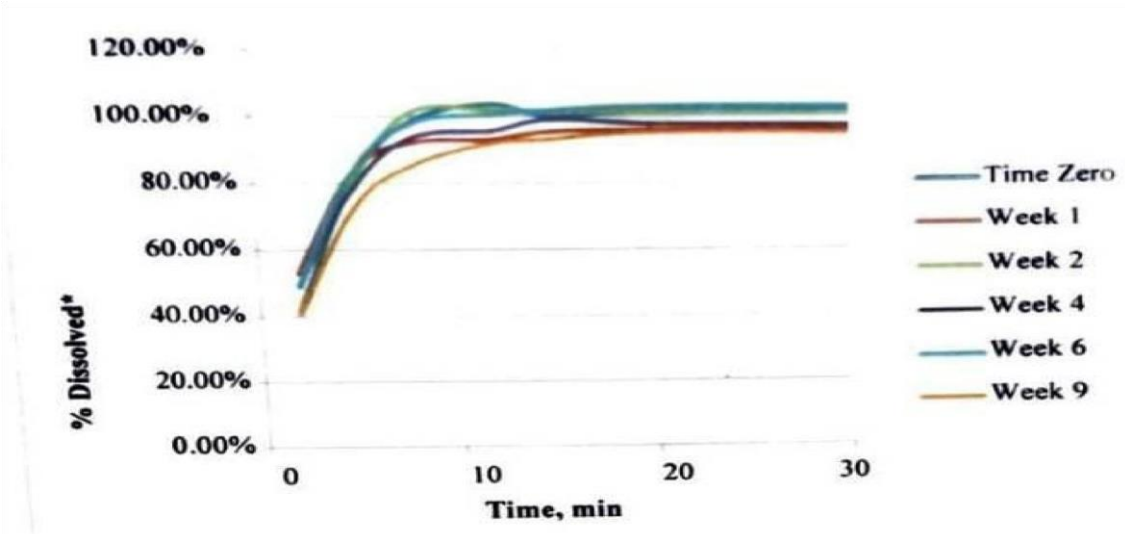

Fig. 17: Dissolution Testing For The 110 mg Diphenhydramine HCI Tablets Under Oven (40°C) Conditions.

The final percent of diphenhydramine HCI dissolved for each dissolution test is represented in All parallels for each temperature condition remained within the specified limits outlined in USP 30. The percent of drug dissolved was between 90 and 110% for each determination.

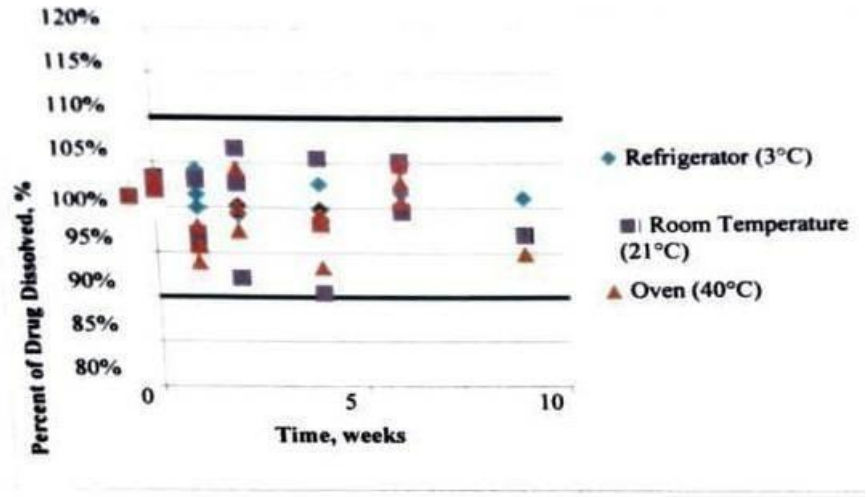

Fig. 18: Combined Stability Testing Results For The 110 mg Diphenhydramine HCI ODT.

4.9 HUMIDITY TESTING

Tablets were weighed prior to and after specific humidity conditions. The percent weight change of diphenhydramine HCl tablets is illustrated in Figure. Tablets stored in 16% and 33% relative humidity chambers maintained the same weight throughout the duration of the study with acceptable error of the electronic balance. Tablets kept at 75% relative humidity swelled over the eight week study and experienced around 2% weight gain throughout the stability testing period.

Fig. 19: Percent Weight Change And Variance Of The 110 mg Diphenhydramine HCI ODT During Humidity Stability Testing.

The same tablets were evaluated for hardness and compared to the average hardness of the final formulation at time-zero in Tablets stored at 16% and 33% relative humidity experienced little change in hardness over the course of the study except for the Week 2 tablets kept at 33% relative humidity. This deviation suggests experimental error such as a non-sealed vessel. Tablets stored in 75% relative humidity had zero Newton hardness and fell apart with minimal effort. As a result, the orally disintegrating tablets of Diphenhydramine HCI are not stable under elevated humidity conditions and easily uptake water from the environment to swell and diminish their structural integrity. The tablets are stable and capable of being stored at or below 33% relative humidity.

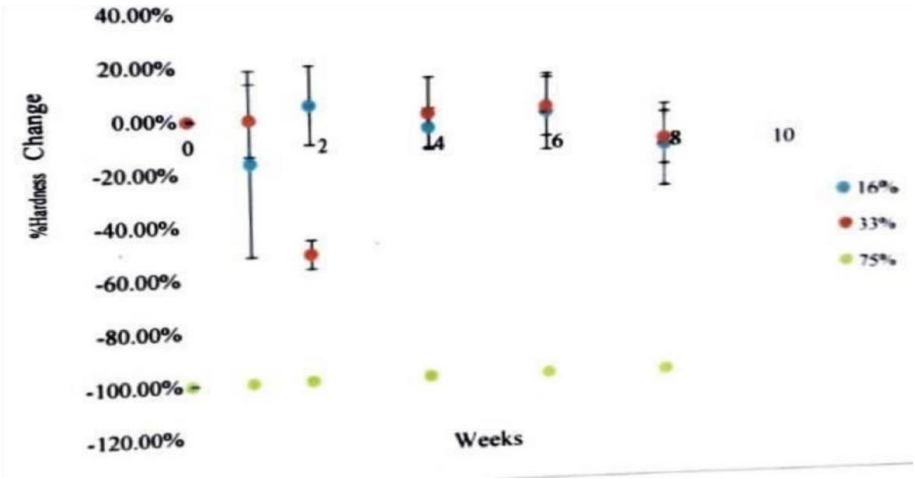

Fig. 20: Percent Hardness Change And Variance In Humidity Stability Testing For 110 mg Diphenhydramine HCI ODT.

DISCUSSION

The DSC analysis confirmed the purity of diphenhydramine HCl by exhibiting a sharp melting endotherm at approximately 170°C, consistent with reported literature values. FTIR studies indicated no significant chemical interaction between diphenhydramine HCl and the selected excipients, confirming their compatibility. UV–Visible spectroscopic analysis established 258 nm as the λmax for diphenhydramine HCl, and Beer–Lambert's law was obeyed over the tested concentration range, enabling accurate quantification.

Among the evaluated super-disintegrants, sodium carboxy methyl cellulose demonstrated the shortest disintegration and wetting times while maintaining acceptable tablet hardness and friability. Polyethylene glycol exhibited poor friability performance, leading to tablet capping and breakage, and was therefore deemed unsuitable as a primary super-disintegrant. The optimized blank formulation contained 5% SCMC; however, incorporation of

diphenhydramine HCl necessitated increasing the SCMC concentration to 10% to counteract reduced water uptake caused by the drug.

Pre-compression flow property analysis of the optimized formulation revealed good to fair flow characteristics, as indicated by angle of repose, compressibility index, and Hausner's ratio. Post-compression evaluation confirmed compliance with pharmacopeial standards for weight variation, hardness, thickness, friability, disintegration time, and wetting time.

Stability studies demonstrated that the optimized ODT formulation remained stable at temperatures ranging from 3°C to 40°C and at relative humidity levels up to 33%. Tablets exposed to high humidity (75% RH) showed significant swelling and loss of hardness, indicating moisture sensitivity. Dissolution studies confirmed consistent drug release within USP-specified limits (90–110%) throughout the stability period, validating the robustness of the formulation.

5. CONCLUSION

An orally disintegrating tablet of diphenhydramine HCl was successfully formulated for pediatric and geriatric use sodium alginate was selected as the diluent for 110 mg tablets containing 0.25 mg diphenhydramine HCl. The DSC and FTIR spectra suggest diphenhydramine HCI becomes amorphous when combined with sodium alginate. The amorphous API lacks rigidity, but can be absorbed readily and has increased bioavailability sodium alginate, poly vinyl pyrrolidine, poly ethylene glycol, were used in addition to diphenhydramine HCI and the ideal super-disintegrant. Sodium carboxy methyl cellulose outperformed the other super disintegrants in nearly all the concentrations and all of the testing parameters. The ideal concentration was 5% sodium carboxy methyl cellulose for the orally disintegrating tablets before the API, diphenhydramine HCl was added. 10% sodium carboxy methyl cellulose was selected for the final formulation. The tablets remained stable and within the acceptable range of drug release (90%- 110%) at the three temperatures analyzed. The final formulation of diphenhydramine HCl tablets was stable between 3-40°C and at 33% relative humidity or less for eight weeks.

Future research can be done to effectively taste mask the bitter diphenhydramine HCI particles and create a suitable orally disintegrating tablet for pediatric and geriatric use. Additional testing can also be done to further confirm the notion that diphenhydramine HCI becomes amorphous when combined with sodium alginate.

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