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Formulation, Optimization and In-Vitro Evaluation of Drotaverine Hydrochloride Mini-Tablet.

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ABSTRACT

Oral route of drug administration is the most popular route to administer a drug and mini-tablets has the advantages such as ease of transportation, high-patient compliance, accurate dosing, ease of manufacturing. Drotaverine hydrochloride is used to treat spasm or twitches of the smooth muscles in stomach and heart also is used to relieve from pain caused due to irritable bowel syndrome, menstrual periods and headache. So, mini-tablets of drotaverine hydrochloride are formulated weighs 75 mg of a single mini-tablet from which 7.5 mg of API is used and excipients such as Gellan gum, Carbopol 940, PVP K30, Talc, Magnesium stearate and Lactose are used. All the pre and post compression parameters are done and the results are within the standard limits. In-vitro drug dissolution study is carried out from which formulation F5 showed a linear and maximum drug release so, are considered as optimized and further studied for stability studies for 0-3 Months under ICH guidelines of Accelerated Stability Studies (40^0 C ± 2^0 C and 75 % RH ± 5 % RH) and the parameters such as Thickness, Hardness, Drug content and % Drug release were studied. The results obtained were within the standard ranges. Further Long-Time stability studies and In-Vitro drug release studies were recommended for futuristic development and optimization of the formulation.

KEYWORDS: DROTAVERINE HYDROCHLORIDE, MINI-TABLET, ANTI-SPASMODIC, PAIN RELIEF.

INTRODUCTION

[1,2,3,4,5,6,7] The advancement in pharmaceutical technology, conventional pharmaceutical dosage forms is being replaced by new drug delivery systems. These systems are improvement over conventional dosage form. Mini-Tablet have many advantages such as Ease of transportation, High patient compliance, Accurate dosing, Ease of manufacturing and dosage forms of equal dimensions. Weight with smooth regular surface can be produced in a reproducible and continuous way. They do not require for any solvent for their production as a result problems with stability can be avoided, they also require less coating material and also there is a great flexibility in formulation development. [8,9,10,11,12,13] Drotaverine is an effective medicine to treat spasm or twitches of the smooth muscles in the stomach and heart. It is used to relieve pain caused due to irritable bowel syndrome, headache, menstrual periods, and is also used to relieve cervical spasm during labor. It is also effective in abdominal pain, chest pain, gallstones pain in the kidneys, pain in renal colic and a few other conditions. Drotaverine may interact with a few other drugs like atropine, diclofenac, levodopa and diazepam. The possible side-effects that may occur on using this medicine are nausea, vomiting, fainting, dry mouth, sleep disorders, constipation, flushing, allergic dermatitis, swelling of face, lips, eyelids, tongue, hands and feets, falling of blood pressure and change in pulse rate.

It comes as an oral medicine with or without food. The recommended dose for adults is usually 40-80 mg, three times a day but it can vary depending on your condition if taken orally as an antispasmodic by children between the age of 1 to 6, the recommended dose is 20 mg, 3 to 4 times daily. In children older than 6 years of age, the dosage is generally increased to 40 mg. [14,15,16,17,18,19,20] Drotaverine Hydrochloride is light yellow crystalline powder which id used to treat as an Antispasmodic agent. It is sparingly soluble in water (96 %) in ethanol, freely soluble in chloroform, slightly soluble in acetone, practically insoluble in petroleum ether. Its bioavailability following oral administration is approximately 91 % and its bioavailability is highly variable, following oral administration of a single 80 mg dose, the absolute bioavailability ranged between 24.5 and 91 % with a mean of 58.2 ± 18.2 %. Drotaverine inhibits phosphodiesterase's hydrolyzing cAMP, thereby increasing cAMP concentration, decreasing ca^+ uptake of the cells and changing the distribution of calcium among the cells. It may also have minor allosteric calcium channel blocking properties. Drotaverine is a selective inhibitor of phosphodiesterase 4 (PDE 4), which is an enzyme responsible for the degradation of cyclic adenosine monophosphate (cAMP) inhibition of PDE 4 leads to elevated levels of cAMP, leading to smooth muscle relaxation. Recent researchers showed that low levels of cAMP have been associated with brain tumorigenesis, leading to the investigation of PDE 4 inhibitors as potential anticancer agents. Drotaverine is mainly eliminated via hepatic metabolism. About 67 % of the drug is found in feces and 20 % of the drug was eliminated with urine. Following oral administration of a single 80 mg dose, the mean half-life was 9.11 ± 1.29 hours. Following, an intravenous dose of 80 mg, the mean half-life 9.33 ± 1.02 hours. In the formulation of Drotaverine Hydrochloride mini-tablet, drotaverine hydrochloride is used as an API (Active Pharmaceutical Ingredient), Gellan Gum is used as a thickener and binder, Carbopol 940 is used as a diluent, PVP K30 is used as binder, Talc is used as a glidant, Magnesium stearate is used as a lubricant, Lactose is used as a filler and binder. For overall study modern instruments such as digital weighing balance, hardness tester, tablet compression machine, vernier calliper, digital pH meter, friability test apparatus, FTIR spectrophotometer, disintegration apparatus, sonicator, tablet dissolution apparatus, UV-spectrophotometer are used. Total weight of a mini-tablet was 75 mg all the pre and post compressions were evaluated and are within their standard

ranges. For the in-vitro release of drug/formulation studies were performed in in-vitro dissolution apparatus of all the batches, i.e., F1-F9. The selected optimized batch of formulation were kept for stability studies, [26] accelerated stability studies as per the ICH guidelines were studied. The stability of the tablets was studied for the duration of 90 days at temperature of 40^0 C ± 2^0 C and 75 % RH ± 5 % RH. Then the tablets were evaluated for various parameters viz. thickness, hardness, weight variation and release studies.

MATERIALS AND METHODS

Drotaverine Hydrochloride was the gift sample of pure active pharmaceutical ingredient (API) by "Shree Swami Samarth pharmaceuticals (Allopathic division), Jalgaon", Gellan gum, Carbopol 940, PVP K30, Talc, Magnesium Stearate and Lactose were purchased from "S.D. Fine Chem. Ltd, Mumbai". All the chemicals used during the study were of Analytical Grade. Preformulation studies such as characterization of pure drug by Fourier transform infra-red spectroscopy (FTIR), differential scanning calorimetry (DSC) and determination of λ-Max by using UV Spectrophotometer were studied and other pre-formulation parameters such as Melting point, organoleptic properties of pure drug, solubility studies were studied and by using software Design Expert the batches of mini-tablets were optimized as given in the table below.

- **Design of Factorial Batches: -** All the batches i.e., F1-F9 were designed with the help of Design Expert software.

Table 1- Factorial Designed mini-tablet batches.

Ingredients (mg/tablet)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Drotaverine Hydrochloride	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Gellan Gum	15	30	45	15	30	45	15	30	45
Carbopol 940	4	4	4	8	8	8	12	12	12
PVP K30	8	8	8	8	8	8	8	8	8
Talc	1	1	1	1	1	1	1	1	1
Magnesium Stearate	1	1	1	1	1	1	1	1	1
Lactose	38.5	23.5	8.5	34.5	19.5	4.5	30.5	15.5	0.5
Total	75	75	75	75	75	75	75	75	75

- **Evaluation of Pre-Compression parameters of powder blend: -**

A. Bulk Density: - Accurately weighed 5 g of powder blends from each formulation which was previously passed through 20 # Mesh sieve, and then transferred in a 10 ml measuring cylinder. The powder in the cylinder was levelled without compacting, and unsettled apparent volume (Vo) was noted. The apparent bulk density (gm/ml) was calculated by the following formula (Bulk Density = weight of powder/ bulk volume).

B. Tapped Density: - Weighed 5 gm of powder blends from each formulation into a 10 ml measuring cylinder. Then the cylinder containing the sample was mechanically tapped by raising the cylinder and allowing it to drop under its own weight using mechanically tapped density tester that provides a fixed drop of 15 ± 2 mm at a nominal rate of 300 drops per minute. The cylinder was tapped 500 times initially and the tapped volume (V1) was measured to the nearest graduated units, the tapping was repeated an additional 750 times and the tapped volume (V2) was measured to the nearest graduated units. If the difference between two volumes is less than 2 % then the final volume (V2). The tapped bulk density in gm/ml was calculated by the following formula (Tapped Density= weight of powder/ tapped volume).

C. Compressibility Index: - The compressibility index of the powder blend was determined by Carr's compressibility index. It is a simple test to evaluate the BD and TD of a powder and the rate at which it is packed down. The formula for Carr's index is (CI = (tapped density – bulk density) × 100 tapped density).

D. Hausner's Ratio: - It indicates the flow properties of the granules and is measured by the ratio of tapped density to the bulk density (Hausner's Ratio = tapped density/ bulk density).

Table 2- Effect of Carr's index and Hausner's ratio on flow property.

Carr's Index (%)	Flow	Hausner's Ratio
5 - 11	Excellent	1.00 - 1.11
12 - 17	Good	1.12 - 1.18
18 - 22	Fair to Passable	1.19 - 1.25

23 - 32	Poor	1.26 - 1.34
33 - 39	Very Poor	1.35 - 1.45
40	Extremely Poor	1.46 -1.59

E. Angle of Repose: - The angle of repose of Drotaverine HCL powder was determined by the funnel method. The accurately weight of powder blend were taken in the funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of powder blend. The powder blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and the angle of repose was calculated using the following equation (Tan Θ = h/ r), where h and r are the height and radius of the powder cone respectively.

Table 3- Effect of Angle of Repose on flow property.

Angle of Repose (Θ)	Flow
< 25	Excellent
25 – 30	Good
30 – 40	Passable
> 40	Very Poor

- **Evaluation of Post-Compression parameters of Mini-Tablet: -** Tablets were evaluated for their thickness, weight uniformity, hardness, friability, disintegration time and dissolution profiles by using standard procedures.

A. Appearance: - The thickness of tablet as a dimensional variable was evaluated. The tablet thickness was controlled within the average value. The colour, odour and any other flaws like chips, cracks, surface texture, etc. are other important of morphological characteristics were observed.

B. Thickness and Diameter: - Thickness of the tablet is important for uniformity of tablet size. The thickness and diameter of mini-tablets were measured with the help of vernier calliper. It was determined by checking the thickness of ten tablets of each formulation. The average diameter and thickness of the tablet was calculated. The test passed if none of the individual diameter and thickness value deviated by ± 5 % of the average.

C. Weight Variation Test: - For the tablet weighing 40 mg or more, the weight of the tablet being made was routinely determined to ensure that a tablet contains the proper amount of drug. The USP weight variation test is done by weighing 20 tablets individually, calculating the average weight and comparing the individual weights to the average. The tablets et the USP specification that not more than 2 tablets are outside the percentage limits and no tablet differs by more than 2 times the percentage limit. The tablets were weighed individually and the weight variation was determined.

D. Hardness Test: - Tablet hardness is defined as force required to shipping or breakage under conditions of storage, transportation and handling before usage depends on its hardness and crushing the tablet in diametric compression test. The hardness was measured with Erwika Hardness tester. The hardness was measured in terms of kg/cm^2. 4 tablets were chosen randomly and tested for hardness. The tablets were placed diametrically between two plungers and the lower plunger is kept in contact of tablet to read as zero. The upper plunger is forced against a spring by turning the screw until tablet fracture.

E. Friability Test: - Friability generally refers to loss in weight of tablets in the containers. Due to removal of fines from the tablet surface. 20 tablets were weighed and subjected to friability test in Roche Friabilator. The pre-weighed sample was placed in Friabilator which revolves at 25 rpm for 4 minutes dropping the tablets through a distance of 8 inch with each revolution. This process was repeated for all formulations and the percentage friability was calculated (% Loss = initial wt. of tablets – final wt. of tablets / initial wt. of tablets × 100) where, w1 = initial weight of tablet, w2 = weight of tablet after rotation.

F. Disintegration Time: - Disintegration test was performed for tablets in 0.1 N HCL at 37^0 C by using USP disintegration apparatus. Triplicate readings were taken and average was computed.

G. Drug content uniformity: - The tablets were tested for their drug content uniformity randomly selected 4 tablets were weighed and powdered. The powder equivalent to 30 mg of Drotaverine HCL was weighed accurately and dissolved in 100 ml of 0.1 N HCL in water. The solution was shaken thoroughly the in-dissolved matter was removed by filtration through Whatman no.41 filter paper. Then the serial dilutions were carried out. The absorbance of the diluted solutions was measured at 234 nm. The concentration of Drotaverine HCL was determined by using UV.

- **In-Vitro Dissolution profile of formulation batches: -** Mini-Tablets were subjected to in-vitro drug release studies in simulated gastric and intestinal fluids to assess their ability in providing the desired controlled drug delivery. Drug release studies were carried out using USP dissolution test apparatus – II at 100 rpm, 37 ± 0.5^0 C, and 0.1 N HCL (900 ml) for 2 hours, since the average gastric emptying time is about 2 hours. The dissolution medium was replaced with 0.1 N HCL (900 ml) and experiment continued for another 10 hours at different time

intervals, 1 ml of the samples were withdrawn and replaced with 1 ml of dissolution medium. The samples withdrawn were analyzed by UV Spectrophotometer using multi-component mode of analysis at 234 nm and 276 nm wave length.

- **Stability Studies: -** on the basis of in-vitro evaluation of all the formulation batches for the various parameters, formulations were packed in thick aluminium foil and stored in stability chambers (Thermo lab) for the accelerated stability studies. The tablets were stored in the stability chamber at the controlled conditions of temperature and relative humidity. The stability of the tablets was studied for the duration of 90 days at temperature 40^0 C ± 2^0 C and 75 % RH ± 5 % RH. The tablets were then evaluated for various parameters viz. thickness, hardness, weight variation and release studies.

RESULTS AND DISCUSSION

A. Determination of Melting point: - The Melting point of Drotaverine Hydrochloride API was determined by Capillary tube method and the melting point was found within the standard range of 206 – 209^0 C and when compared with the official standards it was within its standard range.

B. Standard calibration curves of Drotaverine Hydrochloride (Pure Drug): -

I. Calibration curve of Drotaverine Hydrochloride in 0.1 N HCL: - The standard solution of Drotaverine Hydrochloride showed linear curve with correlation coefficient of 0.993. the UV Spectrophotometric method was selected for estimation of Drotaverine. The UV spectrum exhibited maximum absorbance (λ-Max) at 234 nm. The standard calibration curve exhibited good coefficient of correlation.

Table 4- Standard calibration curve of Drotaverine HCL in 0.1 N HCL

Sr. No	Concentration (µg/ ml)	Absorbance (at 234 nm)
1	0	0.0
2	2	0.047
3	4	0.129
4	6	0.190
5	8	0.259
6	10	0.350

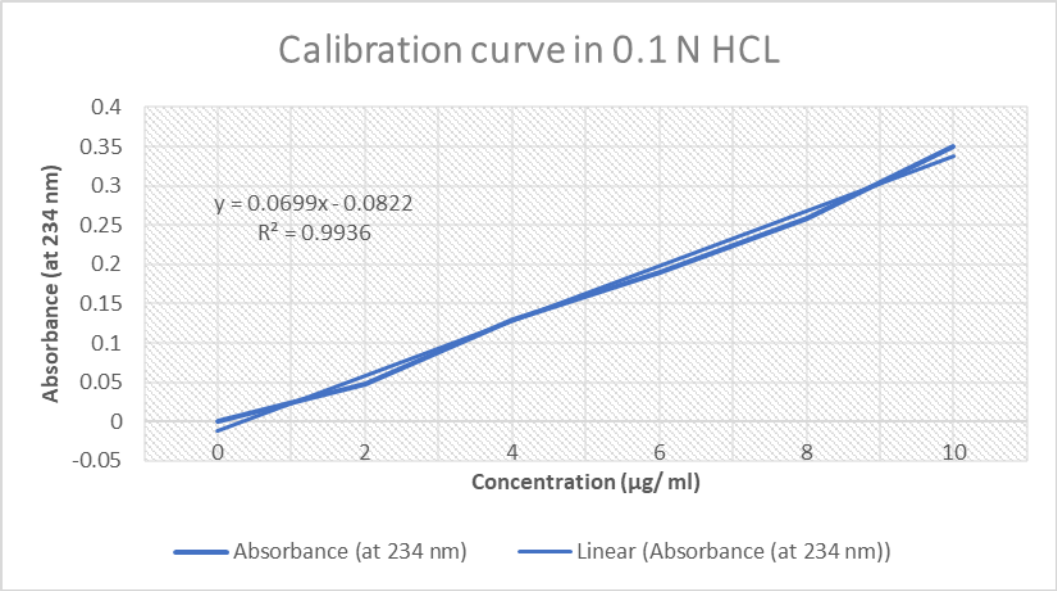

Fig 1- Standard calibration curve of Drotaverine HCL in 0.1 N HCL

II. Calibration curve of Drotaverine Hydrochloride in 6.8 Phosphate buffer: - The standard solution of Drotaverine Hydrochloride showed linear curve with correlation coefficient of 0.957. the UV Spectrophotometric method was selected for estimation of Drotaverine. The UV spectrum exhibited maximum absorbance (λ-Max) at 234 nm. The standard calibration curve exhibited good coefficient of correlation.

Table 5: - Standard calibration curve of Drotaverine HCL in 6.8 Phosphate buffer

Sr. No	Concentration (µg/ ml)	Absorbance (at 234 nm)
1	0	0.0

2	2	0.021
3	4	0.038
4	6	0.065
5	8	0.106
6	10	0.155

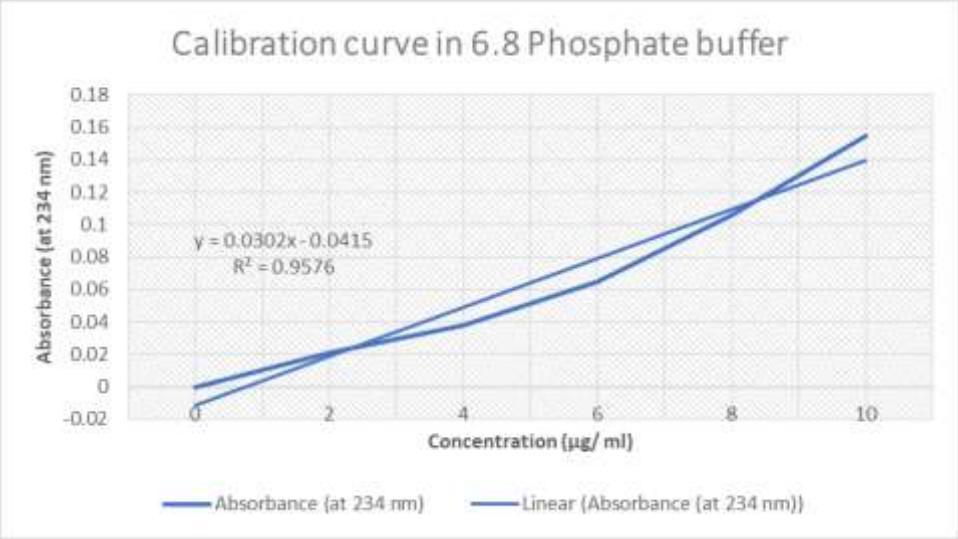

Fig 2- Standard calibration curve of Drotaverine HCL in 6.8 Phosphate buffer

C. FTIR Studies: -

1) FTIR of Drotaverine Hydrochloride (Pure Drug): -

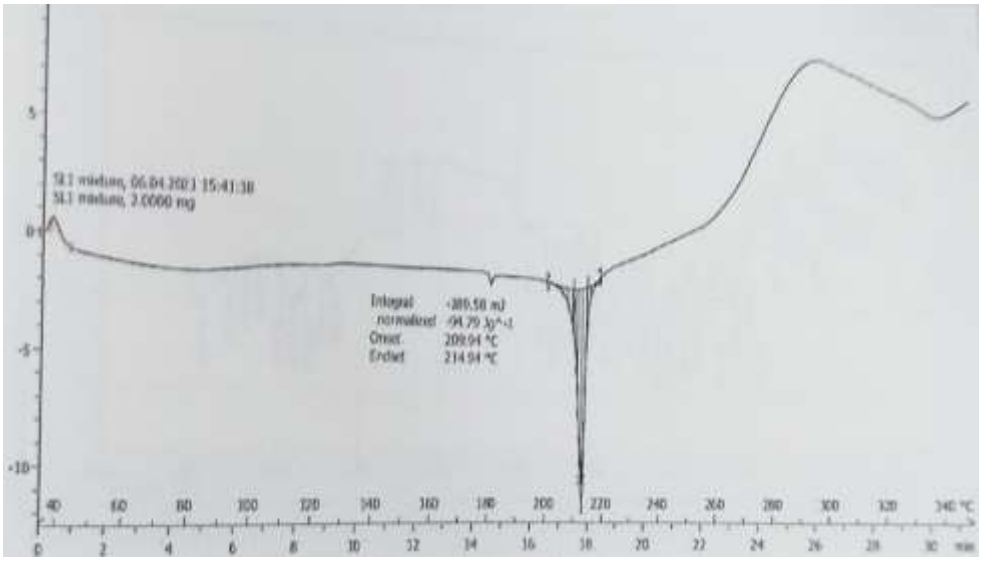

Fig 3- FTIR analysis of Drotaverine Hydrochloride (Pure Drug)

Table 6- Interpretation of FTIR of Drotaverine Hydrochloride (Pure Drug)

Functional Group	Characteristic Peaks cm^{-1}
C=O Carboxylic acid stretching	1647.26 cm^{-1}
C=N Aromatic stretching	1506.46 cm^{-1}
C-H Aromatic stretching	3279.10 cm^{-1}
C=C Aliphatic stretching	1425.44 cm^{-1}

2) FTIR of Drotaverine Hydrochloride with Gellan Gum: -

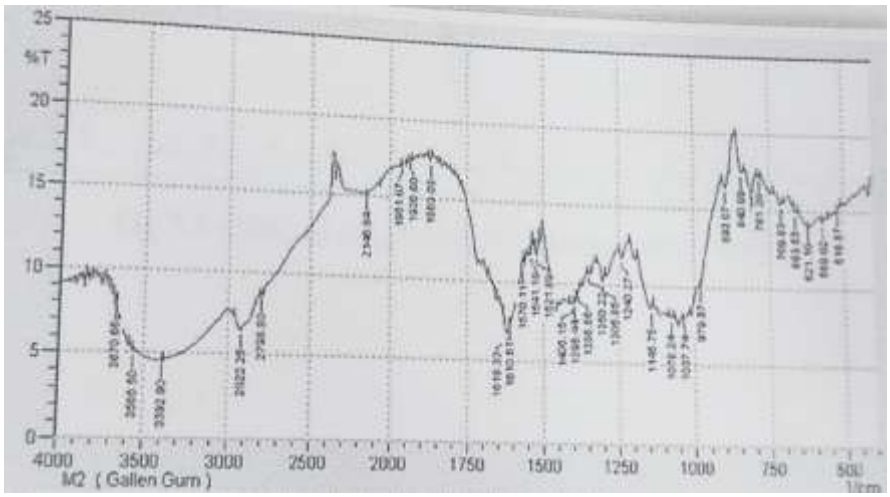

Fig 4- FTIR analysis of Drotaverine Hydrochloride with Gellan gum

3) FTIR of Formulation Blend: -

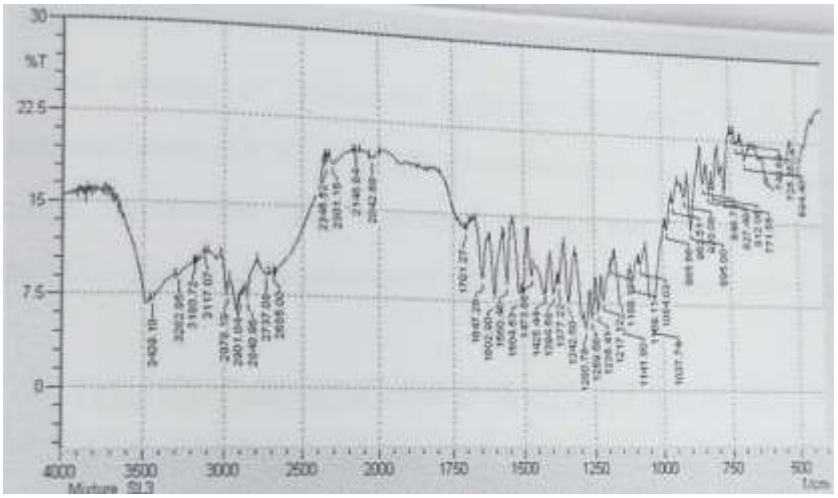

Fig 5- FTIR analysis of Formulation Blend

D. DSC Studies –

I. DSC graph of Drotaverine Hydrochloride (Pure Drug): -

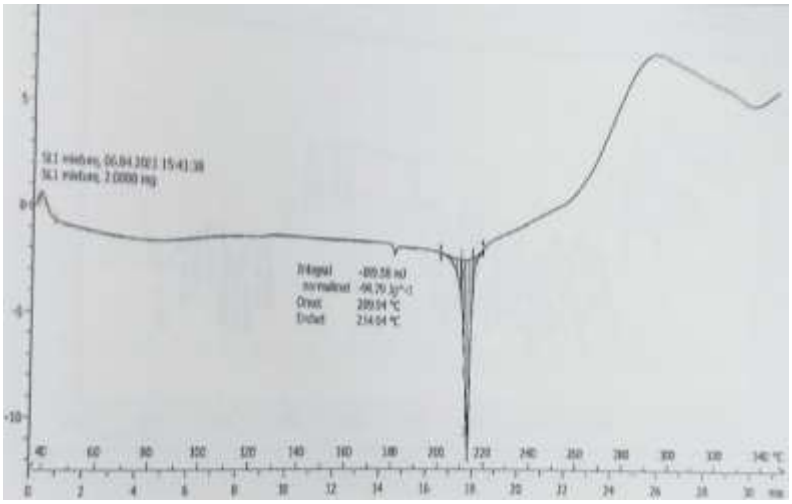

Fig 6- DSC graph of Drotaverine Hydrochloride (Pure Drug)

II. DSC graph of Drug-Excipients compatibility analysis: -

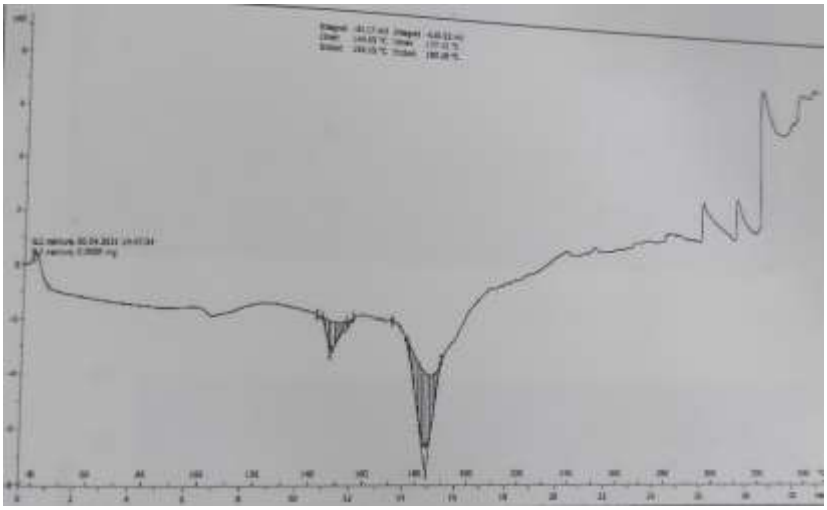

Fig 7- DSC graph of Drug-Excipients compatibility analysis

E. Derived powder properties for Drotaverine Hydrochloride (Pure Drug): -

Table 7- Derived powder properties for Drotaverine Hydrochloride (Pure Drug)

Drug	Angle of Repose	Bulk Density (gm/ cm^2)	Tapped Density (gm/ cm^2)	Carr's Index (%)	Hausner's Ratio
Drotaverine Hydrochloride (Pure Drug)	28.35	0.48	0.61	16.42	1.16

F. Pre-Compression parameters of powder blend: -

Table 8- Pre-Compression parameters of powder blend

Formulation Batches	Bulk Density (gm/ ml)	Tapped Density (gm/ ml)	Carr's Index	Hausner's Ratio	Angle of Repose
F1	0.45 ± 0.013	0.51 ± 0.027	11.76 ± 0.75	1.13 ± 0.058	26^0. 12 ± 0.22
F2	0.50 ± 0.009	0.58 ± 0.025	13.79 ± 0.60	1.16 ± 0.036	27^0. 18 ± 0.49
F3	0.46 ± 0.010	0.53 ± 0.022	13.20 ± 0.38	1.15 ± 0.044	28^0. 34 ± 0.76
F4	0.46 ± 0.010	0.58 ± 0.029	13.59 ± 0.49	1.16 ± 0.012	27^0. 21 ± 0.30
F5	0.48 ± 0.015	0.55 ± 0.034	12.72 ± 0.45	1.14 ± 0.039	26^0. 19 ± 0.88
F6	0.49 ± 0.013	0.56 ± 0.027	12.50 ± 0.30	1.14 ± 0.078	25^0. 22 ± 0.17
F7	0.46 ± 0.019	0.52 ± 0.056	11.53 ± 0.66	1.13 ± 0.080	28^0. 55 ± 0.20
F8	0.51 ± 0.022	0.59 ± 0.017	13.55 ± 0.42	1.15 ± 0.036	29^0. 21 ± 0.20
F9	0.50 ± 0.010	0.53 ± 0.026	13.79 ± 0.18	1.12 ± 0.028	25^0. 41 ± 0.38

G. Post-Compression parameters of formulation batches of Mini-Tablets: -

Table 9- Post-Compression parameters of formulation batches of Mini-Tablets

Formulation Batches	Thickness (mm) (±SD)	Hardness (kg/ cm^2) (±SD)	Friability (%) (±SD)	Weight Variation (mg) (±SD)	Disintegration Time (Sec)	Drug Content (mg) (±SD)
F1	1.87 ± 0.12	3.65 ± 0.319	0.32	76.51 ± 1.78	127	87.43 ± 3.07
F2	2.51 ± 0.059	3.30 ± 0.264	0.60	74.06 ± 0.89	144	94.23 ± 0.65
F3	2.47 ± 0.038	3.30 ± 0.211	0.45	74.61 ± 1.40	162	93.89 ± 0.57

F4	1.98 ± 0.13	3.25 ± 0.078	0.66	73.36 ± 1.14	186	91.53 ± 0.58
F5	2.62 ± 0.021	3.70 ± 0.337	0.62	75.02 ± 0.83	206	97.35 ± 0.89
F6	1.95 ± 0.20	3.10 ± 0.257	0.75	74.16 ± 1.49	220	90.43 ± 3.86
F7	2.37 ± 0.027	4.10 ± 0.564	0.47	73.06 ± 2.07	234	95.35 ± 0.69
F8	2.46 ± 0.054	1.40 ± 0.580	0.59	73.08 ± 1.64	248	88.55 ± 2.94
F9	2.49 ± 0.076	4.20 ± 0.273	0.49	74.08 ± 0.85	278	90.76 ± 3.78

The Pre and Post Compression parameters such as bulk density, tapped density, carr's index, hausner's ratio, angle of repose, thickness, hardness, friability, weight variation disintegration time, drug content was found within all the standard limits. So, the in-vitro dissolution studies were performed by using a USP-Dissolution test apparatus, in that all the designed formulations from (F1-F9) was studied in 0.1N HCL. Each of the tablet of all the formulations contain 7.5 mg of Drotaverine Hydrochloride, Gellan Gum and spray dried Lactose as Direct Compressible vehicle.

The percentage of drug release was found to be in the range of 87.62 % to 99.72 % and 90.68 % to 91.44 % respectively. The results show that is increased rate of release of drug gradually decreases. They rank in the following order F1 to F9. Also, the in-vitro release data was subjected to goodness of fit-test by linear regression analysis according to zero order, first order kinetic equations, Higuchi equation, korsmeyer-peppas and Hixson-crowell models to ascertain the mechanism of drug release. The result of linear regression analysis of data including regression coefficient and the study was showed that mini-tablet of Drotaverine Hydrochloride follows the korsmeyer-peppas release order kinetic. The formulation F5 was the best formulation by using Gellan Gum and Carbopol 940 and it follows zero order kinetics.

Table 10- In-Vitro drug release of Drotaverine Hydrochloride of formulation of Mini-Tablet

Time (Hrs.)	% Drug Release (% CDR)								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	8.30	6.25	9.52	8.77	10.9	6.20	6.30	9.30	12.6
2	16.3	21.3	19.5	16.5	15.2	12.1	9.50	11.3	16.5
3	21.6	24.9	22.5	19.5	18.8	14.4	21.7	18.7	31.4
4	25	29.1	27	23.4	23.3	18.5	28.1	29.7	38
5	33.2	34	32.5	28	29	23.8	36	41	44.3
6	40.3	40.2	37.8	34.2	35.7	30	47.1	53	48.3
7	48.8	46.2	44.7	41.7	43.6	37.2	55.3	56.4	52.9
8	56.6	54.3	52.3	50	52.6	45.8	61.7	60	58.6
9	66.4	63.6	60	60.4	62.7	55.4	70	65.4	65.9
10	71.5	72.7	71.2	71.7	74	66	77.2	71.1	73.8
11	79.5	84.2	80	81.7	86.2	77.2	86.2	77.2	83.2
12	87.6	95.2	92.7	94.7	97.7	90	95.2	93	91.6

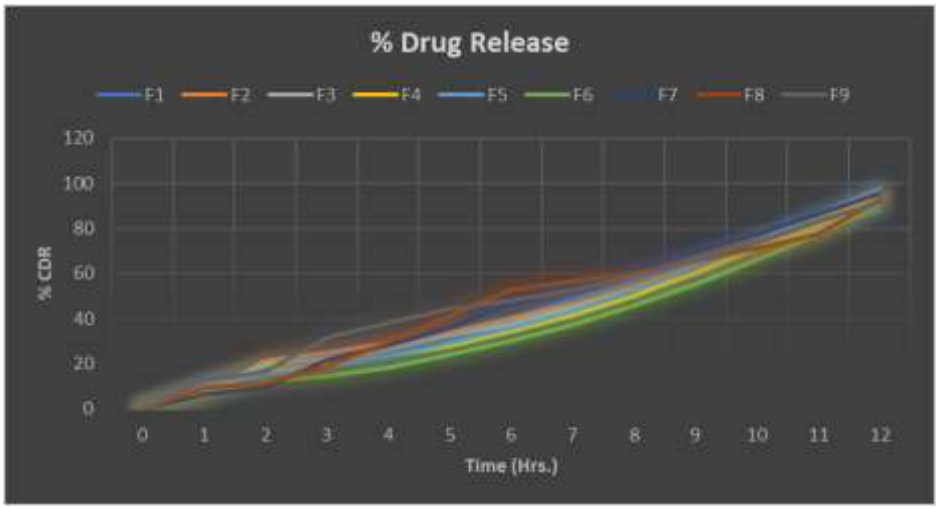

Figure 8- In-Vitro % Drug release of Drotaverine Hydrochloride Mini-Tablets

H. Kinetics of Drug release: -

The results showed that the factorial designed batches followed zero-order models. The rate of drug release from the mini-tablet is rapidly initially followed by progressively slow drug release through the tablet. The slow release of the drug from they may be due to the formulation of Gellan gum and Carbopol 940.

Table 11- Drug release kinetics of the optimized batch

Batch code	R^2			
	Zero order	First order	Peppas	Hixson crowell
F5	0.9848	0.9690	0.9166	0.9814

The optimized batch F5 was selected for further Stability Studies.

I. Stability Studies: -

The Stability of the tablets was studied for the duration of 3 Months at temperature 40^0 C ± 2^0C and 75 % RH ± 5 % RH. The tablets were then evaluated for various parameters viz. thickness, hardness and drug content and release studies.

Table 12- Stability Studies

Sr. No	Parameters	0- Month	After 3 Months
1	Drug Release	97.72 %	96.26 %

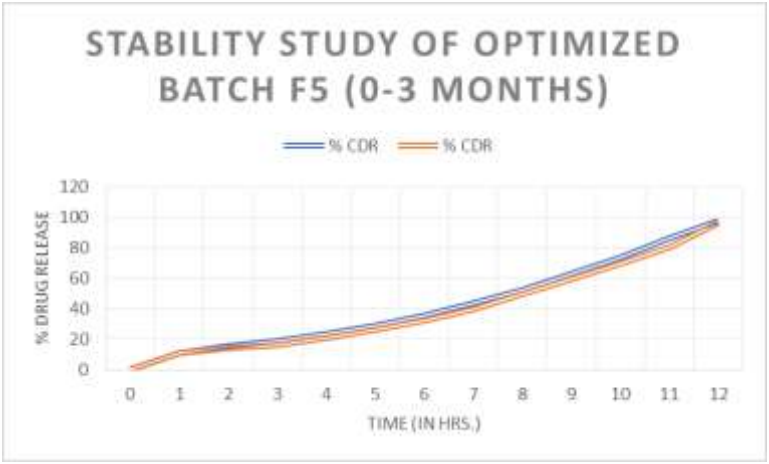

Figure 9- Stability Studies (0-3 Months)

CONCLUSION

The main aim of the study was to formulate, optimize and in-vitro evaluate mini-tablets of Drotaverine Hydrochloride, the tablets were formulated by using direct compression technique. Ingredients such as Drotaverine Hydrochloride as API, Gallen Gum, Carbopol 940, PVP K30, Talc, Magnesium Stearate and Lactose were used.

Pre-compression parameters such as Bulk Density, Tapped Density, Compressibility Index, Hausner's Ratio, Angle of Repose, Post-compression parameters such as Appearance, Thickness and Diameter, Weight variation, Hardness, Friability test, Disintegration time, Drug content uniformity and In-Vitro Dissolution study were performed. From that Formulation F5 showed satisfactory results in release of drug in a linear form, and so from F1-F9 formulation F5 was selected as an optimized formulation. The FTIR and DSC studies also were near the standard references when compared to them. So, formulation F5 were studied for stability studies for 0-3 Months' time period as per ICH guidelines for stability studies (for Accelerated stability study on 40^0 C ± 2^0 C and 75 % RH ± 5 % RH) and the studies also showed satisfactory results/ did not seen much variation or change in any parameters throughout the study period. Best formulation batch i.e., F5 found to be stable. But, Long-Term Stability studies and In-Vivo studies are recommended for futuristic scope of the formulation.

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CONFLICTS OF INTEREST

The Author declares "No Conflict of Interest".

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ABBREVIATIONS

- Hrs/ h- Hours
- SD- Standard Deviation
- GM- Gellan Gum
- PVP- Polyvinyl Pyrrolidone
- µg- Microgram
- IP- Indian Pharmacopoeia
- USP- United States Pharmacopoeia
- ^{0}C- Degree Celsius
- nm- Nanometre
- RH- Relative Humidity
- Min- Minutes
- mm- Millimetre
- PDE- Phosphodiesterase
- Ɵ- Angle of Repose
- mg- Milligram
- DSC- Differential Scanning Calorimetry
- FTIR- Fourier-Transform Infrared Spectroscopy
- ICH- International Council on Harmonization (Previously-International Conference on Harmonization)
- IR- Infrared
- %- Percentage
- GIT- Gastro-Intestinal Tract