FORMULATION AND EVALUATION OF SUSTAINED RELEASE TABLET OF DICYCLOMINE HYDROCHLORIDE

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ABSTRACT

The goal of the present study was to Formulate and evaluate Sustained Release tablet of Dicyclomine Hydrochloride to reduce the dosing frequency to twice daily, thereby increasing patient's compliance and therapeutic efficacy. Sustained release system achieves slow release of drug over prolonged period of time. This system retards the release of therapeutic agent such that its appearance in the circulation is delayed or prolonged and its plasma profile is sustained in duration. Sustained release formulation maintains a uniform blood level of drug with better patient compliance as well as increased efficacy of drug. The Sustained Release Tablets (F1-F9) were prepared by direct compression method and formulated using different concentration of polymers. Combination of polymer, Guar Gum, Xanthan gum, Hydroxyl Propyl Methyl Cellulose (HPMC K15M). FT-IR spectroscopy was done to study the compatibility of the drug with various excipients used in formulation. Formulations were subjected for pre-compression and post compression evaluation. The IR study revealed that there was no chemical interaction between drug and excipients. The tablets were prepared by direct compression method. Pre-compressional parameters i.e. angle of repose, carr's index, bulk density, tapped density and Hauser's ratios were studied. These results indicate that powder mixture had good flow characteristics. After evaluation of physical properties like Weight variation, Hardness, Thickness, Friability of tablet, the different formulations were checked for the percentage Drug content, which showed good uniformity. The compressed tablets were evaluated for post compression parameters and showed compliance with pharmacopoeial limits. Dicyclomine HCl is an antispasmodic and anticholinergic which is used for relief colicky pain caused by intestinal muscle spasm in functional bowel /irritable bowel syndrome (IBS). The objective is to formulate and evaluate the Sustained Release tablets of Dicyclomine HCl containing 30 mg.

In- vitro drug release was performed with USP dissolution apparatus type-II (paddle type) using with 6.8 pH phosphate buffer by temperature maintaining at Room Temperature. Based on results among all formulations, F4 formulation containing drug and xanthan gum in ratio of 1:2 showed maximum drug release of 98.108 %. Thus, drug formulation of F4 has enhanced drug release profile.

Keywords: Sustained Release Tablet, Direct Compression Method, Guar gum, Xanthan gum, HPMC K15M, Dicyclomine Hydrochloride.

INTRODUCTION

For many decades treatment of an acute disease or a chronic illness has been mostly accomplished by delivery of drugs to patients using various pharmaceutical dosage forms, including tablets, capsules, pills, suppositories, creams, ointments, liquids, aerosols, and injectables, as drug carriers. This type of drug delivery system is known to provide a prompt release of drug or immediate release product. Such immediate release products result in relatively rapid drug absorption and onset of accompanying pharmacodynamic effects. However, after absorption of drug from the dosage form is complete, plasma drug concentrations decline according to the drug's pharmacokinetics profile. Eventually, plasma drug concentrations fall below the minimum effective plasma concentration (MEC), resulting in loss of therapeutic activity. Before this point is reached another dose is usually given if a sustained therapeutic effect is desired. An alternative to administering another dose is to use a dosage form that will provide sustained drug release, and therefore, maintain plasma drug concentrations, beyond what is typically seen using immediate release dosage forms.[1]

Sustained release tablet is designed to reduce frequency of dosing by modifying the rate of drug absorption. Sustained release tablets are commonly taken only once or twice daily, compared with conventional forms have to be taken three or four times daily to achieve the same therapeutic effects. Sustained release system achieves slow release of drug over prolonged period of time. This system retards the release of therapeutic agent such that its appearance in the circulation is delayed or prolonged and its plasma profile is sustained in duration. Sustained release formulation maintains a uniform blood level of drug with better patient compliance as well as increased efficacy of drug.[2]

Dicyclomine hydrochloride is an anticholinergic agent having direct smooth muscle relaxant action, and in addition to being a weak anticholinergic, it exerts antispasmodic action. Its plasma half-life elimination 4-6 hrs. It is commonly used for the treatment of irritable bowel syndrome. It is rapidly absorbed after oral administration with peak plasma concentration occurring in 60-90 minutes. Conventional therapy of Dicyclomine hydrochloride requires multiple daily administrations (3-4 times daily).[3,33]

Advantages-[3-7]

- The Bioavailability of drugs should be improved.
- The ability to provide special effects can be improved.
- The fabricate in a wide range of shapes and sizes is very easy.
- Acceptable for the both non-degradable and degradable systems.
- No Dose Dumping.
- Patient Compliance can be upgrade.
- Reduce variation in steady-state drug level.
- The manufacturing process is easy.
- It can release high molecular weight compounds.
- It can maintain therapeutic concentration for an extended period of time.
- High blood concentration can be avoided by the use of a sustained-release dosage form.
- By slow drug absorption, the ill effects can be reduced.
- It is used to increase stability.
- Local and systemic side effects can be minimized.
- Small amount of drugs can be used.

Disadvantages [3-7]

- These dosage forms are designed on the basis of average biological half-life.
- They are costly.
- It does not permit prompt termination of therapy.
- Flexibility in dose adjustment is less.

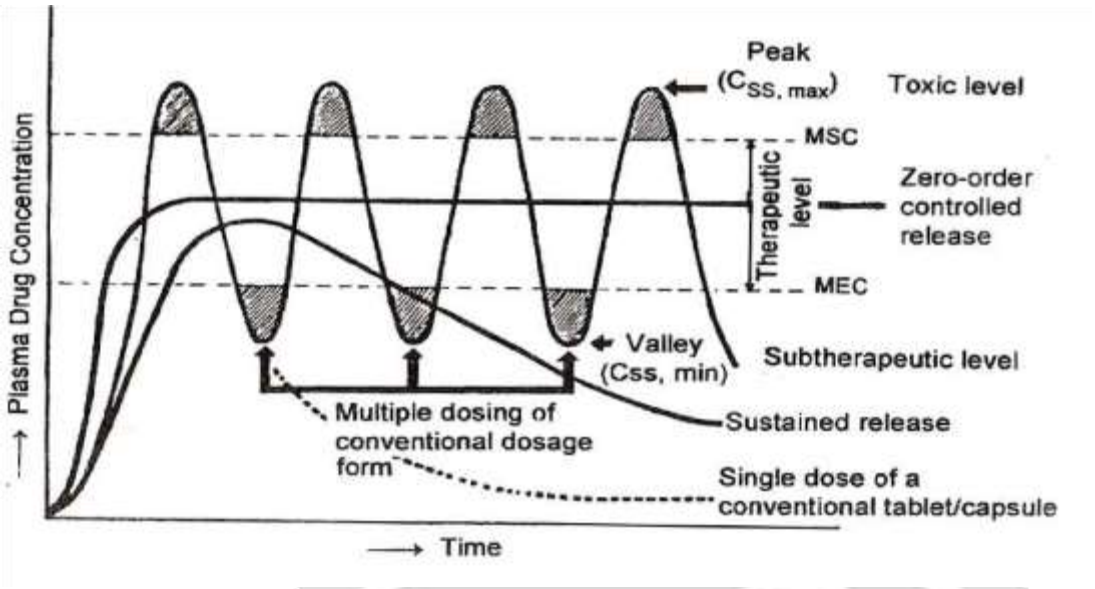


Fig. -1: A hypothetical plasma concentration – time profile from conventional multiple dosing and single doses of sustained and controlled delivery formulations.

CONVENTIONAL TECHNIQUES FOR PREPARATION OF SUSTAINED RELEASE TABLETS: [21-24]

Sustained Release Tablets can be prepared by the following methods:

1) Tablet molding
2) Direct compression
3) Spray drying
4) Sublimation
5) Freeze drying (or) Lyophilization
6) Mass extrusion
7) Taste masking
8) Use of sugar based excipients

1) Tablet Molding:

Moulded tablets are usually prepared by different molding techniques.

A. Compression molding: The powder mixture previously moistened with a solvent like ethanol/water is compressed into mould plates to form a wetted mass.

B. Heat molding: The moulded forms can be obtained directly from a molten matrix in which the drug is dispersed / dissolved.

C. No vacuum Lyophilization: In this process at standard pressure the solvent from a drug solution or suspension is evaporated. Tablets produced by molding are solid dispersion. Moulded tablets disintegrate more rapidly and offer improved taste because the dispersion matrix is in general made from water soluble sugars. The active ingredients in most cases are absorbed through the mucosal lining of the mouth. The tablets prepared by moulding offer more rapid disintegration and improved taste as the dispersion matrix is made from water soluble excipients (sugar) Moulded tablets

typically do not possess great mechanical strength. Erosion and breakage of the moulded tablet often occur during handling and opening of blister packs.

2) Direct Compression:

It is the easiest way to manufacture tablets with low cost, conventional Equipments, commonly available excipients and a limited number of processing steps leading to this technique is preferable one. High doses can be accommodated and final weight of tablet can easily exceed that of other production methods. The disintegration and dissolution of directly compressed tablets depend on single or combined effect of disintegrate, Water soluble excipients and effervescing agents. The optimum concentration of super disintegrant can be selected according to critical concentration of the disintegrate. Below this concentration the tablet disintegration time is inversely proportional to the concentration of superdisintegrants whereas if concentration of superdisintegrant incorporated in tablet is above the critical concentration, the disintegration time remains approximately constant or even increases.

3) Spray Drying:

Spray drying technique produces highly porous and fine powders as the processing solvent is evaporated during the process. This technique is based upon a particulate support matrix that is prepared by spray drying an aqueous composition containing support matrix and other components to form a highly porous and fine powder. This is then mixed with active ingredient and compressed into tablet, which disintegrated in less than 20 seconds when immersed in an aqueous medium.

4) Freeze Drying / Lyophilization: A process in which water is sublimated from the product after freezing is called Freeze drying. Lyophilization results in preparations which are highly porous with a very high specific surface area, which dissolve rapidly and show improved absorption and bioavailability. The use of Freeze drying is limited due to high cost of the equipment and processing. Other major disadvantages of the final dosage forms include lack of physical resistance in standard blister packs.

5) Mass Extrusion: This technology involves softening the active blend using the solvent mixture of water soluble polyethylene glycol, using methanol and expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets. The dried cylinder can also be used to coat granules of bitter tasting drugs and thereby masking their bitter taste.

6) Taste Masking: Taste masking is an essential requirement for Sustained Release Tablets for commercial success. Drugs with unacceptable bitter taste can be microencapsulated into pH sensitive acrylic polymers like Eudragit E, Eudragit L-55 and Eudragit RL.

7) Use of Sugar Based Excipients: Sugar based excipients (e.g. Sorbitol, manitol, dextrose, xylitol, fructose etc.) have been used as bulk agents. Aqueous solubility and sweetness impart pleasing mouth feel and good taste masking. But no sugar based materials have fast dissolution rate and good compressibility and/or compatibility. However technologies are developed to make use of the sugar based excipients in the design of Sustained Release Tablet.[5]

Factors In The Designing Of Sustained-Release Drug Delivery Systems [17-18,29,32]

1. **Biopharmaceutics characteristics of the drug in the design of SRDDS**

- **Molecular size and diffusivity**

The diffusion coefficient of intermediate molecular weight medicine is 100-400 Daltons; through the flexible polymer, the range is 10-6-10-9 cm^2/ sec. For medicines having molecular weight> 500 Daltons, the prolixity measure in numerous polymers is truly lower i.e. lesser than 10-12 cm^2/ sec. samples of medicines that are tough to control the release rate of cure from dosage form are proteins and peptides. Diffusivity depends on the size & shape of the concavities of the membrane.

- **Partition coefficient (P (o/w)**

Composites with a fairly high partition measure are generally lipid-answerable and, accordingly, have veritably low hydrated solubility. Likewise, these compounds can generally persist in the body for long period of time, because they can localize in the lipid membranes of cells. Meaning that the solubility of the medicine may change several orders of magnitude during its releases. The solubility of medicine with the lower limit to be formulated in a sustained release system and it has been reported to be 0.1 mg/ ml.

- **Ionization Drug and pKa at physiological pH**

Medicines subsisting largely in the ionized form are poor aspirants for oral Sustained release medicine delivery systems. Absorption of the unionized medicines is well whereas permeation of ionized medicines is negligible because the unionized medicine is 3-4 times further than the absorption rate of the ionized remedy. The pKa variety for an acidic medicine whose ionization is pH sensitive is about 3.0 -7.5 and the pKa range for an initial medicine whose ionization is pH sensitive is around7.0-11.0 is ideal for optimum positive absorption. The drug shall be unionized at the point to an extent of 0.1-5.0.

- **Drug stability**

Medicines have both acid and base hydrolysis and enzymatic degradation when administered oral route.However, for the medicines that are unstable in the stomach that prolong delivery to the entire GI tract are cost-effective, If the medicine is in a solid state the declination will occur at a reduced rate. If the medicine is administered in an extended- release dosage form that's unstable in the small intestine may demonstrate reduced bioavailability. This occurs due to the fact that a lesser volume of medicine is delivered in the small intestine and is being subordinated to further declination.

- **Aqueous Solubility**

Medicines with low water solubility will be tough to incorporate into sustained release mechanisms. A medicine with high solubility and rapid-fire dissolution rate is frequently relatively delicate to brake its dissolution rate. A medicine of high water

solubility can be dissolved in water or gastrointestinal fluid readily and tends to release its dosage form in a burst and therefore is absorbed fast leading to a sharp increase in the blood medicine attention compared to a lower soluble remedy. It's difficult to include a largely water-soluble medicine in the dosage form and brake the medicine release especially when the cure is high. The pH-dependent solubility in the physiological pH range would be another problem for Sustained release formulation because of the variation in the pH throughout the gastrointestinal tract and variation in the dissolution rate. The biopharmaceutical classification system (BCS) allows estimation of the likely contribution of three major factors solubility, dissolution, and intestinal permeability which affect oral absorption. Class III (High solubility-Low permeability) & Class IV (Low solubility-Low permeability) medicines are poor campaigners for Sustained release dosage form compounds with solubility. The maximum of the medicines are weak acids or weak bases.

2. Pharmacokinetic characteristics of the drug in the design of the Sustained Release Tablet

- **Absorption rate**

The absorption rate constant is an apparent rate constant, and it should be the release rate constant of the medicine from the dosage form. Sustained-release medications may be critical to absorption because if the medicine is absorbed by active transport is limited to a specific region of the intestine.

- **Rate of metabolism**

Medicines that are significantly metabolized before absorption, either in the lumen or tissue of the intestine, bioavailability from slower-releasing dosage forms can show reduced. Utmost intestinal wall enzyme systems are saturated. As the

medicine is released at a slower rate to this regions, the total medicine presented to the enzymatic process during a specific period is less and allows more complete alteration of the remedy to its metabolite.

- **Elimination half-life of SRDDS**

A sustained relaese dosage form is the one from which the rate of medicine absorption is equal to the rate of elimination. The lower the $t_{1/2}$, the larger the quantity of medicine to be incorporated in the dosage form. Medicines with a half-life in the range of 2 to 4 hours make a good aspirant for this system.g propranolol.

3. Pharmacodynamic characteristics of the drug in the design of SRDDS

- **Dose of drug**

The most dose strength for SRDDS is 1gm.

- **Therapeutic index**

In Sustained release formulations, Medicines with a low therapeutic index are unsuitable. However, dose dumping may occur, which leads to the toxin, If the system fails in the body.

- **Therapeutic range**

SRDDS formulation should have a wide therapeutic range.

- **Plasma concentration-response relationship**

The plasma drug concentration is more responsible for pharmacological exercise rather than dose. But the medicine has a pharmacological exertion that's independent of plasma concentrations is a poor aspirant for oral SR drug delivery system.

Ideal properties of drug suitable for SRDDS.

MATERIALS AND METHODS

Dicyclomine HCl drug got from Balaji Drugs, Gujrat. Polymer such as HPMC K15M, Xanthan gum, Guar gum and Microcrystalline cellulose from Karnataka fine chem, Karnataka.

Table No. -4: Formulation for Sustained Release Tablets of Dicyclomine HCl

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Dicyclomine HCl (Equivalent to Dicyclomine 30 mg)	33.5	33.5	33.5	33.5	33.5	33.5	33.5	33.5	33.5
Guar Gum	60	90	120						
Xanthan Gum				60	90	120			
HPMC K15M							60	90	120
Microcrystalline Cellulose	30	30	30	30	30	30	30	30	30
Lactose	120.5	90.5	60.5	120.5	90.5	60.5	120.5	90.5	60.5
Talc	4	4	4	4	4	4	4	4	4
Magnesium Stearate	2	2	2	2	2	2	2	2	2
Total Tablet Weight	250	250	250	250	250	250	250	250	250

PRE-COMPRESSION STUDIES [44-47]

Bulk Density and Tapped Density:

An accurately weighed quantity of powders and/or granules (W) was carefully poured into the graduated cylinder and the volume (V_0) was measured then the graduated cylinder was closed with lid, set into bulk density apparatus which was set for 50 taps. After completion of 50 taps, the volume (VF) was measured and continued until the two consecutive readings are equal. The bulk density and tapped density was calculated using the following formula:

Bulk Density = W / V_0

Tapped Density = W / V_f

Where,

V_0 = Initial volume

V_f = Final Volume

Compressibility Index and Hausner's Ratio:

The compressibility index and Hausner's ratio was calculated using measured values for bulk density (ρ bulk) and tapped density (ρ tapped) as follows:

$$\text{Compressibility index (\%)} = \frac{\text{TBD}-\text{LBD}}{\text{TBD}} X\ 100\%$$

Hausner's ratio:

It is an index of case of powder flow. By formula

$$\text{Hausner's ratio} = \frac{\text{TBD}}{\text{LBD}}$$

Where,

TBD = Tapped bulk density

LBD = Loose bulk density

Table No. -5: Effect of Carr's Index and Hausner's ratio on flow properties

Carr's Index (%)	Flow character	Hausner's ratio
≤10	Excellent	1.0-1.11
11-15	Good	1.12-1.18
16-20	Fair	1.19-1.25
21-25	Passable	1.26-1.34
26-31	Poor	1.35-1.45
32-37	Very poor	1.46-1.59
>38	Very very poor	>1.60

Angle of Repose:

Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and the horizontal plane. The angle of repose of blended granule was determined by the funnel method. Accurately weighed granules blend was passed through a funnel that is fixed in such a way that it just touches the apex of the blend. The blend was allowed to flow through the funnel freely on to the surface. The diameter of the granule cone was measured and the angle of repose was calculated using the equation:

$$\theta = \tan^{-1}(h/r)$$

Where,

θ = Angle of repose

h = height of the pile

r = radius of the base of the pile

POST-COMPRESSION STUDIES [48,-50]

- **Shape and Appearance:**

The formulated tablets were visually observed for its shape and color.

- **Uniformity of thickness:**

Thickness and diameter of the tablets were measured using a Vernier Caliper. Five tablets of each formulation were picked randomly and the dimension of each three tablets were measured in mm. This was done in triplicate and standard deviation was calculated. The tablet thickness was controlled within a ± 5% variation of the standard.

- **Weight Variation Test:**

The weight variation test was carried out in order to verify the uniformity of the weight of tablets in each formulation. Twenty tablets were selected randomly and weighed individually to check for the weight variation. The following percentage deviation in weight was allowed as shown in the table no. 7.

Table No. -7: Limits for weight variation (U.S.P)

Average weight of a tablet	Percentage deviation (%)
130 mg or less	±10
More than 130 mg and less than 324 mg	±7.5
324 mg or more	±5

- **Thickness of Tablets:**

The thickness of the tablets was determined using a Vernier Caliper. Ten tablets from each prepared batch of Dicyclomine HCl were taken and an average thickness value was calculated.

- **Friability of Tablets:**

The friability of the tablets was determined for twenty tablets taken randomly from each formulation. After weighing, the tablets were placed in the plastic chamber of friability test apparatus. The friability was evaluated by the following formula:

$$F = (W_1-W_2)/W_1 \times 100$$

Where,

W_1 = Weight of the tablets before testing.

W_2 = Weight of the tablets after testing.

% friability of the tablets less than 1% is considered acceptable.

Hardness of the Tablets:

The crushing strength of prepared tablets of Dicyclomine HCl was determined using Monsanto tablet hardness tester.

Drug content Uniformity:

From each batch 10 tablets were taken and finely powdered. . A weight equivalent to 100 mg of Dicyclomine HCl was accurately weighed and dissolved in 100 ml of 6.8 Phosphate Buffer. The drug was allowed to dissolve in the solvent, the solution was filtered and 10 ml of the filtrate was suitably diluted to 100 ml with the same buffer (II). Again, from II stock solution 10 ml was pipetted out and diluted to 100 ml with 6.8 Phosphate Buffer and analyzed spectrophotometrically at 213nm. The amount of Dicyclomine HCl was estimated using standard calibration curve of the drug. The study was carried out in triplicate for each batch of formulation. Sustained Release tablet of Dicyclomine HCl should contain not less than 95.0 % and not more than 105.0 % of the labeled amount of Dicyclomine HCl.

Disintegration time:

Disintegration apparatus consists of 6 tubes with 3 inch length and bottom glass tube have # 10 mesh the particles should pass through it, each tablet is placed in each tube and tubes are placed in each tube and tubes are placed in 1 litre of 6.8 Phosphate Buffer. The device is raising and lowering the basket in the immersion fluid at a constant frequency rate of 29 and 32 cycles per minute and is maintained at 37± 2 ^{0}C. The time taken to disintegrate the tablet is determined when all particles should pass through the #10 mesh in glass tube.

In-vitro Drug Release Study: [51]

In-vitro dissolution studies of Sustained Release tablet of Dicyclomine HCl were carried out in USP dissolution test apparatus-II, employing a paddle type apparatus at 50 rpm using 900ml of 0.1N HCl maintained at 37±0.5 ^{0}C and stirred for 2 hours and followed by 6.8 phosphate buffer. At predetermined time intervals, 5 ml of sample was withdrawn and replaced with equal amount of respected buffer. The collected samples were filtered and suitably diluted with buffer solution and analyzed spectrophotometrically at 213 nm to determine the amount of drug released in the dissolution medium.

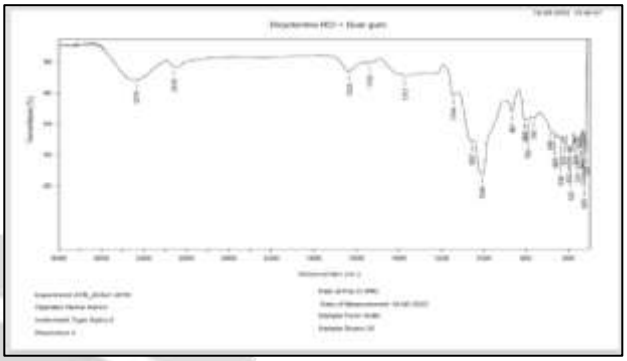
Release Kinetics [52-53]

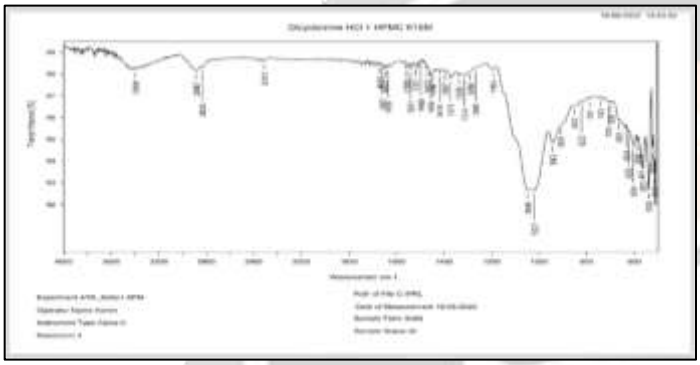
To analyse the mechanism for the drug release and the release rate kinetics of the dosage form, the data obtained was fitted into Zero order, First order, Higuchi's and Korsmeyer-Peppas. By comparing the R^2 values obtained from this, the best-fit model was selected.

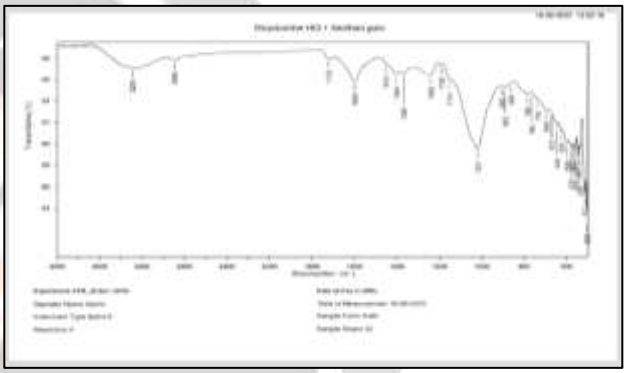
Stability Studies:

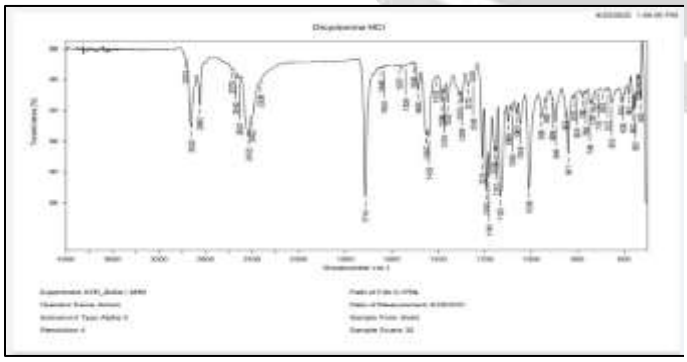
The selection of formulation was tested for its stability studiers. Short term stability studies were performed at Room Temperature over a period of 3 months. 5 tablets were packed in amber colored screw bottle and kept in stability chamber maintained at Room Temperature. Sample were taken at 1 month interval for their drug content estimation including physical parameters. At the end of 3 months periods, dissolution were performed to determine the drug release profile.

RESULTS
Drug and Polymer Compatibility Studies
FTIR Analysis









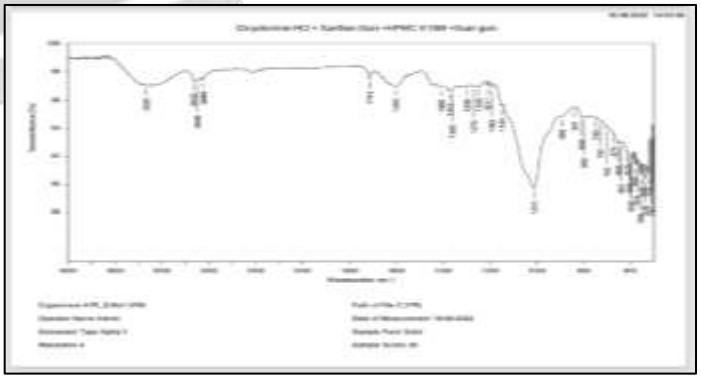


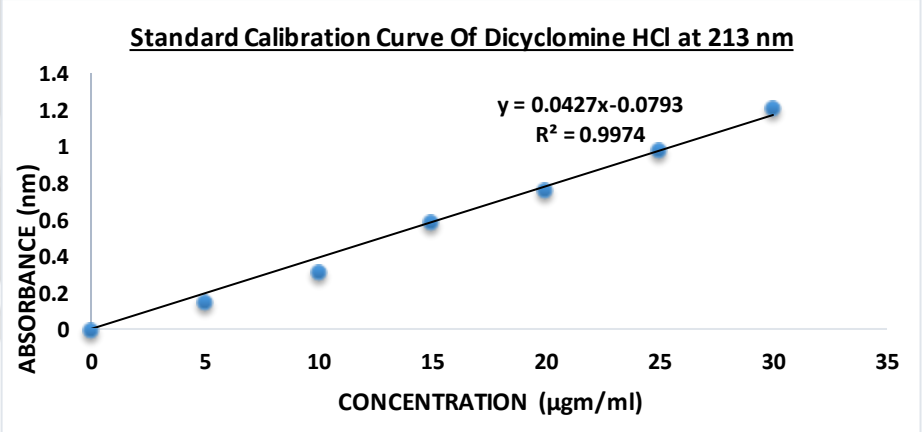
Table No.-8: FT-IR Characteristic peak of Pure Drug and excipients

SI No.	Functional group	IR Observed peaks (cm^{-1})					
		IR range	Dicyclomine HCl	Drug + HPMC K15M	Drug + Xanthan gum	Drug + Guar Gum	Drug+ HPMC K15M +Xanthan gum+ Guar Gum
1.	C-H	3350-3310	3324.47	3323.64	3334.43	3343.29	3343.61
2.	C=O	1685-1666	1674.19	1674.62	1673.26	1673.91	1672.38
3.	O-H	1550-1500	1538.76	1543.27	1536.27	1529.43	1542.23
4.	N-H	1250-1020	1228.67	1229.68	1229.79	1230.37	1229.76

STANDARD CALIBRATION PLOT OF DICYCLOMINE HCL:

Table No. -10: Data for Calibration Curve of Dicyclomine HCl

Concentration (µgm/ml)	Absorbance(nm)
0	0
5	0.1500
10	0.3180
15	0.5870
20	0.7600
25	0.9870
30	1.2100



S. No.	Parameters	Reported	Inferences
1.	Nature	Crystalline powder	Crystalline powder
2.	Color	White	White
3.	Melting point	164°C	164- 166 °C
4.	Odor	Odorless	Odorless
5.	Solubility	Soluble in water, free soluble in ethanol, methanol, dichloromethane, acetonitrile,	Soluble in water, free soluble in ethanol, methanol, dichloromethane, acetonitrile,

Figure -2: Standard Calibration Curve of Dicyclomine HCl in 6.8 Phosphate Buffer at 213 nm

EVALUATION OF SUSTAINED RELEASE TABLETS OF DICYCLOMINE HCl

A. Pre-compression evaluation

Angle of Repose: The angles of repose (θ) for various formulations were calculated and the value of θ for each formulation is shown in the table below:

Table No. -11: Data for Angle of Repose

Sl. No.	Formulation Code	Angle of Repose (θ)
01	F1	30 ± 0.85
02	F2	30 ± 1.09
03	F3	30 ± 0.89
04	F4	29.28 ± 0.85
05	F5	28.14 ± 1.18
06	F6	28.16 ± 0.49
07	F7	31 ± 0.45
08	F8	30 ± 0.46
09	F9	30.52 ± 1.42

Note: All the values are mean of three readings ± SD

From the above table, the angle of repose of pre-compressed powders of Dicyclomine HCl was in the range 28.14 ± 1.18 to 31 ± 0.45, indicating that the studied granules have good flow properties because for a formulation to have good flow properties, θ should be ≤ 30º.

Bulk Density:

The LBD, TBD, compressibility index and Hausner's Ratio for the powders of various formulations were determined and their respective values are shown in the table below:

Table No. -12: Pre- Compression parameter of Sustained Release Tablet of Dicyclomine HCl

Sl. No.	Formulation Code	Bulk Density (gm/ml)	Tapped Bulk Density (gm/ml)	Compressibility Index	Hausner's Ratio
01.	F1	0.38	0.44	13.6	1.16
02.	F2	0.39	0.46	15.2	1.17
03.	F3	0.34	0.41	17.07	1.2
04.	F4	0.35	0.42	16.66	1.2
05.	F5	0.36	0.42	17.07	1.2
06.	F6	0.34	0.42	19.05	1.24
07.	F7	0.34	0.41	17	1.2
08.	F8	0.34	0.41	17.07	1.2
09.	F9	0.34	0.41	17.07	1.2

Note: All the values are mean of three readings ± SD

We can observe from the above table that LBD ranges from 0.34 to 0.39 and TBD ranges from 0.41 to 0.46; compressibility index ranged from 13.6 to 19.05 and Hausner's ratio ranged from 1.16 to 1.24. These results are in agreement with the desired value of compressibility index and Hausner's ratio for a formulation. Hence all the formulations studied exhibited good compressibility index.

Formulation Code	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%w/w)	Weight Variation (mg)	Drug Content (%)	Disintegrating Time (Sec)
F1	3 ± 0.2	5.5 ± 0.41	0.6	250.15 ± 0.45	92.97±0.09	10.4±0.3
F2	3.2 ± 0.24	6 ± 0.5	0.49	250.55 ± 0.34	92.27±0.39	11.2±0.4
F3	3.2 ± 0.36	5.5 ± 0.58	0.49	250.35 ± 0.39	94.54±0.40	12.5±0.2
F4	3.1 ± 0.16	5.5 ± 0.58	0.25	250.1 ± 0.58	99.38±0.42	10.9±0.3
F5	3.2 ± 0.16	5.41 ± 0.94	0.63	250.5 ± 0.87	97.66±0.41	10.6±0.1
F6	3.18 ± 0.1	6.08 ± 0.42	0.47	249.55 ± 0.98	97.42±0.41	12.9±0.4
F7	3.3 ± 0.12	5.9 ± 0.42	0.63	250.35 ± 0.89	95.39±0.40	11.3±0.2
F8	3.44 ± 0.11	5.91 ± 0.28	0.63	249.15 ± 1.12	94.54±0.40	12.6±0.1
F9	3.3 ± 0.2	5.9 ± 0.32	0.48	249.3 ± 0.91	91.73±0.39	11.2±0.5

Table No. -13: Post -Compression parameter of Sustained Release Tablet of Dicyclomine HCl

Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	3.627	4.112	3.567	3.818	4.532	4.976	4.203	4.013	3.676
2	7.955	7.789	6.930	7.868	8.226	8.897	8.207	8.494	8.292
3	16.614	15.828	15.887	15.971	16.905	17.602	17.985	15.899	16.610
4	28.495	27.794	27.568	27.088	28.437	28.733	28.481	28.694	29.570
5	40.215	38.683	38.199	38.054	40.896	41.440	39.919	38.440	17.555
6	49.051	48.262	47.774	46.536	49.754	50.539	50.314	48.461	49.130
7	62.243	61.548	60.744	58.668	62.330	63.798	63.862	61.212	62.498
8	68.933	67.596	66.874	67.898	67.635	68.691	68.193	67.344	69.504
9	81.098	79.844	80.170	78.449	72.321	73.177	71.220	80.643	79.995
10	82.674	82.107	81.722	88.208	74.225	79.200	72.934	81.975	82.959
11	83.802	86.436	82.834	94.626	85.850	86.985	85.494	83.311	86.167
12	94.683	93.070	92.645	98.108	94.515	96.110	94.140	92.679	96.743

Table No. -14: Data for Cumulative % drug release

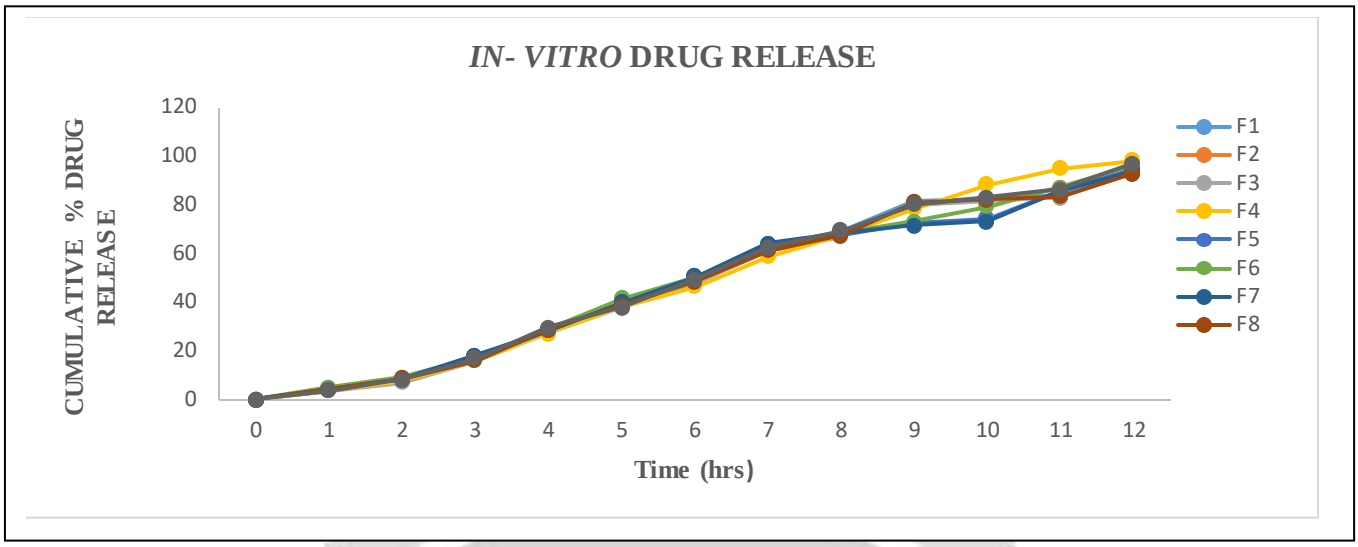


Figure -3: *In-vitro* drug release curve for batch 1- 9

Formulation Code	Zero Order	First Order	Higuchi	Korsmeyer-Peppas		Best Fit Model
	R^2	R^2	R^2	R^2	N	
F1	0.9771	0.9042	0.8142	0.9529	0.6352	Zero Order Korsmeyer-Peppas
F2	0.9789	0.9295	0.81	0.9574	0.6337	Zero Order Korsmeyer-Peppas
F3	0.9755	0.9246	0.8071	0.9563	0.6304	Zero Order Korsmeyer-Peppas
F4	0.9807	0.8292	0.7896	0.9667	0.6355	Zero Order Korsmeyer-Peppas
F5	0.982	0.8771	0.8249	0.9479	0.6337	Zero Order Korsmeyer-Peppas
F6	0.9848	0.8596	0.8273	0.9458	0.6381	Zero Order Korsmeyer-Peppas
F7	0.9792	0.8796	0.8265	0.9455	0.6335	Zero Order Korsmeyer-Peppas
F8	0.9773	0.9273	0.8143	0.9542	0.6339	Zero Order Korsmeyer-Peppas
F9	0.9465	0.846	0.7584	0.9553	0.6267	Zero Order Korsmeyer-Peppas

Table No. -15: Kinetic Models for Sustained Release Tablet of Dicyclomine HCl

$R^{2\,=}$ Regression Constant

N = Release Coefficient

		Observation

S. No.	Parameters	Initial	1st month RT	2nd month RT	3rd month RT
1	Nature	Compact solid	Compact solid	Compact solid	Compact solid
2	Colour	white	white	white	white
3	Hardness (kg/cm2)	5.5	5.5	5.4	5.4
4	Friability (%)	0.25	0.24	0.24	0.23
5	Content uniformity (%)	99.60	99.17	98.86	99.53

Table -16: Stability studies of F4 formulation at Room Temperature.

*RT – Room Temperature

Table -17: *In-vitro* drug release study for stability testing of formulation F4 at Room Temperature.

S. No.	Time (hrs.)	90th day cumulative % drug release
1	0	0
2	1	37.3
3	2	62.5
4	3	77.6
5	4	82.2
6	5	88.71
7	6	92.3
8	7	95.6
9	8	98.01

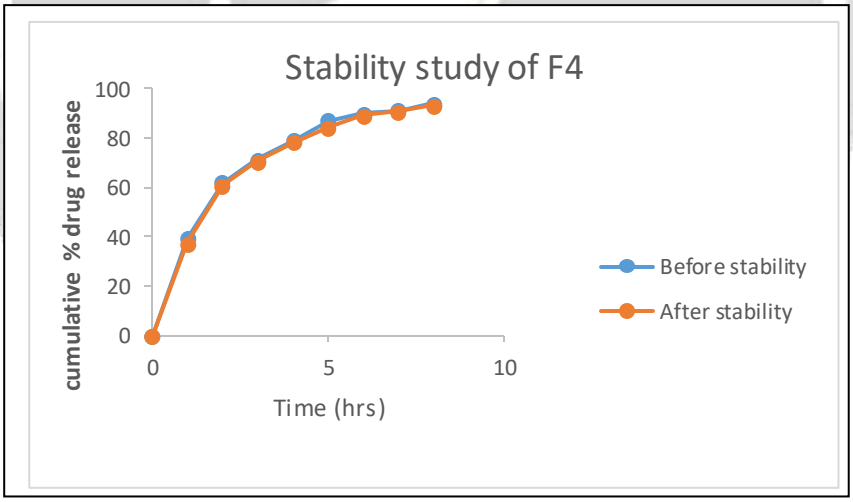


Figure -4: *In- vitro* drug release of F4 Before Stability and After stability at Room Temperature

CONCLUSION AND SUMMARY

The formulation and evaluation of Sustained Release tablet of Dicyclomine HCl was performed in the present study. The Sustained Release tablet of Dicylomine HCl were prepared by using polymers like Guar Gum, HPMC K15M and Xanthan gum, which is used for the treatment of spasm of intestine seen in the functional bowel disorder and irritable bowel syndrome. Sustained Release tablet containing xanthan gum and drug was concluded the best formulation among other formulation, which showing the most desired drug release. It will be considerd as optimized formulation.

The optimized formulation F4 was subjected for stability studies, the formulation was found to be stable in the short term stability study.

Preformulation study was carried out for powder blend, it was evaluated to determine the flow characteristic, angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio. The data obtained from the studies indicated that the powder blend had good flow properties.

The tablet were prepared with different ratios of polymer by direct compression method. All the physical parameters of prepared tablets comply with Pharmacopoeial Specifications.

Evaluation studies of all formulations showed that drug content, weight variation and friability as per the standard given in Pharmacopoeia. The Hardness of all formulations were within the limits.

The *in-vitro* dissolution studies closely indicated that among nine formulations. The formulation F4 was found to be the best in drug release.

The regression correlation co-efficient values was concluded in kinetics modeling of drug dissolution profile for all formulations. The formulation (F4), R^2 value lies between 0.7896 to 0.9807. Hence, it is concluded that the formulation F4 following drug release. From the stability data, it can be concluded that there was no significant change in any parameters. Hence, the formulation F4 is considered to be highly stable formulation.

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