FORMULATION AND EVALUATION OF FAST DISINTEGRATING TABLET CONTAINING HYDROCHLOROTHIZIDE

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ABSTRACT

The aim of this study was to prepare Fast disintegrating tablet containing Hydrochlorothiazide by using Natural disintegrants. The tablets were prepared using micro crystalline cellulose as diluent and aspartame as sweetening agent along with Natural super disintegrant. The superdisintegrant used in this study was Isapghula mucilage and Banana powder. The tablets were evaluated for weight variation, hardness, friability, wetting time, water absorption ratio and disintegration time (DT) and dissolution study. Different concentration of superdisintegrant was used in this formulation as 2%, 4%, 6%, 8%. From the results obtained, it can be concluded that the tablet formulation prepared with 8% with Isapghula mucilage ie. 8 mg showed fast and higher drug release (97.68%) during in vitro dissolution study. Also the hardness, friability, dissolution rate and assay of prepared tablets (batch F8) were found to be acceptable according to standard limits.

Key Word: *Fast disintegrating Tablet, Superdisintegrant, Hydrochlorothiazide, Isapghula mucilage, Banana powder.*

INTRODUCTION

Despite of tremendous innovations in drug delivery, the oral route remains the preferred route for administration of therapeutic agents because of accurate dosage, low cost therapy, self-medication, and ease of administration leading to high level of patient compliance .The most popular dosage forms are being conventional tablets and hard gelatin capsules. Pediatric and geriatric patients may have difficulties in swallowing or chewing pharmaceutical dosage forms for oral administration[1]. Tablets that rapidly dissolve upon contact with saliva in the buccal cavity could present a solution to those problems and so there is an increased interest in fast dissolving dosage forms for buccal, sublingual and oral administration. Fast dissolving/ disintegrating tablet are perfect fit for these patients as these immediately release the active drug when placed on tongue by rapid disintegration/ dispersion, followed by dissolution of drug[2]. The Fast disintegrating tablet technology, which makes tablets dissolve or disintegrate in the mouth without additional water intake. The FDT formulation is defined by the Food and Drug Administration (FDA) as "a solid dosage form containing medical substances whish disintegrates rapidly, usually within a seconds, when placed upon the tongue.[3] According to European Pharmacopoeia, "the FDT should disperse/disintegrate in less than three minutes. Fast dissolving tablets are also called as mouth-dissolving tablets, melt-in mouth tablets, Oro-dispersible tablets, porous tablets, quick dissolving etc.[4]

The basic approach in development of FDT is the use of superdisintegrants, which provide instantaneous disintegration of tablet after putting on tongue and release the drug in saliva. The fast dissolving tablets are rapidly dissolved or disintegrate by the use of superdisintegrants.[5] The faster the drug into solution, quicker the absorption and onset of clinical effect. Some drugs are absorbed from the mouth, as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablets dosage form. The advantage of mouth dissolving dosage forms are increasingly being recognized in both, industry and academics. The basic approach in development of FDT is the use of superdisintegrant like cross linked carboxy methyl cellulose (croscarmellose), sodium starch glycolate (primogel, explotab), polyvinylpyrollidone (polyplasdone) etc, which provide instantaneous disintegration of tablet after putting on tongue, thereby release the drug in saliva.[6]

The bioavailability of some drugs may be increased due to absorption of drug in oral cavity and also due to pregastric absorption of saliva containing dispersed drugs that pass down into the stomach. Moreover, the amount of drug that is subjected to first pass metabolism is reduced as compared to standard tablet. The technologies used for manufacturing fast dissolving tablets are freeze-drying, spray-drying, tablet molding, sublimation, sugar based excipients, tablet compression, and disintegration addition. As a result of increased life expectancy, the elderly constitute a large portion of the worldwide population today. These people eventually will experience deterioration of their physiological and physical abilities.[7]

REQUIREMENTS OF FAST DISINTEGRATING TABLETS

The tablets should be follow different requirements: [8]

1. Not require water to swallow and should dissolve or disintegrate in the mouth within a few seconds.
2. Allow high drug loading.

3. Be compatible with taste masking and other excipients.
4. Have a pleasing mouth feel.
5. Leave minimal or no residue in the mouth after oral administration.
6. Have sufficient strength to withstand the rigors of the manufacturing process and post manufacturing handling.
7. Exhibit low sensitivity to environmental conditions such as humidity and temperature.
8. Be adaptable and amenable to existing processing and packaging machinery.
9. Allow the manufacture of tablets using conventional processing and packaging equipment's at low cost.

IDEAL CHARACTERISTICS ON FAST DISINTEGRATION TABLET

Fast disintegration tablet should following characteristics:[9]

1. They should not require water or other liquid at the time of administration.
2. Should easily disintegrate and dissolve.
3. Mask or overcome unacceptable taste of drug.
4. They should have high drug loading.
5. They should have pleasant feel in mouth.
6. They should have negligible or no residue in oral cavity after administration.
7. They should have low sensitivity against environmental conditions like moisture and temp. etc.
8. Ease of administration for patients who are mentally ill, disable and uncooperative.
9. Should be portable without fragility concern.
10. They should be manufactured using conventional tablet processing and packing equipment at low cost.

ADVANTAGES OF FAST DISINTEGRATING TABLETS

Fast disintegration tablet should have following advantages:[10]

1. Ease to administration to patients who refuses to swallow a tablet such as pediatrics, generatric patients and psychiatric patients.
2. No need or little water is require to swaiiow the dosage from which is highly convenient feature for patients who are traveling and do not have access to water.
3. Free of risk of suffocation due to physical obstruction when swallowed, thus offering improved safety.
4. Rapid disintegration and absorption of drug which will produce quick onset of action.
5. Quick absorption from the GIT improves patient compliance.
6. Drug and dosage stability.
7. New business opportunities like differentiation, line extension and life cycle management. Exclusivity of product promotion although chewable tablet have been on the market for some time.
8. They are not the same as the new fast dissolving tablets. Patients for whom chewing is difficult or painful can use these new tablets easily.
9. Fast dissolving tablet can be used easily children who have lost their primary teeth, but do not have full use of their permanent teeth.

DISADVANTAGES OF FAST DISINTEGRAT-ING TABLET

Fast disintegration tablet should have following disadvantages:[11]

1. Most fast dissolving Tablet lack the mechanical strength common to traditional tablet. Many products are very light weight and fragile requiring them to be individually packaged. Patients should be advised not to push these tablets through the foil film, but instead. Peel the film back to release the fast dissolving tablet.
2. Due to formation of fast dissolving tablets which are also more susceptible to degradation via temp, and humidity, some of newest fast dissolving tablet formulation is dispensed in a conventional stock bottle. Pharmacists are advised to take care when dispensing such formulation to ensure they are not exposed to high levels of moisture or humidity excess handling of tablet can introduce enough moisture to initiate dissolution of tablet matrix.
3. The tablet may leave unpleasant taste and/or grittiness in mouth if not formulated properly.
4. Drug with relatively larger doses are difficult to formulate in fast dissolving tablet. E.g. Antibiotics, like ciprofloxacin(500 mg)
5. Patient who concurrently takes anti-cholinergic medications may not be the best candidates for FDT.
6. Patient with Sjogren's syndrome or dryness of the mouth due to decreased saliva production may not be good candidate for these tablet formulation.

Superdisintegrants: Disintegrating agents are substances routinely included in the tablet formulations to aid in the break-up of the compacted mass into the primary particles to facilitate the dissolution or release of the active ingredients when it is put into a fluid environment. They endorse moisture penetration and dispersion of the tablet matrix. The major function of disintegrants is to oppose the efficiency of the tablet binder and physical forces that act under compression to structure the tablet.[12] Recently new materials termed as "superdisintegrants" have been developed to

improve the disintegration processes. Superdisintegrants are another version of super-absorbing materials with tailor-made swelling properties. These materials are not planned to absorb significant amounts of water or aqueous fluids, but planned to swell very fast. They are physically dispersed within the matrix of the dosage form and will expand when the dosage form is exposed to the wet environment.[6] These newer substances are more effective at lower concentrations with greater disintegrating efficiency and mechanical strength.[13] Superdisintegrants are generally used at a low level in the solid dosage form, typically 1-10 % by weight relative to the total weight of the dosage unit.[4] Their particles are generally small and porous, which allow for rapid tablet disintegration in the mouth without an objectionable mouth-feel from either large particles or gelling. The particles are also compressible which improves tablet hardness and its friability.[14] Effective superdisintegrants provide improved compressibility, compatibility and have no negative impact on the mechanical strength of formulations containing high-dose drugs. Generally, one gram of superdisintegrant absorbs 10-40 g of water or aqueous medium. After absorption, swelling pressure and isotropic swelling of the superdisintegrants particles create stress concentrated areas where a gradient of mechanical properties will exist due to which whole structure will break a part.

TYPES OF SUPERDISINTEGRANTS

The Superdisintegrants can be classified into two categories on the basis of their availability:

1. Natural Superdisintegrants
2. Synthetic Superdisintegrants

PLAN AND WORK

1. To study the preformulation factor of Hydrochlorothozide such as solubility, melting point, pH, max and standard calibration curve of drug in phosphate buffer pH 7.8.
2. To study FTIR spectroscopy of Hydrochlorothizide.
3. To study the pre-compression parameters.
4. Formulation of Hydrochlorothizide Fast disintegrating tablets.
5. To evaluate prepared tablets by different post-compression parameters.
6. To study in-vitro dissolution of dissolving tablets Hydrochlorothizide in phosphate buffer pH 7.8

PREFORMULATION STUDIES

1. Solubility of Drug
2. Partition coefficient
3. UV Spectral Studies

ISOLATION AND CHARACTERIZATION OF POLYMERS

1. Isolation of natural polymers: Isapghula and Banana Powder.
2. Solubility of Polymer.
3. Swelling Index.
4. Moisture absorption.
5. Thermal stability.

METHODOLOGY

1. Preparation of Preliminary formulations
2. Selection of Excipients and Optimization of their Concentration
3. Formulation compositions of preliminary batches

CHARACTERIZATION AND EVOLUTION OF FORMULATION

1. Precompression Parameters
2. Optimization of formulation

PRE-COMPRESSION PARAMETERS

1. Angle of repose
2. Bulk density
3. Carr's index
4. Hausner's ratio

POST-COMPRESSION PARAMETERS

1. Thickness
2. Uniformity of weight
3. Drug Content uniformity
4. Hardness
5. Friability
6. Wetting time
7. Water absorption ratio
8. In-vitro disintegration time
9. In-vitro dispersion time
10. In-vitro Drug Release of final formulations

MATERIALS AND METHODS

Preparation of Isapghula Mucilage: The seeds of Plantago ovata were soaked in distilled water for 48 hours and boiled for few minutes. The collected material was squeezed through muslin cloth to separate them. Then, an equal volume of acetone was added to the filterate for precipitation of the mucilage. The separated mucilage was dried at 40C in a tray dryer. The dried mucilage was powdered and sieved in sieve no # 80.The resultant powder was stored in a dessicator and used for the present study.[15]

Preparation of Banana Powder: The collected fresh whole bananas were cleaned for any debris and weighed. The skin peeled bananas were dipped in ethanol in 5 minutes. Then banana was weighed and squashed to paste, this paste was added with citric acid (2-3%) to remove the sticky nature. Then water is separate by centrifugation and processing. The pressed mass is subjected to drying in tray-dryer. The

dried substances was milled and screened in sieve (#80) to get fine powder.[16]

Preparation of Preliminary Tablet: Fast disintegrating tablet of Hydrochlorothiazide were prepared by direct compression method because of their several advantages:

1. Easiest way to manufacture tablets.
2. Use of conventional equipment.
3. Use of commonly available excipient.
4. Limited number of processing steps.

Selection of Excipients and Optimization of their Concentration: The most important parameter that needs to be optimized in the development of Fast disintegrating tablets is the disintegration time. Fast disintegrating tablets were prepared firstly using different excipients (binders and superdisintegrants) and then evaluated for various parameters like friability, hardness and disintegration time to select the best combination for formulation of fast disintegrating tablets. The combination with lowest disintegration time, optimum hardness and friability was selected for further study. Tablets were prepared by direct compression technique.

In all above formulation, weighed quantities of drugs along with optimized concentration of superdisintegrant and binder along with excipients were mixed in geometric progression in a dry and clean mortar. Then the blend was passed through sieve no. 60 for direct compression. The powder blend was then compressed into tablets using 6mm punch in multi punch tablet compression machine. These fabricated tablets were evaluated.

RESULT AND DISCUSSION

In the present investigation pre-formulation studies was estimated on the drug and superdisintegrants. Banana powder and Isapghula powder in different concentration from 2-8% was added to formulate 100 mg Hydrochlorothiazide Fast disintegrating tablets. Direct compression technique was applied in formulating Fast disintegrating tablets.

Table 1: Formulation Composition for Preliminary Batches

Sr. No.	Composition (mg)	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
1.	Hydrochlorothiazide	2.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5
2.	Banana Powder	2	4	6	8	--	--	--	--
3.	Isapgol Mucilage	--	--	--	--	2	4	6	8
4.	Microcrystalline Celluiose	53.5	51.5	49.5	47.5	53.5	51.5	49.5	47.5
5.	Crosspovidone	5	5	5	5	5	5	5	5
6.	Sodium Starch glycolate	5	5	5	5	5	5	5	5
7.	Magnesium stearate	2	2	2	2	2	2	2	2
8.	Mannitol	20	20	20	20	20	20	20	20

CHARACTERIZATION OF DRUG

Determination of Organoleptic Properties: Physical appearance of Hydrochlorothiazide was evaluated by various organoleptic properties, like appearance, colour, odour as shown in **Table 2.**

Table 2: Interpretation of Physical Properties of Hydrochlorothiazide

S. No.	Physical Property	Interpretation
1	Appearance	Crystalline Powder
2	Colour	Almost White
3	Odour	Odourless

Determination of Solubility Profile: Hydrochlorothizide was soluble in saline (0.9% w/v) and other solubility profile results were shown in **Table 3.**

Table 3: Solubility Profile of Hydrochlorothiazide in Various Solvent Systems

S. No.	Solvent	Solubility
1	Saline	Soluble
2	Ethanol 95%	Springly soluble
3	Acetone	Soluble
4	Alkali Hydroxide	Soluble
5	Water	Slightly soluble

Determination of Melting Point: Melting point of Hydrochlorothiazide determined by Capillary fusion method. Shown in **Table 4.**

Table 4: Melting Point of Hydrochlorothiazide

Method Employed	Experimental Value
Capillary fusion method	140.33 ± 1.527˚C

Mean ± SD, where n=3

Determination of Calibration Curve: Hydrochlorothiazide in 0.01 M NaOH solution yield characteristic curve when scanned in the UV range between 230 to 300 nm. The λ_{max} for Hydrochlorothiazide in 0.01 M NaOH solution was finalized at 273 nm.

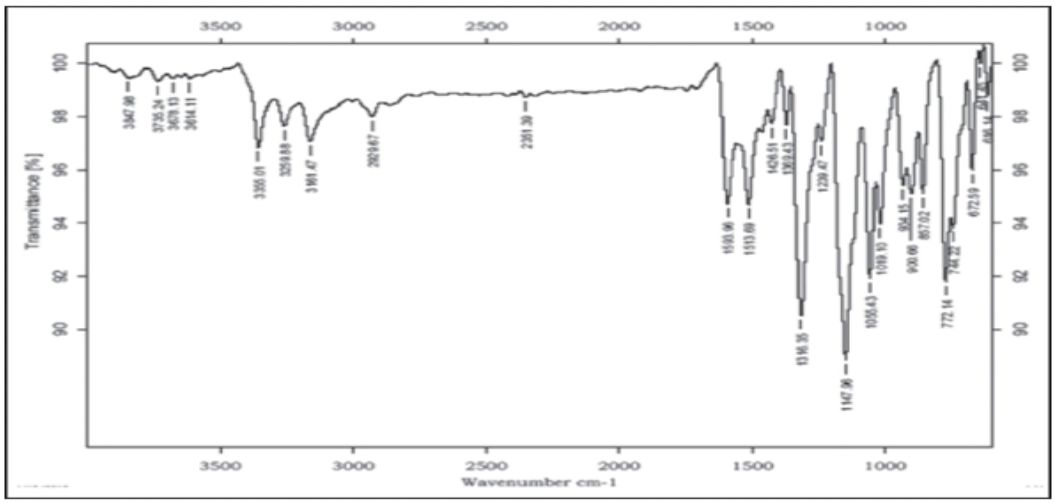

Fig. 1: FTIR of Hydrochlorothizide

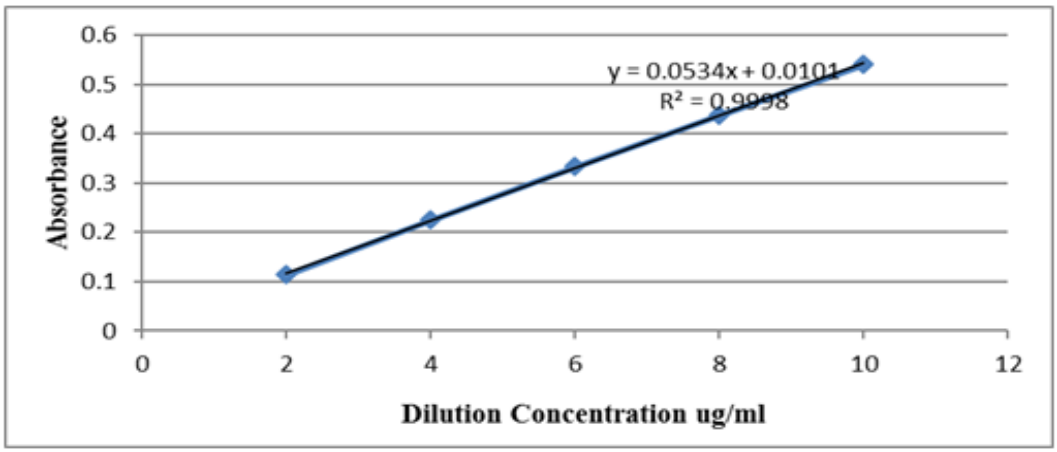

Fig. 2: Standard Plot of Hydrochlorothizide

The standard plot data of Hydrochlorothizide in respective buffer at determined λ_{max} is given in **Table 5**. This data was used for construct the calibration curve **Figure 2**. This showed linear relationship with respect to absorbance values with the correlation coefficient

Table 5: Standard Plot Data for Hydrochlorothizide

Concentration (µg/ml)	Mean Absorbance
2	0.144 ±0.001
4	0.225 ±0.005
6	0.333 ±0.004
8	0.438 ±0.007
10	0.541 ±0.006

Physicochemical Characterization of Isapghula Mucilage and Banana Powder

Identification of Isaphula Mucilage: Powdered mucilage was treated with ruthenium red dye solution and observed pink color passing the test for mucilage.

Identification of Banana Powder: 1gm of banana powder was boiled with15ml of water. After cooling this mucilage solution. Now in 1ml of mucilage solution, 2 drops of 0.1N Iodine solution was added and observed blue color passing the test for mucilage.

Organoleptic Evaluation: The polysaccharide was characterized by various organoleptic properties such as colour, odour, taste, shape, touch and texture and shown in **Table 6**.

Table 6: **Organoleptic Evaluation of the Polymer**

Sr. No.	Property	Inference (Ispaghula)	Inference (Banana)
1	Colour	Light grey	Yellowish
2	Odour	Odourless	Characteristics
3	Taste	Tasteless	Sweet
4	Shape	Irregular	Irregular
5	Touch & Texture	Hard & Rough	Hard & Soft

Phytochemical Screening of the Powder: The basic Phytochemical screening tests for carbohydrates, alkaloids, steroids, flavonoids saponins, tannins and phenols were carried out and shown in **Table 7**. The tests indicated the absence of alkaloids, steroids, flavonoids, saponins, tannins and phenols. Only carbohydrates were found to be present.

Table 7: **Determination of Purity of Polymer**

S. No.	Tests for Phytoconstituents	Results
1	Test for steroids: Libermann – burchard test	Absent
2.	Test for saponins: Foam test	Absent
3.	Test for Carbohydrates: Molisch test, Barfoed's test, Benedicts test	Present
4.	Test for Flavonoids :Shinoda test, Zinc/HCl reduction test	Absent
5.	Test for Tannins/ Phenols: Ferric chloride test, Gelatin test	Absent

Solubility Profile of Powder: The solubility profile of the powder was found to as shown in **Table 8**.

Table 8: Solubility Behavior of the Polymer

Sr. No.	Solvents	Isapghula	Banana powder
1	Acetone	Insoluble	Insoluble
2	Methanol	Insoluble	Soluble
3	Water	Forming a gel	Poorly Soluble
4	Chloroform	Insoluble	Insoluble
5	Ethanol	Insoluble	Soluble

Determination of Swelling Index: Swelling index of powder sample in distilled water was found to as shown in **Table 9**.

Table 9: Swelling Index of Polymer

Method Employed	Isapghula	Banana Powder
Swelling index	68± 1.527	55 ± 1.527

Mean ± SD, where n=3

Determination of Melting Point: Melting point of powder sample was determined by capillary fusion method Shows in **Table 10**

Table 10: Melting Point of Polymer

Method Employed	Isapghula	Banana Powder
Capillary fusion method	139 ± 1.121˚C	88 ± 1.023ºC

Mean ± SD, where n=3

Moisture Absorption: Moisture absorption of powder sample was determined. Shown in **Table 11**.

Table 11: Moisture Absorption of Polymer

Method Employed	Isapghula	Banana Powder
Moisture absorption	2.78 ± 0.7843%	2.91 ± 0.7443%

Mean ± SD, where n=3

Loss of Drying: The powder sample was subjected for determining the LOD in hot air oven is shown in **Table 12.**

Table 12: Loss of Drying of Polymer

Method Employed	Isapghula	Banana Powder
Loss of drying	1.82 ± 0.4532%	0.991± 0.0011%

Mean ± SD, where n=3

Determination of pH of powder: pH of the powder sample was found Shown in **Table 13.**

Table 13: pH of the Polymer

Method employed	Isapghula	Banana Powder
pH	6.6 ± 0.0021	7.16 ± 0.26

Mean ± SD, where n=3

Thermal Stability: Thermal stability study was established and shown in **Table 14**.

Table 14: Thermal Stability of Polymer

Method employed	Isapghula	Banana Powder
Stability(^{o}C)	140^{0}C	110^{0}C

FLOW PROPERTIES OF POLYMER

Micromeritic Properties of Isapghula & Banana Powder: The derived properties such as bulk density, tapped density, compressibility index, Hausner's ratio and angle of repose which depend mainly on particle size distribution, particle shape and tendency of the particles to adhere together results shown in **Table 15**.

Table 15: Characterization of Polymer

Property	Result (Isapghula)	Result (Banana)
Bulk density (gm/cm^3)	0.72 ± 0.002	0.61 ± 0.004
Tapped density (gm/cm^3)	0.76 ± 0.001	0.67 ± 0.003
Compressibility index	5.26 ± 0.003	9.27 ± 0.003
Angle of repose (◦)	29.50 ± 0.004	30.50 ± 0.04
Hausner's Ratio (HR)	1.05 ± 0.002	0.92 ± 0.002

Mean ± SD, where n=3

Tablet Formulation: Drug along with calculated concentration of superdisintegrant and other excipients were mixed together and compressed by direct compression method using 6mm punch in multi compression machine. Before compression the pre-compression parameters were also determined.

Pre-compression Parameter of Tablet: The characterization of mixed blends was done for determination of mass volume relationship parameters. The evaluated parameters were bulk density, tapped density, Hausner's ratio, compressibility index and angle of repose. The bulk density of blend varied between0.43-0.54 g/cm^3. The tapped density was found in the range of 0.52-0.59 g/cm^3. By using these two density data, Hausner's ratio and compressibility index was calculated. The powder blends of all formulation had Hausner's ratio of less than 1.24 indicating good flow characteristics. Blends having value of compressibility index less than 25% were considered as free flowing ones. The values for compressibility index were found between 8.98- 15.95. The flow ability of the powder was also evidenced by the angle of repose. The angle of repose below 35° range indicates good flow properties of powder. Lower the friction occurring within the mass, better the flow rate. The angle of repose was found to be in range 28.791-31.788°. The results for characterization of blend are shown in **Table 16**. The mixed blends were then compressed using rotary tablet punching machine to obtain the mouth dissolving tablets.

Table 16: Characterization of Blended Powder

Formulation Code	Bulk Density (gm/cm^3)	Tapped Density (gm/cm^3)	Angle of Repose (◦)	Carr's Index (%)	Hausner's Ratio (HR)
F1	0.43±0.002	0.56±0.003	30.113	10.87±0.003	1.222±0.002
F2	0.48±0.001	0.53±0.002	31.788	12.08±0.001	1.023±0.002
F3	0.54±0.003	0.59±0.003	29.683	11.97±0.002	1.101±0.001
F4	0.48±0.002	0.53±0.002	30.963	15.95±0.003	1.652±0.003
F5	0.45±0.002	0.52±0.003	30.541	8.98±0.002	1.076±0.002
F6	0.50±0.001	0.58±0001	28.791	9.53±0.001	1.023±0.001
F7	0.51±0.002	0.59±0.001	29.445	9.99±0.002	1.025±0.002
F8	0.52±0.001	0.58±0.001	28.917	9.52±0.001	1.024±0.001

Mean ± SD, where n=3

Post Compression Parameter of Tablet

Uniformity of Thickness: The crown diameters of all the formulations were found to be uniform (6mm).Thickness of all the formulations was in the 1.85mm to 1.89mm (± 5 % of the average thickness of 10 tablets).

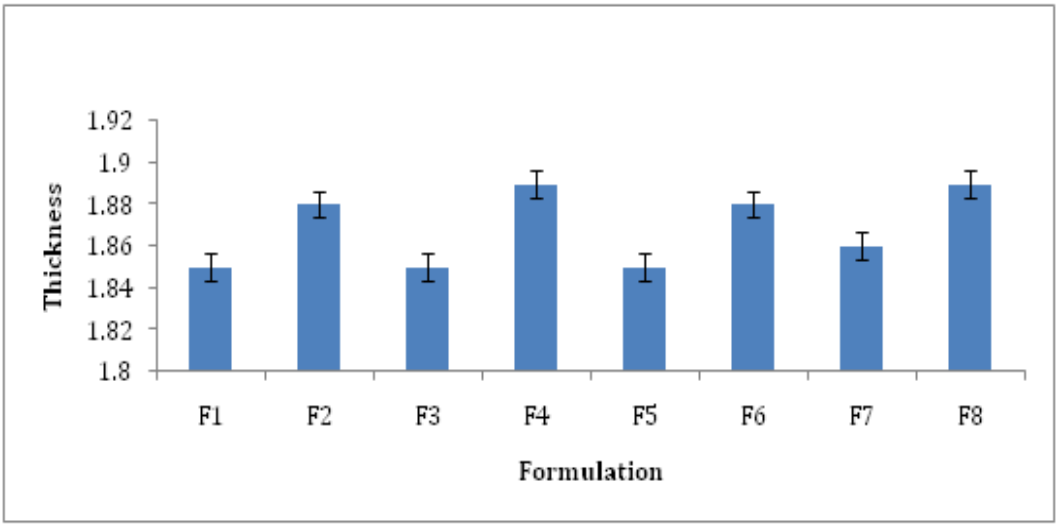

Fig. 3: Thickness Uniformity of Formulations

Weight Uniformity: As the percentage weight variation was within the pharmacopoeial limits of ±7.5%. It is related to tooling of the compression machine, head pressure, machine speed and flow properties of the powder. Inconsistent powder or granulate density and particle size distribution are common sources of weight variation during compression.

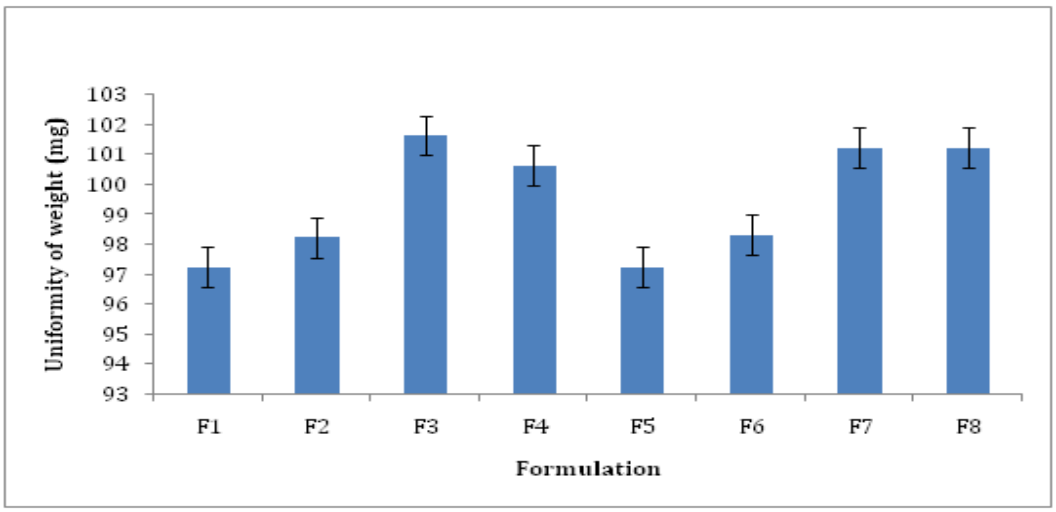

Fig. 4: Weight Uniformity of Formulations

Hardness: In all the formulations, hardness test indicated good mechanical strength, as the hardness of the FDTs was found in the range of 3.2 to 4.2 kg/cm^2.High hardness values increase the disintegration time and reduced dissolution values. By exploiting the correlation between hardness, disintegration, dissolution, friability, percentage defective and weight variation, improves the quality of the tablets.

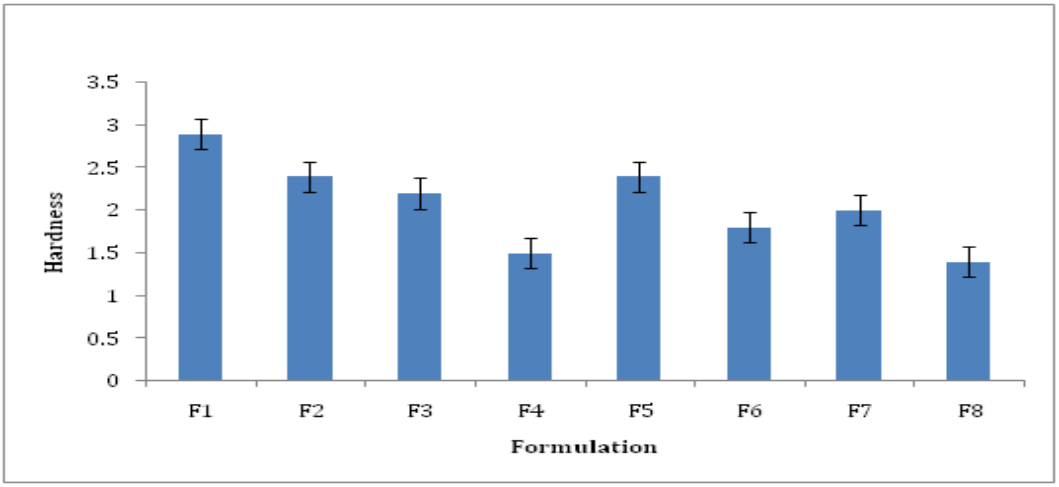

Fig. 5: Hardness of Formulations

Friability: Friability was observed less than 1%, indicated that FDTs had a good mechanical resistance. It is designed to evaluate the ability of the tablet to withstand abrasion in packaging, handling and shipping.

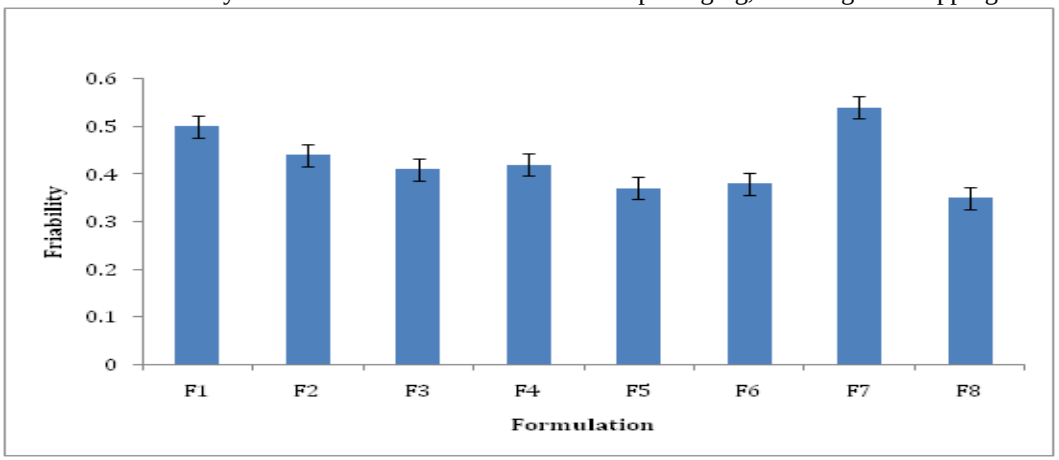

Fig. 6: Friability of Formulations

Table 17: Evaluation Chart of Formulations

Formulation Code	Appearance	Thickness (mm)	Uniformity of Wt. (mg)	Hardness (kg/cm^2)	Friability (%)
F1	Greyish white	1.85±0.005	97.22±0.21	3.6±0.009	0.50±0.017
F2	Greyish white	1.88±0.006	98.23±0.54	4.0±0.007	0.49±0.022
F3	Greyish white	1.85±0.005	101.64±0.45	4.1±0.008	0.41±0.022
F4	Greyish white	1.89±0.003	100.81±0.34	3.7±0.003	0.42±0.024
F5	Greyish white	1.85±0.002	97.23 ±0.48	4.2±0.004	0.37±0.020
F6	Greyish white	1.88±0.002	98.32± 0.23	4.0±0.002	0.38±0.021
F7	Greyish white	1.86±0.003	101.23±0.22	3.2±0.007	0.54±0.019
F8	Greyish white	1.89±0.002	100.32±0.21	3.8±0.001	0.35±0.022

Mean ± SD, where n=3

Wetting time: The wetting time was rapid in all the formulations. Wetting is closely related to inner structure of tablets, this may be due to ability of swelling and also capacity of absorption of water. Among all the formulations F8 showed less wetting time.

Table 18: Wetting Time of Formulations

Formulation code	Time (sec)
F1	11.34±0.008
F2	10.45±0.006
F3	8.23±0.009
F4	5.84±0.007
F5	10.12±0.006
F6	10.09±0.004
F7	8.30±0.004
F8	4.34±0.005

Mean ± SD, where n=3

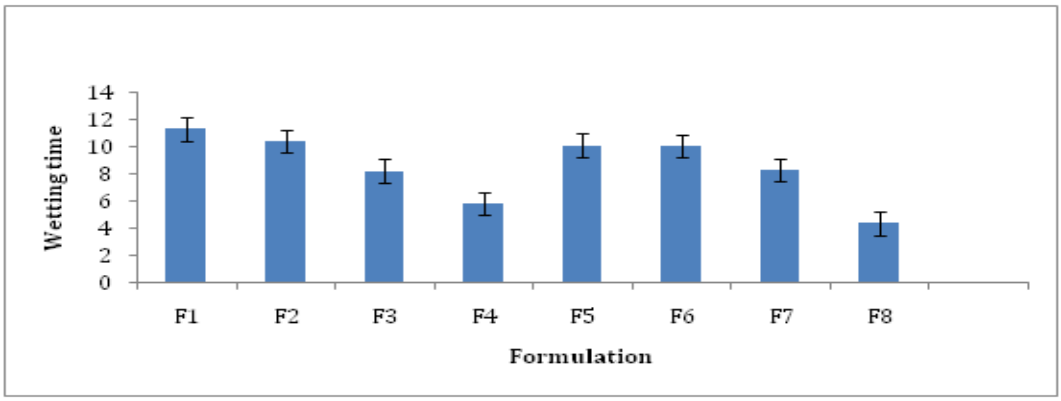

Fig. 7: Wetting Time of Formulations

Water Absorption Ratio: The capacity of disintegrates to swell in presence of little amount of water were found to be in the range of 54-66 %. The water absorption ratio that is the up taking of water was very fast and the ratio was found higher.

Table 19: Water Absorption Ratio of Formulations

Formulation Code	Percentage
F1	55±0.039
F2	57±0.123
F3	62±0.135
F4	65±0.211
F5	54±0.121
F6	60±0.118
F7	63±0.121
F8	66±0.119

Mean ± SD, where n=3

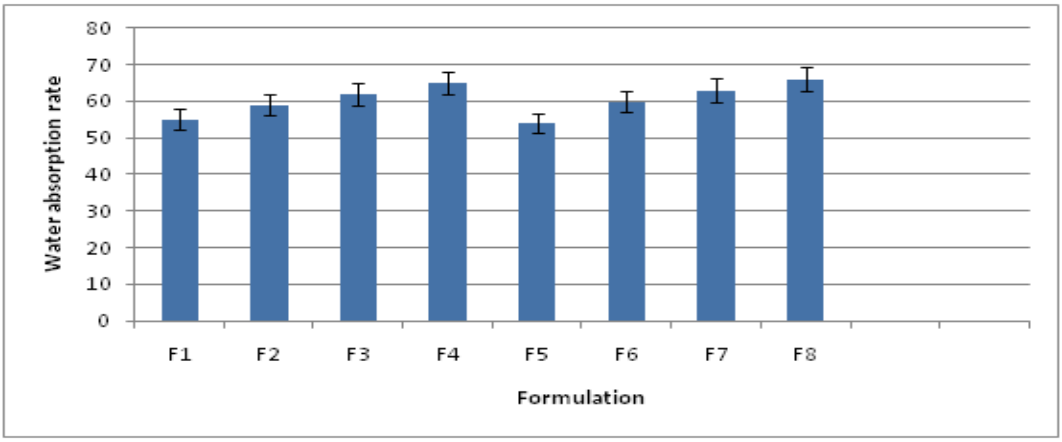

Fig. 8: Water Absorption Ratio of Formulations

In-vitro Disintegration Time: This rapid disintegration of the FDTs was due to the penetration of saliva into the pores of the tablet, which lead to the swelling of superdisintegrants to create enough hydrodynamic pressure for quick and complete disintegration of the tablet. **Plantago Ovate** and **Banana Powder** when comes in contact with water they quickly wicks water into the tablet through capillary action to create internal pressure that disintegrates tablet.

Table 20: In-Vitro Disintegration Time

Formulation code	Time (seconds)
F1	12±0.53
F2	10±0.58
F3	7±0.56
F4	5±0.56
F5	11±0.55
F6	10±0.54
F7	8±0.52
F8	4±0.51

Mean ± SD, where n=3

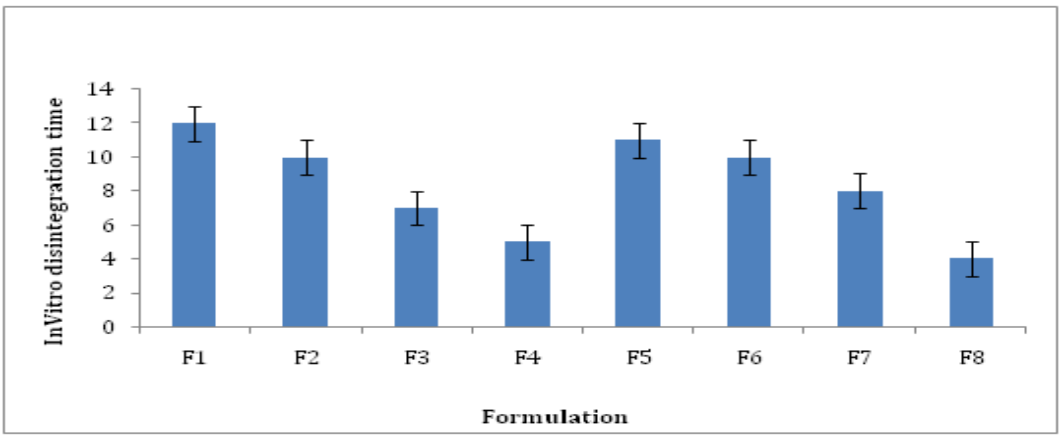

Fig. 9: In-vitro Disintegration Time of Formulations

In-vitro Dispersion Time: The wetting time/dispersion time decreases with increase in the concentration of superdisintegrants. It was observed that as the concentration of superdisintegrants increases water absorption ratio increases and disintegration time decreases.

Table 21: Dispersion Time of Formulations

Formulation Code	Time (Seconds)
F1	14±0.103
F2	12±0.153
F3	10±0.211
F4	8±0.149
F5	12±0.234
F6	11±0.184
F7	8±0.121
F8	4±0.132

Mean ± SD, where n=3

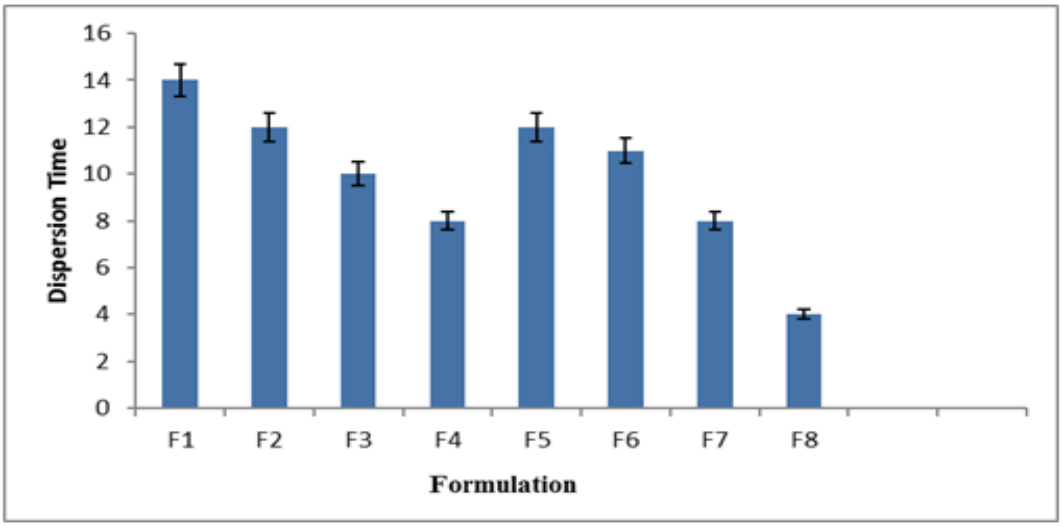

Fig. 10: Dispersion Time of Formulations

Drug Content: The drug content was found to be within the range of 83.40 to 98.9 indicating uniform distribution of drug in the formulated tablets as per pharmacopeia specification.

Table 22: Drug Content in Formulations

Formulation Code	Drug Content (%)
F1	87.4 ± 0.43
F2	92.2 ± 0.49
F3	97.1± 0.72
F4	98.2± 0.69
F5	89.5 ± 0.67
F6	94.2 ± 0.64
F7	96.2 ±0.34
F8	98.9 ±0.22

Mean ± SD, where n=3

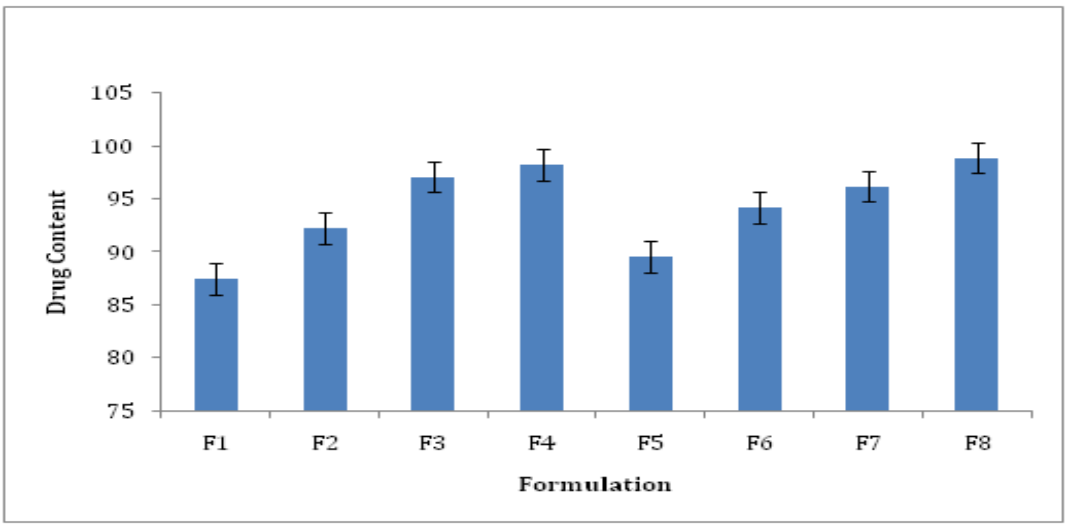

Fig. 11: Drug Content of Formulations

In-vitro Release Studies: The comparative drug release was shown in **Table 23** and in **Figure 12**. Formulations F1 containing superdisintegrant Banana (2%), and F2 containing superdisintegrant Banana (4%) showed a release of 84.01% and 85.62%, F3 containing superdisintegrant Banana (6%) while F4 containing Banana (8%) showed a release of 91.96% and 96.59%. Formulation F5 containing superdisintegrant Isapghula (2%) and F6 containing

superdisintegrant Isapghula (4%) showed a release of 85.01% and 90.12% while F7 containing superdisintegrant Isapghula (6%) while F8 containing superdisintegrant Isapghula (8%) showed a release of 94.46% and 97.68% respectively were selected for preparation of mouth dissolving tablet. Resultant formulation F8 showed best release of 97.68%. The formulation F8, which have good results with high percentage, was selected.

Table 23: Cumulative Percentage of Hydrochlorothiazide

Time	F1	F2	F3	F4	F5	F6	F7	F8
1	20.78±0.98	20.65±0.91	22.92±0.94	25.84±0.65	19.84±0.91	21.06±0.62	21.89±0.49	23.93±0.43
3	31.34±0.64	32.13±0.69	35.62±0.59	36.71±0.89	36.12±0.62	38.18±0.87	40.83±0.72	30.68±0.23
5	48.76±1.21	49.99±0.72	54.01±0.72	56.62±0.91	53.12±0.71	53.74±0.89	55.61±0.82	49.31±0.78
10	72.13±0.37	66.92±0.89	76.09±0.49	82.12±0.98	78.77±0.89	81.89±0.98	83.09±0.49	79.17±0.36
15	84.10±0.62	85.62±0.90	91.94±0.31	96.59±1.02	85.01±0.94	90.12±1.01	94.46±0.31	97.68±0.29

Mean ± SD, where n=3

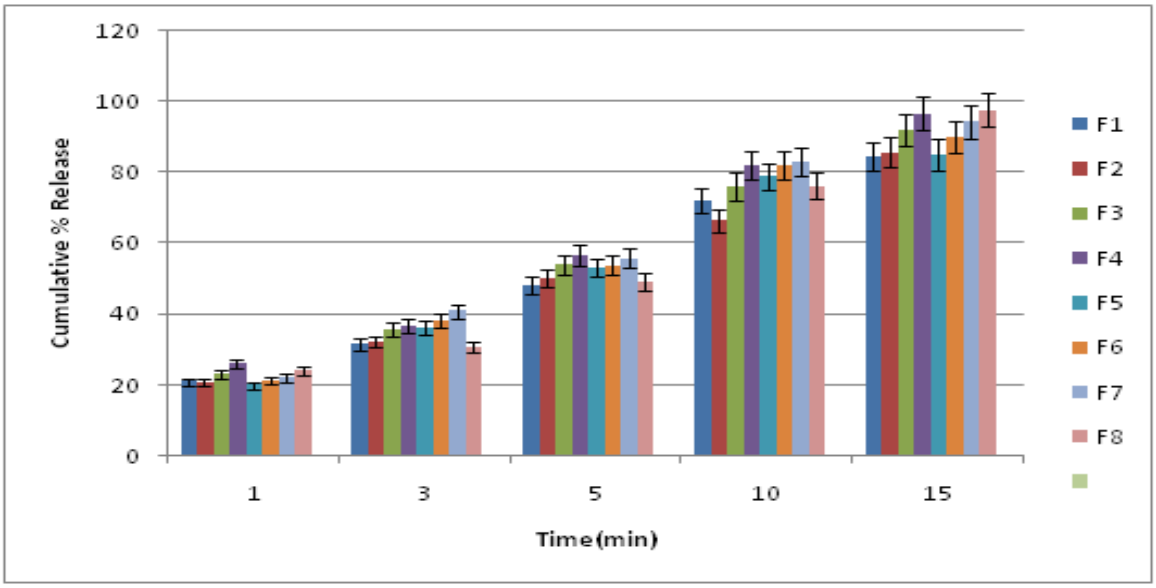

Fig. 12: Cumulative Release (%) of Hydrochlorothiazide

Kinetic Release: Mathematical models that can be applied to the analysis of dissolution data. The models described herein include both empirical and semi empirical models that are applied to the evaluation of dissolution rate data. The use of these models permits the elucidation of the mechanism and type of drug release that can be expected from the mouth dissolving tablets. In order to investigate the mechanism of drug release, the data (F1 to F8) of in-vitro release studies was fitted to various kinetic models representing Zero-order, First order, Higuchi's and Korsmeyer-Peppas model. The applicability of all of these equations was summarized in **Table 24**. The rate constants were also calculated from the slope of the plot of respective models. To find out exact mechanism, dissolution data of all formulations were fitted in Korsmeyer-Peppas equation. All formulations showed good linearity R^2, with slope (n) values. In Korsmeyer-Peppas model, 'n' is the release exponent indicative of mechanism of drug release. The n values are above 0.54 which shows an anomalous drug transport mechanism.

Table 24: Kinetic Value Obtain from In-vitro Release Profile

Formulation	R^2				n-value
	Zero order	First order	Peppas	Higuchi	Peppas
F1	0.941	0.993	0.992	0.986	0.612
F2	0.946	0.997	0.991	0.990	0.582
F3	0.942	0.990	0.996	0.994	0.562
F4	0.942	0.991	0.994	0.992	0.553
F5	0.974	0.967	0.984	0.985	0.549
F6	0.985	0.971	0.989	0.982	0.545
F7	0.973	0.963	0.983	0.973	0.547
F8	0.989	0.974	0.949	0.974	0.544

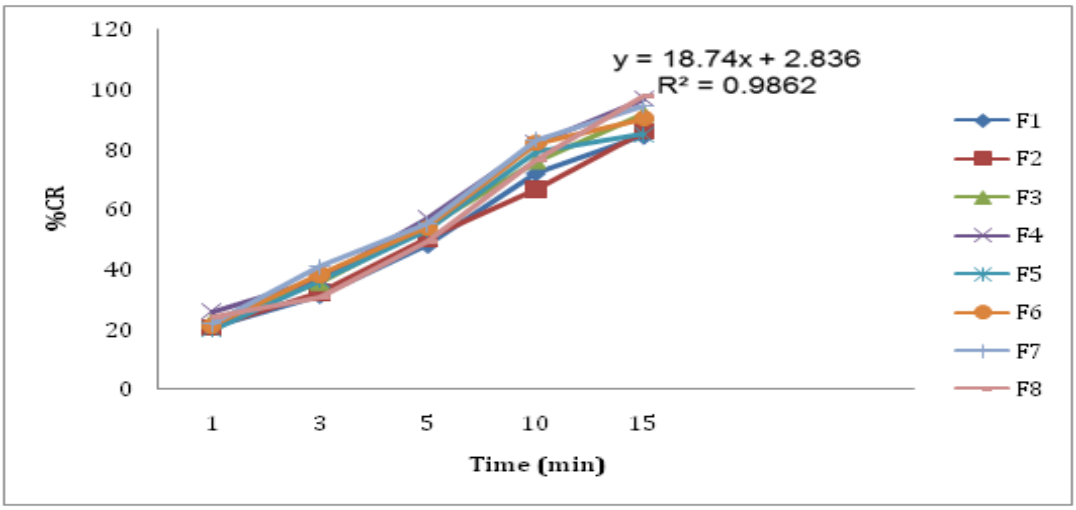

Fig. 13: Zero-order Release Kinetics

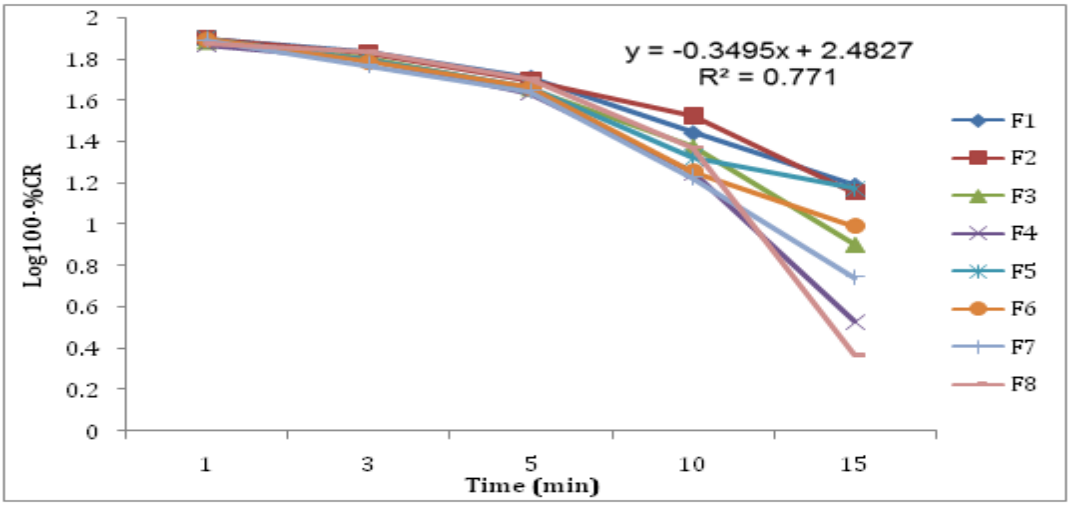

Fig. 14: First Order Release Kinetic

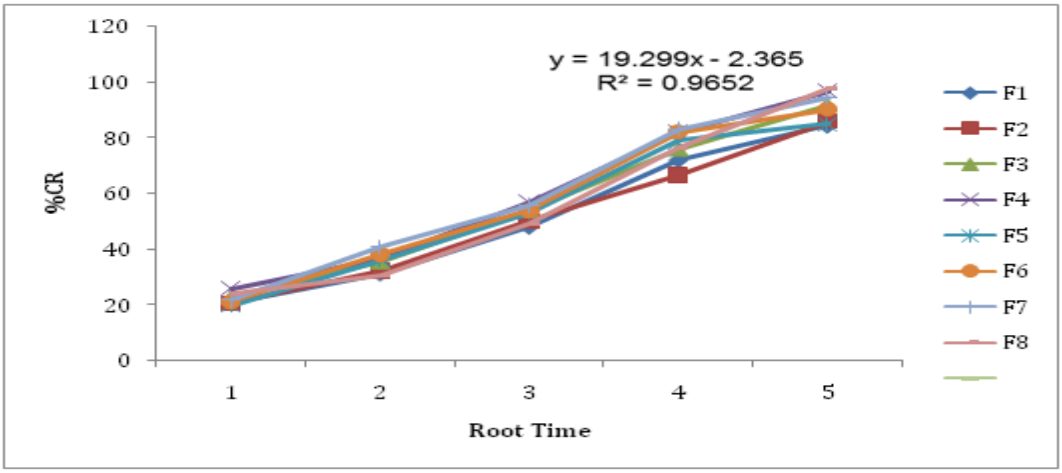

Fig. 15: Higuchi Model Release Profile

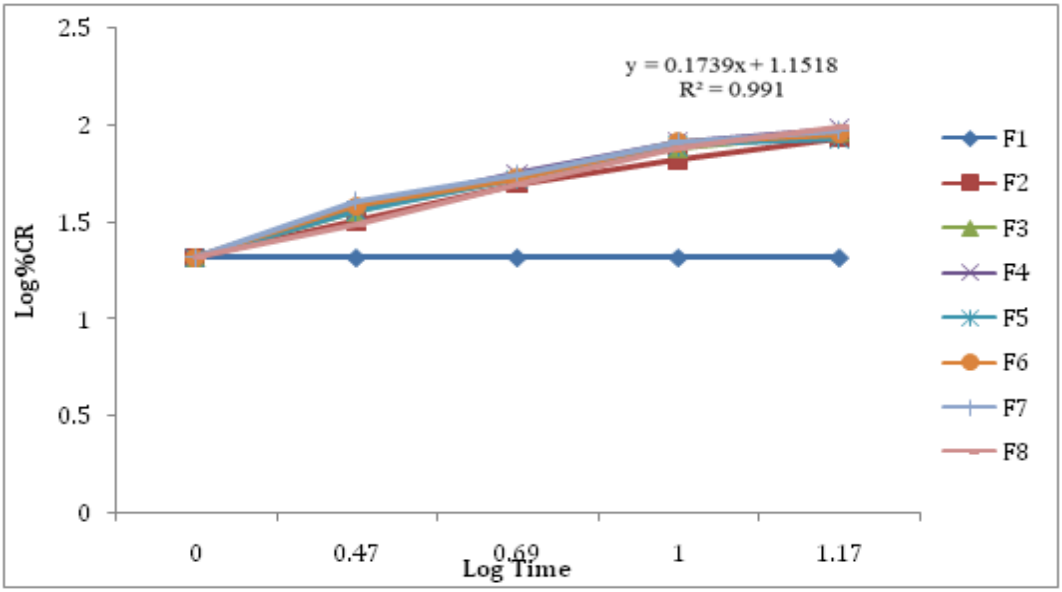

Fig. 16: Pappas Model Release Profile

CONCLUSION

The selection of an ideal batch of Fast disintegrating tablets was made after consideration of the evaluation parameters by dissolution study, disintegration time and wetting time. The batch F8 Fast disintegrating tablets was selected as an ideal batch as its dissolution, disintegration time and wetting time were best among all the formulations. It showed the maximum in-vitro cumulative percentage release of drug 97.68±0.29.

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